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A Combined Review of The Efficacy of Art Therapy as an Intervention for Children and Adolescents with Autism Spectrum Disorder and Trauma-Related Mental Health Challenges By Aiden Wu

Abstract

Previous literature has highlighted the potential for art therapy to improve the psychological well-being of individuals with many conditions. This literature review aims to assess art therapy's application in children and adolescents with autism spectrum disorder (ASD) and trauma related mental health challenges to better understand its effectiveness at addressing psychological and developmental needs in pediatric patients. The result of this literature review indicates that numerous studies find that art therapy may improve hyperactivity, inattention, and assertiveness in pediatric patients with ASD, and it can reduce the avoidance of traumatic memories and trauma-induced anxiety in pediatric patients with trauma-related mental health challenges. By comparing the literature related to both conditions, it is found that art therapy may facilitate emotional expression. These findings enhance the understanding of art therapy's effectiveness across these developmental and psychological conditions and emphasize the necessity for additional high-quality research to provide deeper insights into art therapy's application in pediatric populations.

Introduction

Art therapy is a psychotherapeutic intervention that utilizes the creative process as a therapeutic approach. Participants of art therapy engage with various artistic media and art forms such as drawing, painting, sculpting, collaging, and/or weaving with the goal of improving their psychological and physical well-being. Art therapy may offer unique advantages over other therapies by leveraging the creative process to facilitate for non-verbal communication, multi-sensory interaction, and creative cognition. Art therapy has been applied to many conditions, including autism spectrum disorder (ASD). ASD is a neurodevelopmental disorder which can impact the social communication, cognitive abilities, motor skills, sensory functions, and linguistic functions of an individual. According to the World Health Organization, ASD affects approximately 1 in 100 individuals. Since art therapy can train communication, develop fine-motor skills, and improve sensory functionality, it may be particularly suited for individuals with ASD. In addition, addressing a developmental disorder such as ASD during childhood may correct developmental deficiencies early and improve future patient outcomes. Thus, a review of the literature assessing the effectiveness of art therapy for pediatric patients may provide key insights for clinicians. In addition to ASD, art therapy can be applied to individuals with trauma-related mental health challenges. It is estimated that more than 2 out of 3 individuals experience a traumatic event by the age of 16, with many of these individuals developing increased post-traumatic stress, depression, and anxiety (Lawrence-Sidebottom et al., 2024). Addressing childhood traumatic experiences early is critical since they may affect mental and physical health later in life. (Masachi et. al, 2013). Art therapy may potentially be suited to

pediatric patients with trauma-related mental health challenges because it offers an alternative, non-verbal approach for children to access, process, and express their trauma. A review of the literature focused on art therapy and trauma may establish art therapy as a well-suited intervention for pediatric patients struggling with trauma. ASD and trauma-related mental health challenges were specifically selected for this review because they allow for the assessment of art therapy from a neurodevelopmental and psychological standpoint, providing insights into how art therapy supports emotional and developmental needs in pediatric patients. This review aims to examine the literature on art therapy applied to ASD and trauma-related mental health challenges to compare findings, assess the efficacy of interventions, provide methodological insights and highlight common limitations to offer a comprehensive understanding of art therapy across these conditions.

Methods

ASD & Art Therapy: Literature Search Strategy

Google Scholar and PubMed were used as primary search tools. Search terms included “art therapy”, “autism”, “children”, and “adolescents”. Searches were further narrowed down using words such as “efficacy”, “effectiveness”, “study”, and “case study”. Results were limited from 2000 to 2024 to maintain relevance. Studies were first filtered through by screening titles for relevance. Upon second examination, abstracts were reviewed and non-viable studies were excluded. Finally, full paper readings were used to determine which studies would be included in this review.

ASD & Art Therapy: Literature Inclusion and Exclusion Criteria

To be included in this systematic review, studies needed to primarily focus on participants under the age of 18 diagnosed with autism spectrum disorder (ASD). Studies published before the year 2000 were excluded to maintain relevance. Studies that did not use the creation of physical art as a therapeutic intervention were excluded from this review to maintain consistency with the mission of art therapy. Studies with and without a control group were included. Both quantitative and qualitative studies were included to ensure a comprehensive review of literature.

Trauma & Art Therapy: Literature Search Strategy

Similar to the ASD review section, Google Scholar and PubMed were used as primary search tools. Key search terms included “art therapy”, “children”, “adolescents”, “trauma”, “abuse”, “PTSD”, “effectiveness”, “efficacy”, and “case study”. Results were limited from 2000 to 2024. Studies were initially filtered by screening study titles for relevance. Upon second examination, abstracts were reviewed, and non-viable studies were excluded. Finally, full papers were reviewed to determine which studies would be included in this review.

Trauma & Art Therapy: Literature Inclusion and Exclusion Criteria

To be included in this systematic review, studies needed to primarily focus on participants under the age of 18 who either were diagnosed with PTSD or suffered from a traumatic event(s). Studies that did not utilize the creation of physical art as a therapeutic device were excluded from this review. Studies published before the year 2004 were excluded to maintain relevance. Similar to the ASD review criteria, studies that evaluated interventions not defined as art therapy were excluded from this review. Studies with and without control groups were included. Both quantitative and qualitative studies were included to ensure a broad review of the current literature.

Results

Table 1: Summary of Included Studies Evaluating Art Therapy and Its Benefits for Children with ASD

Study Reference	Participant Details	Methodology	Intervention Details	Key Findings
D'Amico & Lalonde, 2017	6 children with ASD (mean age 10.5 years)	Quasi experimental, pre-and-post design	75 minute weekly group art therapy sessions for a total duration of 21 weeks	Improved assertiveness Reduced hyperactivity and inattention
Prasitwut et al., 2024	23 children with ASD (mean age 12.2 years)	Randomized controlled waitlist trial, pre-and-post design	3 months of individual hospital based weaving therapy followed by 3 months of home based weaving therapy (weekly sessions)	Improved ASD symptoms and quality of life
Epp, 2008	66 children with social and behavioral disorders including with ASD	Longitudinal paradigm, Pre-and-post design	60 minute group art therapy sessions weekly over a total duration of 9 months	Improved assertiveness Reduced hyperactivity and internalizing behaviors
Durrani, 2014	12-year-old male with ASD	Individual Case Study	30-60 minute individual art therapy sessions weekly for a total duration of 1 year	Improved attention span, communication, assertion, attachment, sensory dysfunction Reduced repetitive/self-stimulatory behaviors, sensory dysfunction
Park, 2022	4-year-old female with high functioning autism (HFA)	Individual Case Study	37 personalized art therapy sessions throughout the span of 1 year combined with sporadic parental counseling	Improved communication, socialization, peer relationships, assertiveness, emotional recognition and expression Reduced behavioral problems.

ASD & Art Therapy: Study Characteristics

D'Amico and Lalonde (2017) conducted a quasi-experimental study with a pre-and-post study design. The study aimed to evaluate the effectiveness of group art therapy for a group of 6 children with ASD ($n = 6$). Participant ages ranged from 10 to 12 years, with a mean of 10.5 years. Participants had varying levels of severity of ASD. For this experiment, participants engaged in group art therapy sessions administered by two professional art therapists. The art therapy intervention consisted of 75-minute weekly sessions over 21 weeks, where the participants engaged in collaborative art projects. During each session, participants were encouraged to reflect on their emotions in the artwork and discuss them with their peers. Researchers used the Social Skills Improvement System–Rating Scales (SSIS-RS) to quantify and assess the children's social capabilities and problem behaviors. Children and parents were asked to complete the SSIS-RS before and after the art therapy intervention. Pre-intervention and post-intervention SSIS-RS scores were compared to find improvements in social skills and problem behaviors. Evaluation of student and parent SSIS-RS scores found statistically significant improvements in 2 of the 12 subscales measured by the SSIS-RS (hyperactivity/inattention and assertion subscales). The results of this study suggest that group art therapy may be effective at improving the attention and assertiveness of children with ASD (D'Amico & Lalonde, 2017).

Prasitwut and colleagues (2024) conducted a randomized controlled waitlist trial to evaluate the efficacy of weaving art therapy for children with ASD. The study included a total of 23 children (mean age 12.2 years) with varying severity of ASD. The children were randomly assigned to an intervention group ($n = 11$) or a waitlist control group ($n = 12$) via a random number generator. The intervention group began weaving therapy three months before the waitlist control group. During the weaving therapy program, children participated in three months of hospital-based weaving therapy followed by three months of home-based weaving therapy. During these sessions, children were encouraged to express their imagination through their textiles with parents, promoting social interaction. Participants selected their materials and directed their work to foster a sense of autonomy. Researchers assessed the severity of ASD symptoms and functionality using the Childhood Autism Rating Scale–second edition (CARS-2) and the Pediatric Quality of Life Inventory (PedsQL). CARS-2 evaluated verbal communication, listening skills, and emotional response, while PedsQL measured social, physical, school, and emotional functionality. CARS-2 scores were completed by a clinician, but it is unclear if the PedsQL scores were self-reported or completed by another individual. CARS-2 and PedsQL scores were recorded at baseline, three months, and six months of treatment. Comparison of pre-intervention and post-intervention scores of the intervention group revealed statistically significant improvements in CARS-2 and PedsQL scores. The waitlist control group showed statistically significant improvements only in the CARS-2 scores post-intervention. There was a statistically significant difference in CARS-2 and PedsQL scores between the intervention group and the waitlist control group at three months (when the waitlist control group had not started

treatment). The results of this study suggest that weaving art therapy may improve autism symptoms, social functionality, and quality of life in children with ASD (Prasitwut et al., 2024).

Epp (2008) conducted a quasi-experimental study with a pre-and-post study design to evaluate the effectiveness of an art therapy intervention for children with social deficits characteristic of ASD. Sixty-six children with social and behavioral disorders, including ASD, were enrolled in the art therapy program, which consisted of 1-hour weekly sessions for a total of nine months. The therapy sessions were conducted in small groups and focused on individual and collaborative art projects. Through interactive and creative activities, the children practiced specific social skills such as compromise, conversation, eye contact, recognition of nonverbal cues, emotional recognition, and emotional expression. The study used the Social Skills Rating System (SSRS) to measure the efficacy of the art therapy program. Similar to the SSRS-2, the SSRS evaluates children's social skills and problem behaviors. A total of 44 Parents and 30 teachers completed the SSRS before and after the art therapy intervention. After comparing pre-intervention and post-intervention scores, the study found significant improvements in three of eight subscales (assertion, internalizing behaviors, and hyperactivity). The findings of this study suggest that group art therapy intervention may enhance assertiveness while reducing internalizing behaviors and hyperactivity in children with ASD (Epp, 2008).

Two qualitative studies were identified in this review. Both present individual case studies. The first explored both the social and sensory benefits of art therapy. The case study was on a 12-year-old male diagnosed with autism. Previously, the patient engaged in speech and occupational therapy with limited success. During the case study, the patient participated in weekly creative art therapy sessions administered by an art therapist. The sessions initially lasted 30 minutes but eventually lengthened to 60 minutes. The patient primarily interacted with paint, brushes, and rollers. The therapist tailored the intervention program to emphasize sensory immersion and communication. The results of the art therapy intervention were assessed through the art therapist's observations and statements from the patient's primary caregivers. At the beginning of the case study, the patient exhibited severe sensory dysfunction, repetitive self-stimulatory behaviors, poor eye contact, poor communication skills, limited attention span, aversion to novel textures and materials, and minimal engagement with the art therapist. After the art therapy intervention, the patient's art therapist and primary caregivers reported drastic improvements in his communicative skills, inattention, self-regulation, and assertiveness. They also observed reduced repetitive, self-stimulatory behaviors and aversion to certain textures. The patient enjoyed creating and presenting art in the presence of the therapist and primary caregivers, suggesting that the art therapy intervention served as a bridge for attachment. The findings of this case study suggest that individualized art therapy sessions may improve social skills, reduce problem behaviors, improve sensory dysfunction, and foster connection in children with ASD (Durrani, 2014).

The second case study by Park (2022) explored the social and communicative benefits of art-based therapy combined with parental counseling and psychoeducation. The participant of the study was a 4-year-old female who was diagnosed with high-functioning autism (HFA). The

patient and their mother participated in an intervention program known as the Individual Therapeutic Educational Plan (ITEP), which included 37 1-hour art therapy sessions and parental counseling for the patient's mother. During the sessions, the art therapist utilized a variety of two and three-dimensional art forms to improve the patient's social deficits. For example, the patient drew faces to practice emotional communication and recognition. The patient's mother was provided three interventions: (a) emotional support, (b) education about ASD, and (c) encouraged to use the arts to bond with the patient. The ITEP included 8 group art therapy sessions conducted with another child diagnosed with HFA, focusing on collaborative art creation and games. Before the ITEP intervention, the patient exhibited social communication deficits, unusual language usage, limited self-expression, poor emotional recognition, and poor emotional expression. Throughout the ITEP, the patient had become verbally assertive, interactive, and emotionally expressive. During peer art therapy sessions, the patient developed appropriate communication, collaborative socialization, and behavioral awareness. A post-intervention speech assessment revealed that the patient had age-appropriate receptive and pragmatic language abilities, and evaluation by a clinical psychologist and K-CARS (Childhood Autism Rating Scale) revealed that the patient's functional status had improved. A follow up diagnosis a year later found that the patient exhibited no symptoms related to autism. The results of this case study suggest that art therapy, combined with parental counseling and collaborative art therapy, can effectively improve social skills, language abilities, and emotional awareness in children with HFA (Park, 2022).

Trauma Reviewed Studies

Table 2: Summary of Included Studies Evaluating the Effectiveness of Art Therapy for Traumatized Children and Adolescents

Study Reference	Participant Details	Methodology	Intervention Details	Key Findings
Chapman et al., 2001	58 hospitalized, pediatric trauma patients (mean age 10.7 years)	Randomized cohort study design	Approx. 1-hour individual art therapy session	No statistically significant difference in improvement to overall PTSD symptoms compared to standard hospital care; However, there was a reduction in avoidance related symptoms
Pretorius et al., 2010	25 females with a history of sexual abuse (mean age 9.6 years)	Solomon four-group study design	8 group art therapy sessions	Reduction in depression, anxiety, and sexual trauma symptoms
Feen-Calligan et al., 2020	15 Syrian refugee children and adolescents (age range 7-14)	Quasi-experimental pre-and-post test design	Weekly group art therapy session for 12-weeks	Statistically significant improvements in separation anxiety Reductions in post-traumatic stress symptoms, social anxiety, and

				general anxiety were observed but did not reach statistical significance
Rowe et al., 2017	30 Burmese or Thai refugee adolescents (age range 11-20)	Pre-and-post test study design	16, 50 minute group or individual art therapy sessions administered over the course of 6 months	Statistically significant improvements in anxiety symptoms Reductions in school difficulties and improvements in self-concept were observed but did not reach significance
Mills et al., 2012	11-year-old female who witnessed repeated domestic violence	Individual case study	Group art therapy sessions for a total duration of 27 weeks.	Reported improvements in avoiding, expressing, and accepting past traumatic memories related to domestic violence

Art Therapy & Trauma Study Characteristics

Chapman and colleagues (2001) conducted a randomized cohort study to evaluate the effectiveness of the Chapman Art Therapy Treatment Intervention (CATTI) as a treatment for psychologically distressed pediatric trauma patients. The study included a total of 58 pediatric ICU patients who had received traumatic injuries and presented symptoms consistent with PTSD. Participant ages ranged from 7 to 17 years, with a mean age of 10.7 years. Of the 58 patients, 27 were randomized into a control group, and 31 were randomized into an intervention group. The control group received standard hospital care (psychiatric consults, Child Life services, social work, ect.) while the intervention group underwent the CATTI. Participants of the CATTI engaged in a single, one-on-one session with an art therapist. During the session, the participant was encouraged to use artistic and verbal expression to build a narrative of the traumatic event. Throughout the narrative, the art therapist addressed pressing issues such as shame, guilt, misconceptions, coping mechanisms, and reintegration strategies. Researchers used the Children's Post Traumatic Stress Disorder Index (PTSD-I), a self-reported rating, to measure the severity of PTSD symptoms presented by the control and intervention groups. PTSD-I scores were taken at baseline, 1-week post-intervention, and 1-month post-intervention for both groups. No statistically significant difference was found in the mean improvement of PTSD-I scores between the intervention group and the control group. However, a sustained reduction of mean PTSD-I scores was observed in both groups after treatment. Additionally, the intervention group saw a greater sustained reduction in avoidance symptoms. The results of this study suggested that art therapy may be equal to or slightly more effective than traditional treatment methods for traumatized children displaying symptoms of PTSD.

Pretorius and colleagues (2010) conducted a Solomon four-group study design, which aimed to evaluate the effectiveness of an art therapy intervention as a treatment for sexually abused girls. The study included a total of 25 girls with a history of child sexual abuse (CSA). Participant ages ranged from 8 to 11 years, with a mean age of 9.6 years. The 25 participants

were non-randomly sorted into four groups based on which children's homes they lived. Two of the four groups were experimental groups, receiving the art therapy intervention, while the other two did not. The art therapy intervention was designed for CSA victims and lasted a total of eight sessions. The sessions were conducted in a group setting. They used both artistic and verbal expression to discuss topics related to CSA, such as sentiments associated with sexual abuse, appropriate sexual behavior, and prevention of revictimization. Participants used various artistic mediums, such as clay and paint to express their ideas and emotions. Researchers used the Trauma Symptom Checklist for Children (TSCC) and the Human Figure Drawing (HFD) to measure the intervention programs' efficacy. TSCC and HFD scores were taken by a psychologist who was unaware of the intervention. This study consistently found statistically significant improvements in post-test anxiety and depression scores between experimental and control groups. Their findings revealed statistically significant improvements in anxiety, depression and sexual trauma between intervention and control groups. In addition, the findings also suggest that art therapy may be effective at reducing anxiety, depression, and sexual trauma symptoms in female victims of CSA.

Feen-Calligan and colleagues (2020) conducted a quasi-experimental pre-and-post test study to determine art therapy's effectiveness as an intervention for Syrian refugee children. The study included an intervention group of 15 Syrian refugee children, ages 7 to 14, and a no-treatment control group of 12 individuals with similar demographics and symptom severity. The intervention group underwent a 12-week art therapy program consisting of 90-minute weekly group sessions. The program aimed to reduce anxiety, depression, and PTSD symptoms in the participants through creative art therapy activities. Such activities were collaborative, used various materials, and allowed the participants to express themselves verbally and nonverbally. The sessions were conducted by an art therapist and facilitated by art therapy interns and an Arabic translator. To determine the effectiveness of the art therapy intervention, IRB-approved bilingual clinicians and Arabic-speaking research assistants administered two self-reported rating scales: the Screen for Child Anxiety Related Emotional Disorders (SCARED) and the UCLA Child/Adolescent PTSD Reaction Index (UCLA). The SCARED and the UCLA were administered at baseline and post-intervention. An analysis of SCARED and UCLA scores revealed statistically significant improvements in separation anxiety for the intervention group. Additionally, the findings reveal reductions in post-traumatic stress symptoms, total anxiety symptoms, panic disorder symptoms, social anxiety, and generalized anxiety that did not reach significance. The control group saw no statistically significant changes, suggesting that the improvements in the SCARED and UCLA scores may be attributed to the intervention program itself rather than time to process. The findings of this study suggested that art therapy may improve trauma-related symptoms such as post-traumatic stress, separation anxiety, social anxiety, and generalized anxiety in refugee youth. This study also suggested that art therapy may prove suitable for crossing language barriers.

Rowe and colleagues (2017) conducted a pre-and-post test study to evaluate the effectiveness of the Burma Art Therapy Program (BATP) as an intervention for traumatized

adolescent refugees from Thailand and Burma. This study included a single intervention group consisting of 30 adolescents with ages ranging from 11 to 20 years. The participants had been in the United States for an average of 5 years, and 83% were enrolled in English as a second language classes. Eighty-three percent of participants had experienced at least one traumatic event, while 90% reported witnessing a traumatic event. Such traumatic experiences included starvation, rape, and warfare. The art therapy program included 16 fifty-minute sessions over the course of 6 months total. Sixty percent of the intervention group received individual therapy, while the remaining forty percent received group art therapy. The art therapy sessions aimed to address traumatic experiences, improve anxiety, and reduce depression through artistic expression. The sessions were tailored to support the participants' behavioral, emotional, and therapeutic goals. To evaluate the effectiveness of the BATP, researchers used the following self-reported standardized rating scales: The Piers-Harris Self-Concept Scale (PHSCS), the Hopkins Symptom Checklist (HSC), and the Harvard Trauma Questionnaire (HTQ). The PHSCS, HSC, and HTQ evaluated self-image, anxiety and depression symptoms, and past traumatic experiences, respectively. Additionally, researchers utilized the Strengths and Difficulties Questionnaire (SDQ), a teacher-reported rating scale that evaluated participants' behavior and performance in school settings. A comparison of baseline and post-intervention scores revealed a statistically significant improvement in anxiety symptoms. In addition, this study found reductions in school difficulties and improvements in self-image that did not reach significance. Discussions with the art therapy clinicians revealed that quantitative rating scales may not be the most effective method to evaluate art therapy treatments due to cultural and linguistic barriers. The clinicians suggested that qualitative-based evaluation tools, such as the Diagnostic Drawing Series (DDS), may capture the effects of art therapy more thoroughly by bypassing these barriers. The findings of this study suggested that art therapy may be an effective treatment for anxiety in child and adolescent refugees, with potential benefits for self-image and school difficulties, emphasizing the necessity for qualitative assessment tools to better capture these effects.

Mills and colleagues (2012) conducted a case study that followed the art therapy treatment of an 11-year-old female who had a history of witnessing domestic violence. The participant and her mother had recently moved to a women's aid refuge. During the case-study, the participant engaged in group art therapy sessions over 27 weeks. The duration and frequency of each session were left unspecified, likely due to her inconsistent attendance. The art therapy program focused on using artistic media as a vessel for the participant to access, process, and express her traumatic memories and emotions related to domestic violence. Throughout the 27 weeks, the participant created a variety of art, each interpreted by the art therapists as representations of her sentiments regarding her traumatic experiences and violent family dynamic. At the beginning of the case study, the participant was completely uncommunicative with the art therapist and the other children in her art therapy group. For example, the participant refused to elaborate upon her artwork or express her thoughts. However, as the art therapy program progressed, the participants became increasingly interactive, expressive, and playful.

She began to access her traumatic experiences through the symbolism in her artwork and openly verbalized her feelings with the group. By the end of the program, the participant had reconciled many of her complicated feelings and past trauma associated with her history of witnessing domestic violence. The outcomes of this case study suggested that art therapy may provide the opportunity for traumatized children to access and explore traumatic memories, ultimately allowing for expression and processing.

Art Therapy & ASD Discussion

Interpretation of Findings

The included studies collectively suggest that art therapy may be effective at improving specific social skills and behavioral outcomes in children with ASD. Among the included studies, the most noteworthy pattern emerged concerning enhanced assertiveness. Specifically, four out of five studies—D’Amico and Lalonde (2017), Durrani (2014), Epp (2008), and Park (2022)—reported improvements in assertiveness after art therapy interventions. Such a consistent finding suggests that art therapy may be particularly effective at empowering children with ASD to be assertive in social situations. The self-directed aspects of art therapy, such as requesting materials, may foster confidence and personal expression in children with ASD, subsequently enhancing their assertiveness in social situations. The most consistent behavioral improvements were in hyperactivity and inattention, as reported in studies by D’Amico and Lalonde (2017), Durrani (2014), and Epp (2008). Art therapy may have been especially effective at improving hyperactivity and inattention due to its focus-demanding activities such as drawing, painting, and weaving. During art therapy, children learn to manage their attention and focus, and these same skills can be applied to manage their behavior. The reviewed studies collectively suggest that art therapy leads to improvements in assertion, inattention, and hyperactivity in children with ASD. In addition, other less consistently reported, yet notable, findings have been highlighted by included case studies. Park (2022) reported that its participants had become more emotionally expressive throughout the art therapy intervention. This improvement was not identified in other included studies, yet it highlights art therapy’s unique potential as a nonverbal emotional outlet for children with ASD. Art therapy gives children with ASD the opportunity to practice expressing and recognizing emotions, a valuable skill for social interaction. Another noteworthy finding not addressed by other studies was improved sensory dysfunction and repetitive/self-stimulatory behaviors after art therapy intervention (Durrani, 2014). Unlike conventional forms of therapy, art therapy directly appeals to the senses and introduces new textures, smells, and sights in a more relaxed manner. This aspect makes art therapy particularly suited for children with ASD as it addresses sensory dysfunction, which can be distracting during social interactions. Art therapy also provides a socially acceptable form of “play”, potentially reducing the dependency on repetitive, self-stimulatory behaviors sometimes presented by children with ASD (Eason et al., 1982). It is important to note that case studies uniquely reported improved emotional expression and sensory dysfunction following a single individual, so future

work is needed to examine if these findings may be broadly applicable. There was also a notable discrepancy in findings between the studies with individual art therapy sessions and group sessions. While the case studies by Durrani (2014) and Park (2022) reported broader social skill improvements, the quantitative studies only reported a few statistically significant improvements in individual social skill categories. The exception was Prasitwut and colleagues (2024), which did not evaluate individual social skill categories. This discrepancy can be explained by the individualized art therapy programs used in the case studies by Park (2022) and Durrani (2014), which likely addressed social skill deficits more directly than the broader group therapy used by D'Amico and Lalonde (2017) and Epp (2008). While inconclusive, the reviewed literature suggests that art therapy may enhance assertiveness and reduce inattention in children with ASD. Additionally, art therapy shows potential for improving emotional expression, managing sensory dysfunction, and decreasing repetitive, self-stimulatory behaviors, although more data is needed to substantiate these findings.

Discussion of Methodologies

This review included five studies with various designs and art therapy programs for ASD, each with their advantages and disadvantages. All included studies featured an art therapy program that offered a variety of artistic mediums or activities, except the study by Prasitwut and colleagues (2024), which strictly focused on weaving. The studies by D'Amico and Lalonde (2017) and Epp (2008) conducted their art therapy intervention in group settings. In contrast, the studies by Durrani (2014) and Prasitwut and colleagues (2024) conducted their art therapy sessions one-on-one. Finally, the study by Park (2022) conducted most sessions one-on-one, but a few took place with another child with high-functioning autism. This study's intervention program was also unique because it combined art therapy with parental counseling and psychoeducation. Interestingly, the reviewed studies featuring more individualized art therapy programs reported broader social and behavioral outcomes than their group setting counterparts. This trend is likely because individualized art therapy programs can more specifically address their participants' social and behavioral deficits, unlike larger group programs. The duration of intervention among the reviewed studies aired on the lengthy side, with programs ranging from 21 weeks to 1-year of consistent art therapy sessions. Long intervention timelines may be most suited to children with ASD because it allows them to sufficiently adjust to the novel experiences and routines of art therapy. The method of data collection also varied among the studies. The quantitative studies conducted by D'Amico and Lalonde (2017), Epp (2008), and Prasitwut and colleagues (2024) utilized standardized rating scales to measure participant outcomes. Such rating scales are advantageous—they are practical for group evaluations, quantify improvements in numerical scores, and facilitate standardized comparison. However, they are susceptible to biased reports and can only measure changes within predefined categories. In contrast, the case study by Durrani (2014) relied solely on therapist observations and primary caregiver interviews to evaluate the effectiveness of art therapy intervention. This data collection method is adaptable, has reduced bias, and can capture a broader range of findings; however, it lacks the capability for

standardized comparisons. Park (2022) used a combination of different standardized rating scales, therapist's observations, and medical evaluations to report its findings. This multifaceted approach was highly effective, allowing evaluation from multiple perspectives, and combining standardized and individualized findings to draw conclusions. In summary, this review compared studies with varying methodologies, providing further insight into the types of art therapy programs and data collection methods utilized for examining art therapy's benefits for children with ASD.

Comparison to Current Literature

The findings of this review suggest that art therapy may be particularly effective at improving assertiveness and attention in children with ASD. Additionally, art therapy shows potential for improving sensory dysfunction, fostering emotional awareness, and reducing repetitive, self-stimulatory behaviors. A 2024 systematic review evaluating the efficacy of art therapy as a treatment for children with ASD concluded similar findings, stating that the current literature reports improvements in assertiveness, hyperactivity, and inattention. The review also reported benefits to motor and communication skills, which were either not found or consistently reported by the studies included in this review (Vogel et al., 2024). These findings further supported the conjecture that art therapy may particularly enhance assertiveness and attention in autistic children. Another 2014 systematic review that evaluated clinical case descriptions reported that art therapy may improve repetitive behavior patterns, attention-abilities, and social communicative abilities in children with ASD (Schweizer et al., 2014). These findings supported the potential benefits of art therapy to repetitive, self-stimulatory behaviors and attention reported in this review. Schweizer and colleagues (2014) also found that art therapy potentially improves flexibility and self-image in children with ASD. Both systematic reviews agree that more high-quality empirical research is needed to draw conclusive findings about art therapy's benefits to children with ASD. A comparison of this review's findings to those of Vogel and colleagues (2024) and Schweizer and colleagues (2014) further substantiated art therapy's potential to improve attention and assertiveness in children with ASD. It also highlighted potential benefits of art therapy that were not identified in this systematic review, such as improvements in motor function, flexibility and self-image.

Limitations of Included Studies

There were several limitations to the studies included in this systematic review. First, the sample size of the included studies was small. The two case studies followed only a single participant, while the three quantitative studies included between 6 and 66 participants. These relatively small sample sizes limited the applicability and strength of the reported outcomes. Second, none of the included studies featured a control group that underwent conventional interventions for children with ASD. The lack of control comparison makes it difficult to determine whether art therapy offers any advantage or disadvantage compared to traditional ASD intervention methods. Third, the methods of data collection used by the included studies affected

the reliability of the findings. The standardized rating scales were susceptible to respondents' biases. For example, the study by D'Amico and Lalonde (2017) solely relied on parent-reported scores and child-reported scores. Including teacher-reported scores, as done in the study by Epp (2008), would have provided a more comprehensive assessment of participant outcomes. Child-reported scores, parent-reported scores, and teacher-reported scores all carry their own biases; However, collectively integrating data from all three groups can provide a well-rounded evaluation of art therapy interventions because of combined subjective and objective components.

Recommendations for Future Research

There is a scarcity of literature testing the potential benefits and effectiveness of art therapy as a treatment option for children with ASD. Thus, more studies of high methodological quality are necessary to draw robust conclusions about this topic. This review has two recommendations for future research. The first recommendation includes studies evaluating the efficacy of art therapy relative to conventional interventions for children with ASD. This may be done by including a control group that receives only conventional intervention and an experimental group which receives solely art therapy. A third hybrid group could be included, which receives both conventional and art therapy interventions. Evaluating the effectiveness of a combination of standard treatments and art therapy intervention is important because art therapy can address emotional expression and sensory dysfunctional issues in ways that standard treatments cannot, while standard treatments can provide structured behavioral and social interventions that art therapy may not entirely cover. The second recommendation reflects studies using diverse methods for data collection. Quantitative studies should include multiple respondent groups for standardized rating scales to ensure comprehensive results and diverse perspectives. If practical, future quantitative studies should also feature therapist observations since they can capture findings beyond the scope of standardized rating scales. Therapist observations are beneficial because they can convey nuanced art therapy results that are often not reflected by subjective rating scales. Similarly, case studies should collect quantitative and qualitative data to draw more detailed conclusions about the effectiveness of art therapy interventions

Implications for Practice

While not entirely conclusive, this review's findings may be relevant to the practice of art therapy for children with ASD. The reviewed literature collectively suggests that art therapy may be particularly effective at improving assertiveness, hyperactivity, and inattention, though it provides limited support for improvements in other categories. Therefore, medical providers treating children with ASD should consider using art therapy in conjunction with other standard treatments.

Art Therapy & Trauma-Related Mental Health Challenges Discussion

Interpretation of Findings

The reviewed studies suggest that art therapy may lead to positive psychological outcomes in children and adolescents with trauma-related mental health challenges, although the results were mixed. The sources of trauma featured in the reviewed studies included physical injury, sexual abuse, fleeing warfare, and domestic violence. The most frequently reported finding was improvements in trauma-related anxiety following art therapy intervention, which was assessed in three studies—Pretorius et al. (2010), Feen-Calligan et al. (2020), and Rowe et al. (2017). Art therapy may have been particularly effective at reducing anxiety symptoms because of the therapeutic nature of its creative activities. This is because the creative process may serve as an emotional outlet for children and adolescents with stored trauma-induced anxiety. Another notable outcome was reduced avoidance of traumatic memories as reported in the studies conducted by Chapman and colleagues (2001) and Mills and colleagues (2012). Art therapy may be particularly effective at reducing avoidance because it offers a non-confrontational opportunity for children or adolescents to symbolically express their traumatic past through artwork. Individuals who have experienced trauma can use the creative process in art therapy to access difficult memories and emotions, laying the groundwork to address them with more direct methods like verbalization. Learning to access trauma is a crucial step in processing it, making this aspect of art therapy particularly beneficial. However, the studies by Chapman and colleagues (2001) and Feen-Calligan and colleagues (2020) found no statistically significant improvements to post traumatic stress symptoms after art therapy interventions. This lack of improvement may be attributed to the therapeutic process of accessing and processing traumatic memories, which can temporarily increase negative emotions and stress, making it challenging to see improvements in post traumatic stress symptoms in the short-term. Outcomes for trauma-related depression were mixed, with the study conducted by Pretorius and colleagues (2010) reporting statistically significant improvements while the study conducted by Rowe and colleagues (2017) did not find any substantial improvements in depression. Similarly to post traumatic stress, the therapeutic process may have induced negative emotions, making it difficult to improve depression in the short-term. While not entirely conclusive, the reviewed literature suggests that art therapy may potentially improve trauma-induced anxiety symptoms and facilitate the accessing of traumatic memories in children and adolescents who have experienced trauma. In addition, art therapy may have limited effectiveness for trauma-related depression and post traumatic stress symptoms in the short term, although more research is needed to substantiate such claims.

Discussion of Methodologies

This literature review included five studies with various designs and art therapy interventions for children or adolescents who had experienced trauma. The studies by Pretorius and colleagues (2010), Feen-Calligan and colleagues (2020), and Mills and colleagues (2012) all conducted art therapy in group settings. Group art therapy may be advantageous because it can foster a sense of community and shared experience, preventing the feelings of loneliness that

individuals who have experienced trauma can develop (Stickley et. al, 2024). For instance, Pretorius and colleagues (2010) focused on group cohesion and discussion, allowing the participants to relate to each other's emotions associated with sexual trauma. The peer support aspect of group art therapy was particularly beneficial for children who had psychological trauma from sexual abuse because they often struggle with intimacy and distrust of adults. In contrast, the study by Chapman and colleagues (2001) utilized a one-on-one approach, and the study by Rowe and colleagues (2017) provided individual or group art therapy to its participants. Individualized sessions can offer tailored art therapy, allowing art therapists to address trauma-related psychological issues more directly. For example, Chapman and colleagues (2001) conducted one-on-one sessions featuring a bespoke, narrative-based art therapy session focusing on patients' individual traumatic stories. However, while individualized art therapy may be effective at addressing personal trauma, it may lack the capacity for collaborative creative activities and discussions, which may be particularly beneficial for traumatized individuals. Perhaps a hybrid of individualized and group art therapy sessions may be most effective as an intervention program for children and adolescents with traumatic experiences, as it can offer opportunities for profound personal growth and prevent trauma induced loneliness. The total duration of intervention ranged from 1-hour to 27-weeks across the five studies. Lengthier program durations may improve the perceived psychological outcomes of art therapy interventions because, in the short-term, the therapeutic process may increase negative emotions in traumatized individuals, leading to mediocre results (Tong et al., 2017). For instance, the single 1-hour session featured in the study by Chapman and colleagues (2001) was likely too brief, explaining the limited post-intervention improvements in post traumatic stress symptoms. Conversely, the extended 27-week art therapy program featured in the case study by Mills and colleagues (2012) allowed for sustained therapeutic engagement, providing participants sufficient time for processing traumatic memories and achieving long-term positive emotional outcomes. To evaluate the effectiveness of the art therapy interventions, the quantitative studies utilized a variety of standardized rating scales. As mentioned in the study by Rowe and colleagues (2017), relying solely on numerical scores from such rating scales may not produce a fully comprehensive evaluation of art therapy interventions. Many nuanced psychological outcomes and delayed improvements in traumatized individuals may be undetected by quantitative rating scales. This review included studies with diverse designs and intervention programs, highlighting the most effective characteristics of art therapy treatments and methods for traumatized youth.

Comparison to Current Literature

The aim of this literature review is similar to that of a 2007 review conducted by Mallay and colleagues, which also examined the effectiveness of art therapy as a treatment for children who had experienced trauma.. The review similarly included a variety of traumatic experiences, including physical injury, domestic violence, sexual abuse, death of a loved-one, exposure to war, and the World Trade Center 9-11 terrorist attacks. Mallay and colleagues (2007) concluded

that art therapy interventions may lead to positive psychological outcomes for children who have experienced trauma in a variety of contexts. Specifically, the studies reviewed by Mallay and colleagues (2007) found that art therapy facilitated the controlled recollection and expression of emotions related to past trauma as well as improved symptoms of anxiety. These findings of Mallay and colleagues (2007) are consistent with the conclusions drawn by this review; However, there is a notable discrepancy between the methodology of the reviewed studies—Mallay and colleagues (2007) reviewed literature dominated by qualitative case studies, while this review evaluated literature primarily of quantitative studies. The perceived shift in methodology among the literature focused on art therapy as a treatment for traumatized children may be attributed to an increased interest in this treatment option throughout the period between both reviews, and a subsequent recognition of the need for empirical evidence to support it. Indeed, Mallay and colleagues (2007) call for an increase in statistical analysis of group data to substantiate the findings of the reviewed case studies. This review not only substantiates the findings of Mallay and colleagues (2007) with similar conclusions but also expands upon their work by focusing on more recent qualitative studies that provide the empirical evidence necessary to advance the understanding of art therapy as a treatment for children and adolescents who have experienced trauma.

Limitations of Included Studies

The results of the reviewed studies focusing on art therapy and trauma had four limitations. The first limitation involved the sample sizes of the included group studies being relatively small (ranging from 15 to 58), and several studies had multiple participants drop out. The small sample sizes combined with the attrition of participants in some of the studies introduced potential biases, and future studies should have larger sample sizes and improved participant retention. Participants who left the studies prematurely due to reasons related to the art therapy may have been able to provide key insight into the shortcomings of the treatment; thus, failing to collect their evaluations may create survivorship bias. The second limitation encompassed the reviewed studies lacking long-term follow-ups, which made it difficult to observe the long-term effects of art therapy. In addition, all but one of the reviewed studies lacked continuous data points, preventing researchers from determining if the results from art therapy treatment were sustained, improved, or worsened. The third limitation included studies that involved refugee participants who encountered cultural and linguistic barriers, which limited the accuracy of the assessment tools used to evaluate art therapy treatment. The final limitation involved the fact that the reviewed studies primarily relied on self-reported standardized rating scales that are prone to measurement bias. In summary, the findings of the reviewed studies should be interpreted within the context of their limitations related to sample-size, cultural barriers, and data collection methods.

Recommendations for Future Research

This review presents two main recommendations for future research into art therapy as a psychological intervention for children and adolescents who have experienced trauma. (1) Future studies should compare the effectiveness of different art therapy program designs. The reviewed art therapy treatment designs varied but fell into two categories: collaborative discussion-based interventions, or deep, individualized therapy. A future study comparing the two designs could yield critical insights into which method provides the most effective results. Such a study could include a collaborative treatment group, an individualized treatment group, and a combined treatment group to determine if using one or both art therapy methods in tandem provides the best outcomes. (2) Future studies should incorporate an extended longitudinal design to thoroughly capture the long-term effects of art therapy on children and adolescents who have experienced trauma. Long-term data collection is especially relevant for studies focused on individuals undergoing trauma-focused art therapy because some psychological improvements may only be evident at an extended period post-intervention. In conclusion, future studies should compare the effectiveness of different art therapy designs and incorporate an extended longitudinal study design to provide deeper insight into future art therapy treatments for children and adolescents experiencing trauma-related psychological symptoms.

Implications for Practice

The findings of this literature review may be relevant to the practice of art therapy as a treatment for children and adolescents who have experienced trauma. The reviewed literature suggests that art therapy may be most effective at improving patient outcomes related to trauma-related anxiety; However, the short-term improvements in depression and post-traumatic stress are not widely supported by the included studies. Thus, medical providers treating children and adolescents who have experienced trauma should anticipate a delayed improvement of these symptoms and focus on leveraging art therapy's ability to reduce anxiety and facilitate the controlled access and expression of traumatic memories.

Combined Discussion

The purpose of this section is to synthesize the findings from both sections of this review to provide a comprehensive discussion of the efficacy of art therapy within the context of multiple conditions. This section will identify common findings between both parts of this literature review. The scientific literature suggests that art therapy can lead to positive psychological outcomes for both children with autism spectrum disorder (ASD) and past-traumatic experiences. While the reported improvements for children with ASD were different from the reported improvements for individuals who had suffered traumatic experiences, a common trend emerged concerning art therapy's ability to facilitate expression. The literature focused on ASD suggested that art therapy served as a socially non-confrontational outlet for emotional expression, and the literature concerned with trauma similarly indicated that art therapy promoted the access and expression of a traumatic past. Given that art therapy appears to support both children with ASD, a neurodevelopmental disorder, and youth with

trauma-related psychological symptoms in expressing themselves, it is reasonable to hypothesize that art therapy may be similarly effective at promoting expression across a range of other conditions. The different improvements reported in the studies that focused on children with ASD compared to those that focused on youth struggling with past-trauma may be attributed to their respective art therapy interventions being tailored to treat the distinct symptoms and needs of each group. Also, individuals with ASD may not suffer the same issues as individuals with trauma related psychological symptoms. Across the literature, a common theme emerged: a methodological contrast between small qualitative, which and larger quantitative studies. Smaller qualitative studies seemed to offer individualized intervention and detailed, narrative reports. In contrast, larger quantitative studies provided the benefits of collaborative art therapy along with measurable and standardized results. The strengths and weaknesses of both methodological variations were consistent across the literature. The common methodological limitations observed in both sections were the small sample sizes, the measurement bias associated with self-reported standardized rating scales, and the methodological diversity. These limitations affected the reviewed studies' generalizability, reliability, and comparability s. Future research in art therapy should aim to improve upon these limitations and address any constraints related to a specific patient population (such as cultural and linguistic barriers in refugees). In addition, future research should use diverse approaches for data collection to provide a comprehensive and well-rounded evaluation of art therapy interventions. The literature supports the efficacy of art therapy in certain aspects, but its effectiveness in other areas are not robustly established. Consequently, medical providers should be cautious in entirely replacing standard treatments with art therapy until further evidence supports its broader applicability. The literature focused on art therapy as a treatment for both children with ASD and for youth suffering from past trauma reveals common findings, shared limitations, and methodological insights which underscore the need for future research to establish the efficacy of art therapy.

Conclusion

By assessing the literature focusing on art therapy's application to pediatric populations with ASD and trauma-related psychological challenges, this review identified shared outcomes, common methodological limitations, and suggestions for future research. The literature focused on art therapy and ASD revealed improvements to assertiveness, hyperactivity, and inattention as well as positive social-communicative and behavior outcomes. For trauma-related conditions, art therapy showed a potential in reducing avoidance of traumatic memories and anxiety symptoms in children and adolescents. The findings of this review can be used by clinicians treating pediatric patients with ASD or trauma-related mental health challenges to develop the most optimal art therapy approaches to yield the greatest benefits.

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Members of the American Legal Profession on the Political Spectrum By Sahana Dasgupta

Abstract

This paper is the reevaluation of a study that focused on the political ideologies of workers within the legal profession (Bonica, Chilton and Sen 2014). I use the DIME dataset, which is a comprehensive ideological mapping of political elites, interest groups, and donors within society. This data will be able to provide a comprehensive understanding as to the factors influencing political ideologies, and whether variables like region or gender might make a difference in how liberal or conservative someone can be. I will be focusing primarily on lawyers, and my results demonstrate that lawyers' ideologies vary by state. In addition, the amount of money someone donates by election varies by individual or corporation status. One of the weaknesses in this project would definitely be the disparity in gender within the data, since the men outnumber the women almost 2 to 1, which could result in skewed analyses. Given more time, one of the further areas that could have been explored within this paper would have been how the political ideologies of certain demographics changed over the election cycles, and whether there was any singular factor that caused that change to occur.

Introduction

Lawyers have a large influence on American public life, with 8% of the nation's lawyers working within the government (American Bar Association 2012). They make up a significant portion of the Fortune 500 CEOs and CFOs (Claybourn 2024), and occupy "crown jewel" positions at prestigious universities such as Harvard, UCLA, Yale, and more (Winterhalter 2013). With this much representation within society's powerful groups, the American Bar Association is one of the most powerful lobbying groups in the US (Bonica et al., 2016). Due to their established importance, the ideologies of lawyers have been a consistent source of debate for academics: the ideologies of law firms, schools, and even judges have been evaluated to help answer these longstanding questions (Roeder 2014).

Currently, registered voters are evenly split between the Republican and Democratic parties, with 48% leaning towards Republicans and 49% leaning towards the Democrats (Nadeem 2024). However, "a greater share of registered voters say they are both ideologically **conservative and associate with the Republican Party (33%)** than say they are **liberal and align with the Democratic Party (23%)**," (Nadeem 2024). Namely, this is because many voters that associate with the Democratic Party describe their views as being conservative or moderate (Nadeem 2024).

The goal of this study is to understand the ideologies and political contributions of members of the American legal profession and I use the same data as the original Bonica et al (2014) paper to complete this task. Since the publication of the original study, Adam Bonica has been updating the Database on Ideology, Money and Elections (DIME) dataset to include elections in subsequent years (Bonica 2023). The DIME dataset is a comprehensive ideological mapping of political elites, interest groups, and donors within American society. The dataset

contains political contributions made by both individuals and organizations for local, state, and federal elections from 1979 to 2022. It contains separate databases with information on all the political contributors, all the recipients, the specific contributions made, as well as a combined database with the overall data.

The dataset that I'll be using in this paper is the contributor database, which contains important variables such as names, professions, CFscores that represent donor political ideology, geographic locations, gender, and more. This data will be able to provide a comprehensive understanding as to the factors influencing political ideologies, and whether variables like region or gender might make a difference in how liberal or conservative someone can be. By splitting the overall dataset into smaller data frames organized by the variables that will be compared, a direct analysis can be drawn by comparing the resulting mean CFscores of these lawyers.

This paper will feature graphs for the following variables: gender, geographic region, profession, contributor employers, states, and individuals vs. corporations. These graphs will come together to tell a compelling story about the different factors that can be unknowingly influencing our political ideologies. The graphs will show if one gender is generally more liberal than the other, if the region one was born in and their surroundings affect their views, if working for a big corporation is different from working for smaller companies in terms of ideology, as well as the distribution of political ideologies across America. This will provide a detailed analysis of the political landscape in our society today. Using this analysis using the more recent data, I verify whether Bonica's original conclusion remains true in the status quo: that the political spectrum within lawyers in our society is majorly heterogenous.

Methods

The DIME dataset has over 500 million entries in itemized political contributions made by individuals and organizations to support numerous election campaigns, whether they be local or federal. Consequently, this meant that there were many databases available to use for this paper. In order to make this decision, I first analysed Bonica's study, and what his results failed to consider with the new data that the DIME dataset provides in the status quo.

The dataset is composed of three major databases: the contributor database, the contribution database, and the candidate/recipient files. The contributor database lists all the political campaign monetary contributions that were made during campaign elections, and which individual or firm made that donation. The contribution database lists the organization or group that the monetary donations were made to, alongside the contributors. The candidate/recipient files list all the cycle-specific entries for those that met and didn't meet the requirements to be included within this study.

I chose the contribution database because it would give me both the contributors and the organizations that were donated to, allowing me to gauge whether the individuals that donated were liberal or conservative. This would allow me to group data based on gender, state, location, and more, and would allow me to conduct a comparative analysis on the political spectrum within the status quo.

Bonica's study concluded that the political spectrum among all of society was generally heterogenous – meaning that there were generally an even amount of liberal and conservative donations, and neither ideology overpowered the other. In my research, I narrowed Bonica's study of general society to only focus on the lawyers and legal firms within society, to analyse how the ideologies within one of the major branches within American society pan out.

Since his research, we have had many social and political changes within the United States, ranging from a global pandemic to having the century's highest voter turnout in a presidential election in 2020. This led me to hypothesize that the social and political climates within society may have been dramatically altered as well. To test this hypothesis, the purpose of my review article is to refine Bonica's conclusion by including data from more recent election cycles that he was unable to consider, and determine whether his theory still stands true today.

Results

For this study, I present three different perspectives of the ideology and political contributions of members of the American legal profession. First, I examine the ideological differences between men and women of different states. Second, I examine the ideological distribution (based on contribution) of individual lawyers versus legal firms. Finally, I look at the distribution of contributions across different presidential elections based on contributor status as an individual or as a firm. The analyses and results are discussed further along with each figure below.

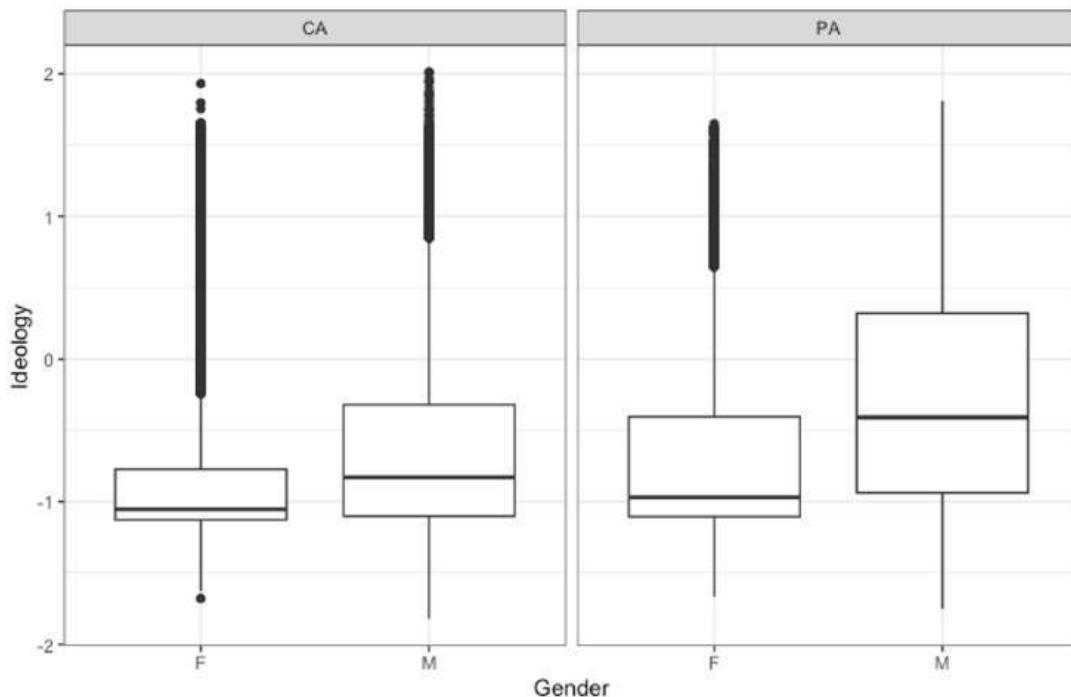


Figure 1: Ideology by Gender

Note. Generated graph that shows the density of conservatives and liberals amongst men and women in California and Pennsylvania.

In Figure 1, I am interested in whether there is an ideological split between men and women in the legal profession and whether such split is more stark depending on the place where someone practices.

To do this, I group the data by gender and state in which the donor was from. I compute the average ideology (as reported by Bonica's CFscore) and plot it as a boxplot, shown in Figure 1. I chose California and Pennsylvania because they represent somewhat two different political spectrums in the United States.

In the status quo, California is largely considered to be a Democratic state, with the democrats representing 46 of the state's congressional districts and holding supermajorities in both legislature chambers. While the red and blue regions within California may seem geographically even, adjustment of the state's map shows that the state is actually more Democratic when the areas with eligible voting residents are emphasized (McGhee, 2020).

Additionally, Pennsylvania is generally known as a battleground state despite its recent Democratic votes, and has earned itself the reputation of being known as a Keystone state in elections to this day (270ToWin, 2024).

In Bonica's (2023) CFscore, negative values indicate liberalism, or being left of center, whereas positive values indicate conservatism, or being right of center.

For California, Figure 1 shows that on average, male lawyers are slightly more conservative (less liberal) than their female counterparts. However, their average ideology for male lawyers remains generally liberal (mean and 75% Interquartile range is less than 0). There is higher variability in the ideological distribution of male lawyers compared to female lawyers as shown by the broader interquartile range for male lawyers.

Moving to Pennsylvania, we again see that male lawyers are more likely to be more conservative (or less liberal) than their female counterparts, though the average lawyer remains liberal (mean less than 0 on the CFscore). However, there is a greater variation in male lawyer ideology as the 75 percentile of male lawyers are slightly conservative compared to their female counterparts, where conservative lawyers are the outlier.

Comparing the two states, we see that female lawyers in both California and Pennsylvania are roughly the same in their average ideology, though there is more ideological diversity among female lawyers in Pennsylvania. On the other hand, male lawyers in Pennsylvania are significantly more conservative than male lawyers in California, and, like women, there is more ideological diversity among male lawyers in Pennsylvania compared to male lawyers in California.

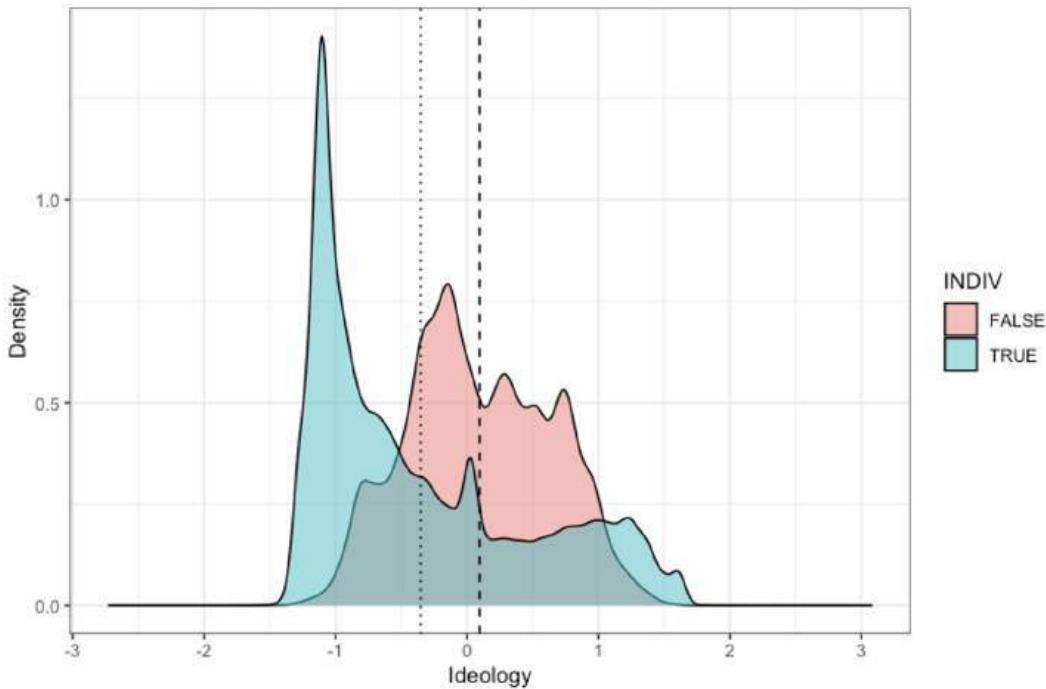


Figure 2: Ideologies- Corporations vs. Individuals

Note. Generated graph that shows the density of conservatives and liberal amongst both legal firms and individual lawyers.

In Figure 2, I am interested in whether there is a clear difference between the ideologies that are sustained by corporations, and the ones that are sustained by individual lawyers.

In order to do this, I first group the data into corporations and individual lawyers. I compute the average ideology (as reported by Bonica's CFscore) and plot it as a smooth curve, shown in Figure 2. I chose to compare corporations and individual lawyers because I've always held the belief that corporations tend to be very politically extreme in their views, especially if they have a large influence, and I wanted to confirm whether that held true when it came to elections. I wanted to compare the ideologies between corporations and individual lawyers to see if that statistically held true.

In Bonica's CFscore, negative values indicate liberalism, or being left of center, whereas positive values indicate conservatism, or being right of center. The blue curve represents the individuals, while the red curve represents the corporations.

Observing the curves as a whole, Figure 2 shows that individuals ideologies' tend to peak at the liberal -1 value, with very few individuals on the conservative side of the graph. The corporations have a peak at the liberal -0.5 value and the conservative 0.5 value, but overall tend to have more conservative values.

To compare the ideologies, Figure 2 shows that there is a difference between the two means of both corporations and individuals. The mean for corporations is represented by the dashed line, while the mean for individuals is represented by the dotted line. On average, the

mean of individuals shows that they tend to be more liberal, while the mean for corporations show that they fall firmly in the center.

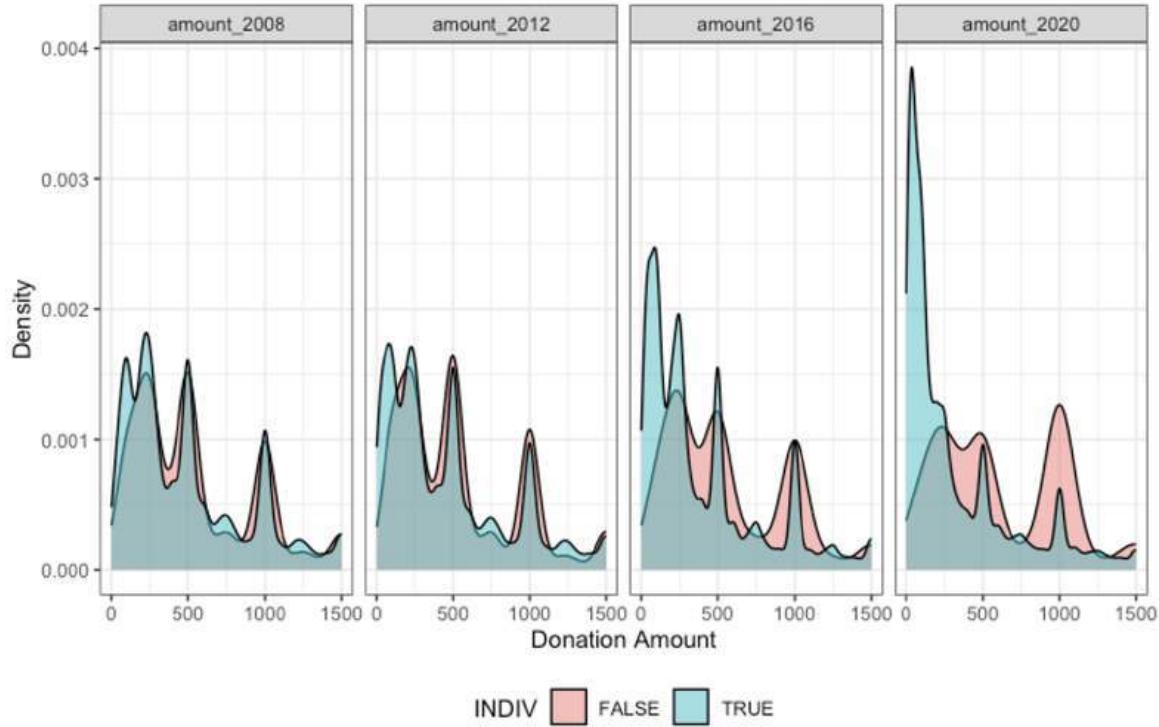


Figure 3: Amount Donated Per Presidential Election Year

Note. Generated graph that shows the amounts of money donated to political campaigns during presidential elections by both legal firms and individual lawyers.

In Figure 3, I am interested in whether the amount of money that was donated by both individual lawyers and corporations in the last four Presidential elections changed or stayed relatively the same. I'm also interested to observe whether individuals or corporations tend to donate more money during elections to political campaigns.

To do this, I take data from the election years of 2008, 2012, 2016, and 2020. I group the data into corporations and individual lawyers, and I had to remove all corporations and individual lawyers that did not pay any money in the election year to help remove outliers from the dataset. I then narrowed the range of values for donation amounts from 0 to 1500 in order to help capture the full spectrum of the curves, as that was where most of the data was concentrated. I compute the average ideology (as reported by Bonica's CFscore) and plot it as a smooth curve, shown in Figure 3. I chose to compare the amounts from the last four election years so I would have enough data to be able to notice an observable difference between the amount of money donated, as well as be able to hypothesize why the amounts may be smaller or bigger.

The blue curve represents the individuals, while the red curve represents the corporations. The donation amounts increase from left to right, with the least amount donated being 0 dollars,

and the highest amount donated being 1,500 dollars. Since most political contributions are small, this allows us to focus on small donations in the analyses.

Observing the curves as a whole, Figure 3 shows that corporations generally tend to donate higher amounts of money than individuals do. While in 2008 and 2012, the donation amounts for both corporations and individuals remained relatively the same, Figure 3 shows that in 2016 and 2020, corporations donated more money as a whole. In the graph for 2016, we see that individuals peak at around 100, 250, and 500 dollars, while corporations peak at 250, 500, and 1000 dollars. A similar situation can be seen in the graph for 2020, where individuals peak at around 100 dollars, while corporations peak at 250, 500, and 1000 dollars.

Figure 3 also shows that individuals donated less money in 2020 than they did in 2016 while corporations remained unaffected, a reasonable conclusion for that being the effects of the COVID-19 pandemic on the financial incomes of a majority of individuals within society. This could be because legal firms tend to remain unaffected during financial crises and hold their income steady, as seen through precedent in past economic downturns. “Of the past three downturns, only the global financial crisis of 2008–09 resulted in a decline in aggregate Am Law 100 revenue”, showing the resilience that law firms have when managing their finances in times of economic crisis (Babbitt et al., 2020).

As a whole, both individuals and corporations donated more money in 2016 and 2020 than they did in the years of 2008 and 2012. While a certain conclusion cannot be drawn as to the reason why just from the data itself, it is reasonable to infer that it may be because of the candidates that were running during the election, prompting more people to get involved.

Discussion

Across the three analyses, I found that:

- Women lawyers generally tend to be more liberal, however the average CFscore for both men and women remain generally liberal regardless of the state (California vs. Pennsylvania).
- Individual lawyers tend to contribute to more liberal recipients, while corporations are more moderate with their donations to either side.
- Most individual lawyer contributions tend to be small dollar amounts, as seen in Figure 3, with many new donors participating in the 2020 election.

Overall, my research confirmed Bonica’s old conclusion that society had mainly heterogenous political views, and no ideology dominated over the other. This can be seen within the legal field through the data represented in the graphs, where it is clear that even in states with entirely different political climates, the amount of lawyers that are either conservative or liberal remain approximately the same despite some lawyers expressing slightly more liberal views on average. This same conclusion held true for both lawyer individuals and legal firms as well, contradicting my previous belief that legal firms had strongly left or right-leaning views. As the data has shown, firms tend to be more neutral in their views than the individual lawyer.

Therefore, considering recent data of all the elections that wasn't in Bonica's previous study, his conclusion that the political climate in the status quo is heterogenous remains accurate to this day.

One of the main shortcomings of the data is the disparity in gender within the data, since the men outnumber the women almost 2 to 1, which could result in skewed analyses. For instance, the lower amount of available data for women in the legal field may result in an inaccurate comparative analysis of the ideologies between women and men, as the sample sizes I am comparing are not equal. This, however, may be a reflection of the fact that the American legal profession is predominantly male. Furthermore, the DIME dataset is a wealth of data covering political contributions over half a century's time in political campaigns and elections. That said, data files are massive, and the resources available for this project meant that there are more avenues to explore than there was computing capacity. With more time and more resources however, it would have been possible to work around this issue and work with all of the data to create a more comprehensive analysis of society's political climate today.

Additionally, given more time one of the further areas that could have been explored within this paper would also have been how the political ideologies of certain demographics changed over the election cycles, and whether there was any singular factor that caused that change to occur. Furthermore, another avenue that could be pursued is to compare the political ideologies of lawyers to those not in the legal field and analyse if there is a difference, and if so, why that is the case. It would also be possible to expand outside just the legal field and map the ideologies of society in general to judge the general political climate of the status quo.

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How can Convolutional Neural Networks Analyze Handwriting Data? By Palak Tiwari

Abstract

Identifying authorship handwriting analysis—a basic subset of forensic document examination—plays a critical role in criminal investigations. This study aims to identify writers by analyzing the features of their handwriting through the creation and implementation of a handwriting recognition model. The study uses convolutional neural networks (CNNs) for feature extraction and classification and uses a dataset that contains handwriting samples. The research attempts to improve writer identification accuracy through model training on a wide range of handwriting styles, including forensic samples. With implications for forensic science and document authenticity verification, the results show how well the model differentiates between different writers.

Introduction

1.1 Background

For centuries, forensics has used handwriting analysis as a primary technique for document validity, determination, and person identification. Handwritten documents, ranging from ancient manuscripts to legal contracts, have been essential sources of information throughout history. The unique qualities of handwriting have been crucial in determining the authorship and authenticity of these documents.

Ancient scribes used unique handwriting styles that reflected their training, geography, and individual quirks to meticulously transcribe religious texts, literary works, and historical records. To identify authors and verify the authenticity of ancient texts, handwriting analysis in historical contexts involved examining variations in script types of ink and parchment composition. Handwriting analysis still to this day, remains a crucial tool in contemporary forensic contexts. An example is the Lindbergh kidnapping, where Bruno Hauptmann's handwriting in ransom notes was discovered at the crime scene, which led to Hauptmann's conviction (Bhargav, Ramachandran, & Karthikeyan, 2023). In more recent times, forensic handwriting analysis has proven helpful in confirming the legitimacy of court documents, identifying forgeries in financial fraud cases, and connecting suspects to handwritten communications containing anonymous threats or extortion attempts. These days handwriting analysis is a specialized area of forensic science that is vital to criminal and legal investigations. To identify, writers confirm signatures and spot changes in legal documents like contracts, wills, and financial records, forensic document examiners examine handwritten samples. Handwriting comparisons are significant proof in circumstances involving fraud forgeries and challenged papers, where the reliability of handwritten evidence can influence court decisions and legal proceedings.

1.2 Research Objective

By increasing efficiency and accuracy through automated processes, advances in artificial intelligence (AI) have completely changed several industries, including business analytics and medicine. AI offers a revolutionary chance to advance authentication procedures and investigative methods in the field of forensic science. Handwriting recognition, facial recognition, voice analysis, and pattern recognition in blood splatters, open up new possibilities for forensic investigations beyond more conventional techniques like fingerprint analysis and DNA profiling. This work investigates using convolutional neural networks (CNNs) in AI-powered handwriting analysis to extract and analyze fine details from handwritten samples. This method improves writer identification accuracy and helps identify forged documents which increases the evidentiary value of documents in court. Additionally, developments in facial recognition algorithms allow law enforcement to identify suspects from surveillance footage with previously unheard-of accuracy allowing for prompt interventions and crime prevention. Artificial intelligence (AI) can also be used to analyze intricate patterns in voice recordings and blood splatters, giving forensic experts quantitative insights into crime scene reconstruction and perpetrator identification. Through the automation of tedious operations, the decrease in human error, and the quickening of the investigation process, these technologies supplement conventional forensic methods. This study attempts to advance the broader use of machine learning in forensic science by investigating the incorporation of AI technologies in forensic handwriting analysis. In doing so, the study hopes to improve writer identification techniques' dependability and effectiveness, which will help the forensic community solve crimes and uphold the rule of law, streamline document authentication processes, improve forensic investigation methodologies, and provide reliable evidence in legal proceedings. The outcomes of this research have practical applications in enhancing the reliability of forensic evidence in an increasingly digital age.

Methodology

2.1 Dataset

The study uses the handwriting dataset from the Center for Statistics and Applications in Forensic Evidence (CSAFE), a data collection created especially for testing and training handwriting recognition algorithms in forensic settings. The research aims to train a convolutional neural network (CNN) architecture using supervised learning techniques by concentrating on a binary classification task between two authors. By accurately differentiating and classifying handwriting samples, the CNN will be trained, advancing the field of forensic document examination.

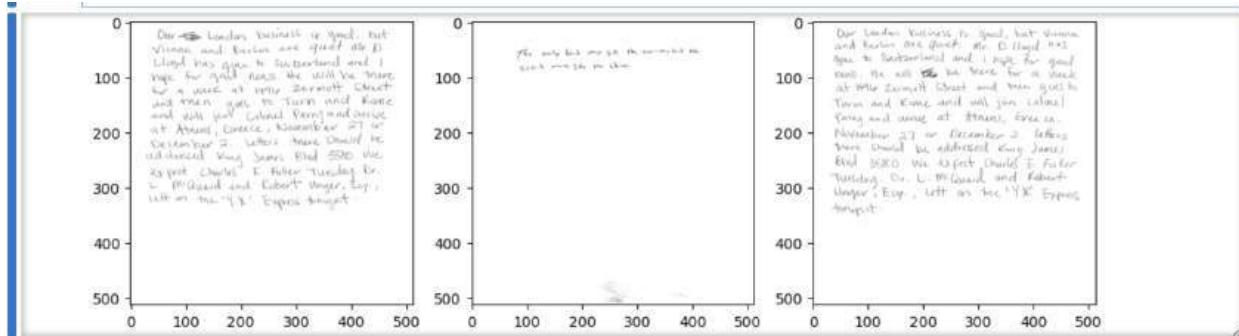


Figure 1: These are sample images of handwriting data being analyzed for patterns and similarities.

2.2 Data Preprocessing

To standardize and improve the quality of handwritten samples, the dataset is heavily preprocessed before model training. Image normalization is one of the preprocessing stages that guarantees consistency across samples. Handwritten documents are scanned at high resolutions and converted into binary or grayscale formats. (Lewandowsky, 2018) Using optical character recognition (OCR) tools, handwritten samples can be divided into individual characters or words, allowing for more precise feature extraction and granular analysis during model training. Character segmentation improves authorship attribution and forgery detection tasks by allowing the model to concentrate on identifying distinctive handwriting characteristics within smaller units.

2.3 Feature Extraction

A key component of capturing unique handwriting traits required for forensic analysis is feature extraction. To quantify the distinctive stylistic elements of each author, conventional features from segmented handwriting samples are extracted, including stroke width, slant angle, and baseline variability. Convolutional neural networks (CNNs) are used in advanced feature extraction techniques like texture analysis and deep feature learning to automatically extract hierarchical features from handwritten images. This allows the techniques to capture subtle patterns and spatial relationships within handwriting strokes. (Lewandowsky, 2018) By utilizing transfer learning, the model can refine CNN layers to extract handwriting-specific features that are important for authorship attribution and document authentication. This is achieved by leveraging learned representations from general image recognition tasks. To enable effective model training and reliable performance across various handwriting datasets, feature vectors taken from CNN layers encode semantic information about handwriting styles.

Results

The CNN model was able to correctly classify 90.91% of the handwriting samples that it examined. This high accuracy shows that the model could identify and distinguish between different handwriting styles within the dataset. This means that practically speaking, the model is very trustworthy for forensic applications where precise handwriting identification is essential. A

dataset of resized and normalized grayscale images was used to train the CNN model, which used a dense layer for classification and a sequence of convolutional and pooling layers to extract features. This allowed for the accuracy of the results. By adding new data, the model was further refined and improved, increasing its generalizability and robustness.

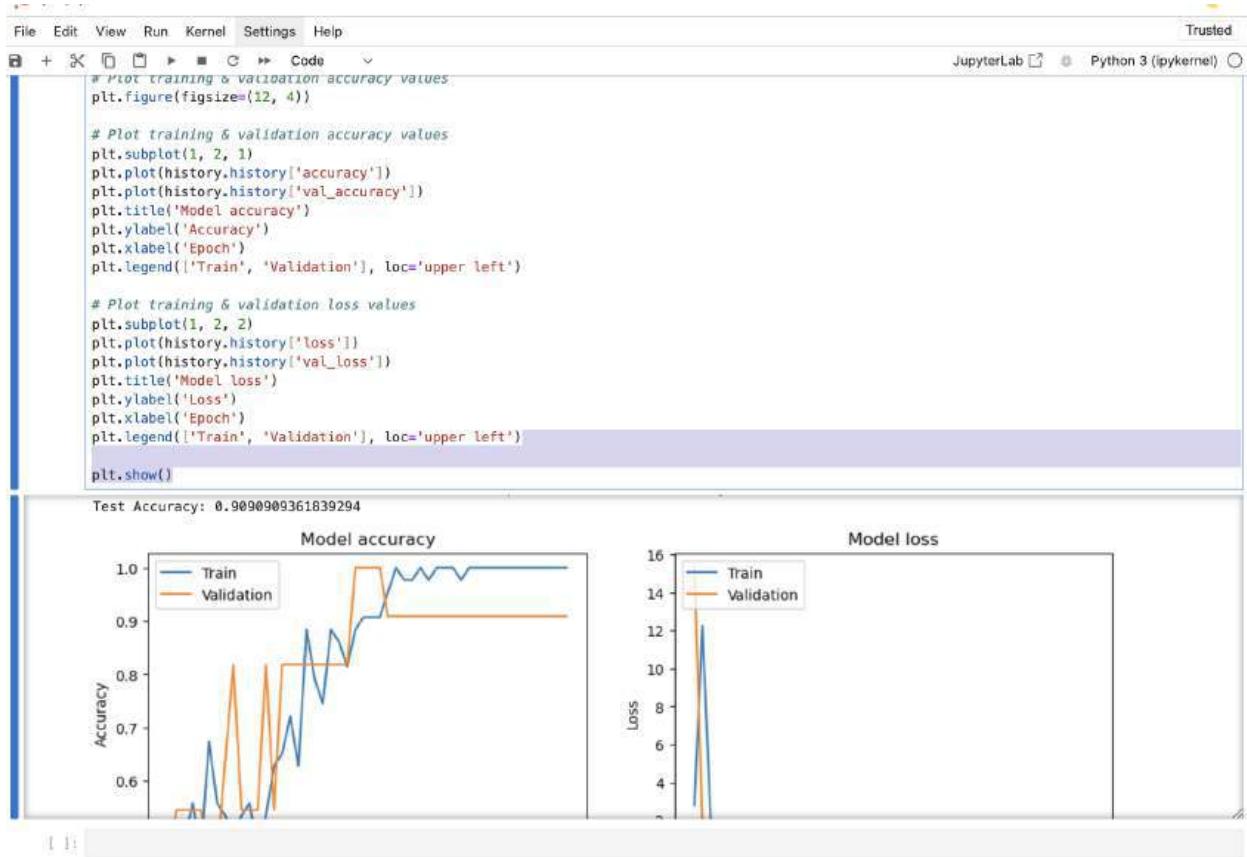


Figure 2: This graph shows the training and validation accuracy and loss for the CNN. The blue line represents the training performance, whilst the orange line represents validation. The graph helps us understand the model's generalization ability, indicating how well it learned to classify the handwriting during trial, versus how it performs on unseen data.

Instead of getting 90.91% accuracy, the error was noted to be 9.09% of the test samples covered. This level of error underlines the fact that a potential for improvement in the analyzing machine learning model's complexity is still there. Prospectively, the research related to enhancing the model's architecture, adding more samples to the training set, and implementing new technologies in image processing and augmentation to further the reduction of these errors might be the potential directions of future work.

Hence, the 90.91% performance shows that the CNN model is a powerful handwriting analysis tool with real-world forensic applications, which is very much expected.

Discussion

The success recorded by the CNN in handwriting analysis, with a performance rate of 90.91%, serves as convincing evidence of the remarkable progress that forensic document examination has gained.

3.1 Improved Reliability and Accuracy

The CNN model proved to be genuine, demonstrating an accuracy of 90.91% and successfully differentiating between different handwriting styles. The necessity of forensic work, which demands argumentation from the very basic level to the point of being central to the case, suggests that the highly accurate handwriting identification process will prove decisive.

3.2 Forensic process automation

The application of handwriting analysis in law enforcement has the potential to revolutionize technology. The traditional method of handwriting analysis, which relies solely on the human eye, is time-consuming, easy to make mistakes, and even results in the public release of convictions. This examination procedure, when combined with the CNN method, creates a more efficient and consistent pattern of work for forensic experts, enabling them to finish more analyses faster and contribute to the speedier resolution of criminal cases.

Conclusion

With a remarkable success rate of 90.91%, this research demonstrates that convolutional neural networks (CNNs) are effective in the field of handwriting analysis. Machine learning is presented as a dependable and effective tool for handwriting recognition while also showing promise as a tool for forensic document examination. Differentiating handwriting samples using the CNN model accurately is a crucial first step toward enhancing forensic processes and offers a notable boost to efficiency and accuracy. Although the model exhibits good performance further research and development are required to address the remaining misclassification issues and improve the model. Overall, this study lays the groundwork for future automated handwritten examinations that may prove beneficial in various domains of forensic science.

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What are the Underlying Factors Contributing to the Heterogeneity In Spinal Muscular Atrophy (SMA) and How Do These Factors Influence the Variability in Disease Severity and Progression Among Affected Individuals? By Aryahi Padmavati Narvekar

ABSTRACT

Spinal Muscular Atrophy (SMA) is a complex neurodegenerative disorder characterized by the degeneration of motor neurons, leading to varying degrees of muscle weakness and atrophy. This review aims to investigate the heterogeneity in SMA, focusing on understanding why the disease can manifest with different levels of severity and progression among affected individuals. Genetic modifiers, environmental influences, and other biological mechanisms could influence the varying clinical manifestations of the disease. Many treatment options regarding SMA tackle symptoms such as broken bones, limited mobility, or breathing problems. However, the root cause of the disorder is a lack of SMN1 genes. These genes carry instructions to create motor neurons. Without motor neurons, muscles undergo atrophy, meaning they become smaller and weaker through their disuse. Although helpful, these treatment options do not tackle the foundation and root cause of the disorder. The findings suggest the importance of considering genetic, environmental, and other factors in SMA research and highlight the need for personalized approaches to diagnosis and treatment. As this study is exploratory in nature, it serves as a foundation for future investigations to unravel the complexities of SMA and improve the lives of those affected by this debilitating condition.

INTRODUCTION

Spinal Muscular Atrophy (SMA) is a neuromuscular disorder characterized by the decline in production or the rapid decay of motor neurons. SMA is an autosomal recessive disorder; it manifests when a child inherits two faulty SMN1 (Survival Motor Neuron 1) genes from each parent (James et al., 2015; Hansen et al., 2019). SMN1 encodes the ubiquitously expressed, multifunctional survival motor neuron protein (SMN) (Singh et al., 2018). Decreased expression of SMN results in the loss of spinal cord motor neurons, ultimately leading to muscle weakness and atrophy. Atrophy is defined as the inability to use a muscle due to a lack of use.

In order to understand the complexities of SMA, scientists have used both animal models and human patient research. Mice are genetically engineered to mimic the human condition of SMA, enabling researchers to study the disease's progression and evaluate the efficacy of therapeutic interventions in these animal models. In humans, SMA research has included observational research, clinical trials, and genetic studies. By employing such models, we have gained a better understanding of the genetic mutations responsible for SMA, the molecular mechanisms leading to motor neuron degeneration, and the resultant muscular atrophy. The employment of animal models, particularly mice and zebrafish, has been pivotal in uncovering the disease's pathophysiology and testing the efficacy and safety of potential treatments. Concurrently, direct human research, through genetic studies and clinical trials, has facilitated the development of groundbreaking therapies that offer hope and improved quality of life for

individuals affected by SMA. From this, interventions for SMA have significantly improved, and several therapeutic modalities are currently licensed or under development. The most striking example is Zolgensma, which introduces a normal copy of the SMN1 gene into the motor neurons. Other modalities include SMN2 splicing modifiers, such as Nusinersen (Spinraza), and risdiplam (Evrysdi), that modulate the splicing of the SMN2 gene to increase the production of fully functional SMN protein.

Heterogeneity is the inheritance of 2 different genes that code for a specific trait (or phenotype). In the context of SMA, heterogeneity involves the inheritance of at least one faulty SMN1 gene. Those that inherit 1 faulty gene can still pass on SMA to their progeny but do not exhibit symptoms as those with two faulty genes do. Because of this, there are various stages at which SMA can show, each having different severity levels and therefore different symptoms and levels of immobilization. In medicine, understanding heterogeneity is essential for personalized treatment plans. Patients differ in genetics, lifestyle, and response to treatments. Tailoring medical interventions to individual patient characteristics can lead to more effective and safer healthcare. In order to treat this heterogeneity among SMA patients, we need to identify the underlying mechanisms involved.

1.0 IMPACT ON SMN PROTEIN DEFICIENCY ON MOTOR NEURONS

Motor neurons play a crucial role in the neuromuscular system, and any disruption in their function can lead to various motor impairments. Motor neurons control muscle contraction. When motor neurons degenerate due to SMN protein deficiency, the muscles they innervate become weak and atrophied. This muscle weakness is a hallmark of SMA and can affect various muscle groups throughout the body. As motor neurons are lost, individuals with SMA experience a decline in motor function. This can result in difficulties with basic motor skills, such as crawling, walking, sitting, and eventually even breathing and swallowing, depending on the severity of the condition (Singh & Howell, 2018).

2.0 GENETIC FACTORS INFLUENCING DISEASE SEVERITY

2.1.1 SMN1 Gene: Structure and Function

Located on chromosome 5q13, the SMN1 gene is responsible for the production of the SMN protein. The SMN protein participates in the assembly and upkeep of small nuclear ribonucleoproteins (snRNPs), which are essential parts of the spliceosome, the cell machinery involved in pre-mRNA splicing. This process is critical for proper gene expression in most cells, but particularly in motor neurons. In addition to its role in RNA splicing, the SMN protein is also involved in other crucial cellular processes, such as the axonal transport of mRNAs and the assembly of stress granules. These functions are essential for localized protein synthesis and cellular stress responses, both of which are vital for motor neuron survival and function. Disruptions in these processes due to insufficient SMN protein contribute to the neurodegenerative nature of spinal muscular atrophy (SMA). Therefore, understanding the

structure and function of the SMN1 gene is key to developing therapies that can restore SMN levels or compensate for its loss (Singh et al., 2018).

2.1.2 SMN2 Copy Number

The most significant genetic modifier of SMA severity is the number of copies of the SMN2 gene that an individual has. SMN2 is a paralogous gene to SMN1, but it usually produces less stable and functional SMN protein due to a single nucleotide difference. The more copies of SMN2 an individual has, the more SMN protein they can potentially produce. Thus, individuals with more SMN2 copies generally have milder forms of SMA, while those with fewer copies have more severe forms. In order to study SMA, researchers have developed transgenic mouse models by genetically modifying mice to have mutations or deletions in their SMN1 gene, similar to the genetic alterations seen in human SMA. These mouse models often incorporate varying copies of the SMN2 gene, which modulates the severity of the disease phenotype in a manner analogous to humans. The most common SMA mouse model is the "SMN Δ 7" model, which carries a deletion of the Smn1 gene and a human SMN2 transgene along with a modified SMN Δ 7 gene. SMA mouse models exhibit a range of symptoms and defects that mirror the human disease- SMA mice show progressive muscle weakness and wasting, particularly noticeable in the proximal muscles. Additionally, similar to humans, mice models exhibit a significant loss of motor neurons, mobility issues, and a decreased lifespan.

2.1.3 Variability in disease severity and progression

There are several genetic factors that may change the age of onset and severity in a patient with SMA. Besides a broken or missing SMN1 or SMN2 gene, the presence of modifier genes can act as basic modifiers. These genes could affect various biological pathways, including those involved in neuronal survival, inflammation, muscle function, and cellular stress responses. Additionally, the overall genetic background of an individual, which includes the cumulative effect of thousands of genetic variations, can influence the phenotype of SMA.

3.0 AGE OF SYMPTOM ONSET

The age at which SMA symptoms first appear can also influence disease severity. SMA is classified into different types based on the age of onset and clinical symptoms. Generally, earlier onset forms of SMA tend to be more severe, while later onset forms are milder. Generally, SMA is categorized into three main types: Type I, Type II, and Type III. Type I, often referred to as Werdnig-Hoffmann disease, manifests in infancy, usually before six months of age. Infants with Type I SMA exhibit severe muscle weakness, difficulty swallowing, and respiratory issues. The rapid progression of symptoms in Type I often leads to significant challenges in motor function and necessitates immediate medical attention. Type II SMA, also known as Dubowitz disease, typically presents between six and 18 months of age. Children with Type II SMA experience a milder form of the disease compared to Type I, but they still face significant motor challenges. While they may achieve certain motor milestones, such as sitting unassisted, the disease

progression may result in the loss of these abilities over time. Type III SMA, or Kugelberg-Welander disease, has a later onset, usually in childhood or adolescence. Individuals with Type III SMA may initially exhibit normal motor development but later experience a gradual decline in muscle strength. Despite motor challenges, many individuals with Type III SMA maintain the ability to walk, although they may require mobility aids as the disease progresses.

Motor function in patients with SMA is measured using different scales, including the Hammersmith Functional Motor Scale (HFMS), which assesses motor functions relevant to daily living activities (Mercuri et al., 2014). Another commonly used scale is the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), which is primarily used for infants with SMA, especially those with Type I SMA (Kolb et al., 2017). The CHOP INTEND scale measures motor skills and is sensitive to even small changes in motor abilities, making it crucial for monitoring this rapidly progressing form of SMA. The scale is scored from 0 to 4, with 0 indicating a complete lack of ability to perform a motor task and 4 indicating the ability to fully perform the task.

4.0. BIOMOLECULAR MECHANISMS

4.1 Contributing to heterogeneity

The clinical heterogeneity in spinal muscular atrophy (SMA) is influenced by various molecular pathways, which play crucial roles in the disease's pathogenesis. One of the critical factors contributing to SMA's heterogeneity is the variable copy number of the SMN2 gene among patients. Therefore, therapeutic strategies often focus on modulating SMN2 gene expression or splicing to increase SMN protein levels.

Research has also highlighted the importance of other genetic and epigenetic modifiers that impact SMA severity. For example, variations in genes involved in muscle maintenance and neuronal survival can influence disease progression. The NAIP gene, for instance, has been implicated in modifying SMA severity. Patients with deletions in both the SMN1 and NAIP genes tend to have more severe forms of the disease, suggesting a synergistic effect in motor neuron degeneration (Cancès et al., 2020).

4.2 Role of Cellular Stress Responses

Cellular stress responses play a significant role in the pathogenesis and progression of spinal muscular atrophy (SMA). The deficiency in SMN protein not only affects motor neurons but also leads to widespread cellular dysfunction, invoking various stress response pathways.

One key cellular stress response implicated in SMA is the unfolded protein response (UPR). The UPR is activated due to the accumulation of misfolded proteins in the endoplasmic reticulum (ER), which is a common occurrence in cells with insufficient SMN protein. Studies have shown that UPR activation can lead to increased cell death in motor neurons, exacerbating SMA symptoms. For instance, the activation of PERK (Protein Kinase RNA-like Endoplasmic

Reticulum Kinase), a key UPR sensor, has been observed in SMA mice models, suggesting that targeting UPR pathways might mitigate some of the cellular damage in SMA (Ceylan et al., 2020; Cho and Dreyfuss, 2010).

Oxidative stress is another crucial factor in SMA pathology. The lack of SMN protein disrupts mitochondrial function, leading to increased production of reactive oxygen species (ROS). Elevated ROS levels can cause oxidative damage to cellular components, including DNA, proteins, and lipids. This oxidative stress is particularly detrimental to motor neurons, which are highly susceptible to oxidative damage. Therapeutic strategies that reduce oxidative stress, such as antioxidants, have shown promise in preclinical studies (Chen et al., 2020; Collén et al., 2022).

Additionally, impaired autophagy has been noted in SMA. Autophagy is a critical cellular process for degrading and recycling damaged organelles and proteins. SMN protein deficiency hampers autophagic flux, leading to the accumulation of damaged cellular components. Enhancing autophagy through pharmacological means has been explored as a potential therapeutic approach, aiming to alleviate cellular stress and improve motor neuron survival (Chen et al., 2020; Chiriboga et al., 2019).

Lastly, the heat shock response, mediated by heat shock proteins (HSPs), is another cellular stress pathway affected in SMA. HSPs function as molecular chaperones, assisting in the proper folding of proteins and the prevention of aggregation. The reduced levels of SMN protein in SMA impair the expression and function of HSPs, leading to increased protein misfolding and aggregation. Enhancing HSP activity through small molecule chaperones or gene therapy could offer therapeutic benefits by stabilizing protein homeostasis in motor neurons (Chen et al., 2020; Chiriboga et al., 2023).

4.3 Impact of RNA Processing Defects

RNA processing defects play a crucial role in the pathogenesis of spinal muscular atrophy (SMA), significantly contributing to cellular stress responses. The SMN1 gene is essential for the assembly of the spliceosomal complex and the proper splicing of pre-mRNA. Defective splicing of the SMN2 gene, which results in the exclusion of exon 7 in most transcripts, produces a truncated, unstable SMN protein that lacks full functionality. Thus, therapeutic strategies have focused on incorporating exon 7 in SMN2 transcripts. This is exemplified by drugs like nusinersen, which modulate splicing to increase the production of functional SMN protein (Cartegni et al., 2006; Chiriboga et al., 2016).

RNA processing defects in SMA also extend beyond the SMN genes. SMN protein is involved in the biogenesis of small nuclear ribonucleoproteins (snRNPs), which are crucial for splicing. The mis-splicing of genes involved in the cytoskeleton and axonal transport contributes to motor neuron degeneration observed in SMA.

The connection between RNA processing defects and cellular stress responses is evident in how these splicing abnormalities induce cellular stress. Mis-spliced RNAs can produce dysfunctional proteins that accumulate and form aggregates, triggering the unfolded protein

response (UPR) and other stress pathways. This aggregation can exacerbate the ER stress already present in SMA, further compromising motor neuron health (Chen et al., 2020; Collén et al., 2022). Additionally, the reduced efficiency of autophagy in SMA, partly due to RNA processing defects, leads to the accumulation of damaged proteins and organelles, contributing to cellular stress and motor neuron degeneration (Chiriboga et al., 2019).

4.4 Neuroinflammation and Immune System Responses

Neuroinflammation and immune system responses are critical components in the pathophysiology of spinal muscular atrophy (SMA). The interplay between motor neuron degeneration and immune responses significantly impacts the progression and severity of SMA, connecting closely with cellular stress responses and RNA processing defects. Microglial activation is a prominent feature of neuroinflammation in SMA. Microglia, the resident immune cells of the central nervous system (CNS), become activated in response to neuronal injury and stress. In SMA, the deficiency of SMN protein leads to increased neuronal stress and subsequent activation of microglia. Activated microglia release pro-inflammatory cytokines such as TNF- α and IL-1 β , which exacerbate motor neuron degeneration and contribute to the inflammatory environment in the spinal cord (Cho and Dreyfuss, 2010; Chen et al., 2020). This inflammatory response creates a vicious cycle, where motor neuron death further activates microglia, leading to increased inflammation and cellular stress.

Astrocytes, another type of glial cell, also play a role in the neuroinflammatory response in SMA. Astrocytes become reactive in the presence of neuronal damage and contribute to the production of inflammatory mediators. They also exhibit altered RNA processing due to SMN deficiency, which can affect their function and exacerbate neuroinflammation (Ceylan et al., 2020). The cross-talk between astrocytes and microglia further amplifies the inflammatory response, impacting motor neuron survival.

The systemic immune response is also implicated in SMA. Studies have shown that peripheral immune cells, such as macrophages and lymphocytes, are involved in the disease process. These cells can infiltrate the CNS and contribute to the inflammatory milieu. Additionally, systemic inflammation can exacerbate CNS inflammation, creating a feedback loop that worsens SMA pathology (Chen et al., 2020; Collén et al., 2022).

Therapeutic strategies targeting neuroinflammation are being explored to mitigate its effects on SMA progression. Anti-inflammatory treatments, such as corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs), have been investigated for their potential to reduce neuroinflammation and improve motor neuron survival. Additionally, more specific approaches targeting microglial activation or cytokine production are under development (Chiriboga et al., 2019). These strategies aim to break the cycle of inflammation and neuronal stress, thereby slowing disease progression.

The connection between RNA processing defects and neuroinflammation is also noteworthy. Mis-spliced RNAs resulting from SMN deficiency can lead to the production of aberrant proteins that trigger immune responses. This link highlights the importance of

addressing RNA processing defects to reduce cellular stress and inflammation. For example, enhancing SMN2 splicing not only increases functional SMN protein levels but also reduces the production of mis-spliced RNAs that could contribute to inflammation (Cartegni et al., 2006; Chen et al., 2020).

4.5 Disruption in mRNA Transport

The mechanisms of neuronal death and survival in spinal muscular atrophy (SMA) are multifaceted and intricately connected to the molecular and cellular deficiencies caused by SMN protein depletion. Understanding these mechanisms is crucial for developing effective therapeutic strategies. As mentioned above, disrupted assembly of snRNPs can lead to splicing defects which in turn can result in motor neuron death (Schmid and DiDonato, 2007; Burghes and Beattie, 2009). SMN protein also plays a vital role in mRNA transport and localization within motor neurons. This function is crucial for the maintenance and repair of axons, which are the long projections of neurons that transmit signals to muscles. Reduced SMN levels impair the transport of mRNA and other essential molecules along the axon, leading to axonal degeneration and synaptic dysfunction. These disruptions at the neuromuscular junction further contribute to motor neuron death (Monani et al., 2000; Mentis et al., 2011). In addition to impairing mRNA transport, SMN protein depletion affects the stability and function of the cytoskeleton within motor neurons. The cytoskeleton is responsible for maintaining cell shape, enabling intracellular transport, and supporting axonal growth and repair. When SMN levels are reduced, cytoskeletal dynamics are altered, resulting in further axonal damage and compromised synaptic transmission. This creates a detrimental feedback loop, where ongoing synaptic dysfunction exacerbates motor neuron degeneration.

5.0 TREATMENTS AND THEIR MECHANISMS

5.1 AAV Gene Therapy for SMA

The use of adeno-associated viruses (AAVs) as viral vectors has revolutionized gene therapy for spinal muscular atrophy (SMA), providing a means to deliver functional copies of the SMN1 gene directly to affected motor neurons. This approach has shown remarkable efficacy in both preclinical studies using mouse models and in human clinical trials.

In mouse models, AAV-mediated gene therapy has been instrumental in elucidating the mechanisms of SMA and testing therapeutic interventions. For instance, Foust et al. (2010) demonstrated that systemic delivery of AAV9 carrying the SMN1 gene significantly increased survival and motor function in SMA mouse models. The AAV9 vector was chosen for its ability to cross the blood-brain barrier and target motor neurons effectively. Treated mice exhibited improved motor function, increased muscle mass, and prolonged survival, highlighting the potential of AAV9-mediated gene delivery as a therapeutic strategy for SMA.

5.1.1 Onasemnogene Abeparvovec (Zolgensma)

Onasemnogene abeparvovec (Zolgensma) is one of the most promising AAV-based therapies by Novartis Gene Therapies for SMA. Zolgensma is an AAV vector-based gene therapy designed to deliver a functional copy of the SMN1 gene to patients' motor neurons, addressing the root cause of SMA by restoring SMN protein levels.

Zolgensma's efficacy has been demonstrated in multiple clinical trials, which have shown significant improvements in motor function and survival in SMA patients. In the pivotal phase 1 START trial, Zolgensma was administered to infants with SMA type 1, the most severe form of the disease. The results were remarkable, with treated infants achieving motor milestones that are typically unattainable for SMA type 1 patients, such as sitting unassisted and even standing or walking independently (Mendell et al., 2017). Moreover, the survival rates of treated infants were significantly higher compared to historical controls, with many patients remaining free from ventilatory support.

The long-term benefits of Zolgensma have also been evaluated, showing sustained improvements in motor function and continued survival benefits. In follow-up studies, patients treated with Zolgensma in infancy continued to demonstrate motor function improvements years after the initial treatment, suggesting that a single dose of this gene therapy can provide long-lasting benefits (Day et al., 2021). This highlights the potential of Zolgensma to alter the natural course of SMA and provide a near-normal life expectancy for patients.

However, the administration of Zolgensma is not without challenges. One significant concern is the potential for immune responses against the AAV vector used in the therapy. The immune system can recognize the viral vector as a foreign entity and mount an immune response, which may reduce the efficacy of the therapy or cause adverse effects. To mitigate this, patients are often pre-treated with corticosteroids to suppress the immune response during the critical period of gene transfer (Al-Zaidy et al., 2019). Despite these precautions, careful monitoring for liver enzyme elevations and other immune-related complications is necessary during and after treatment.

The cost of Zolgensma is another substantial consideration, as it is currently one of the most expensive treatments available, with a single dose priced at over \$2 million. The financial burden poses a challenge for healthcare systems and necessitates innovative funding mechanisms to ensure broad patient access (Pham et al., 2020).

Zolgensma's success has paved the way for further advancements in gene therapy for SMA and other genetic disorders. Ongoing research aims to improve vector design, enhance delivery methods, and address the limitations of current therapies. Additionally, combination therapies that include Zolgensma and other SMN-targeted treatments, such as nusinersen (see below), are being explored to maximize therapeutic benefits (Finkel et al., 2017).

5.2 SMN2 Splicing Modifiers: Nusinersen (Spinraza) and Risdiplam (Evrysdi)

SMN2 splicing modifiers, such as Nusinersen (Biogen) and Risdiplam (Genentech), represent critical advancements in the treatment of spinal muscular atrophy (SMA). These

therapies focus on modifying the splicing of the SMN2 gene to increase the production of functional SMN protein, thereby addressing the underlying cause of the disease.

Nusinersen was the first FDA-approved treatment for SMA and works by modifying the splicing of the SMN2 pre-mRNA to promote the inclusion of exon 7, which is normally excluded due to a splicing defect. By including exon 7, Nusinersen increases the production of full-length, functional SMN protein. Clinical trials have demonstrated efficacy of Nusinersen in improving motor function and survival across various types of SMA. In the pivotal ENDEAR trial, infants with SMA type 1 treated with Nusinersen showed significant improvements in motor milestones and overall survival compared to the control group (Finkel et al., 2017). Similarly, the CHERISH trial demonstrated the efficacy of Nusinersen in later-onset SMA patients, with treated children showing improvements in motor function scores and reduced disease progression (Mercuri et al., 2018).

Risdiplam is an orally administered small molecule that also targets the splicing of SMN2 pre-mRNA. It stabilizes the spliceosome complex, facilitating the inclusion of exon 7, thus increasing the levels of functional SMN protein. Risdiplam offers the advantage of oral administration, which can be more convenient compared to the intrathecal injections required for Nusinersen. The SUNFISH and FIREFISH trials have shown that Risdiplam significantly improves motor function in patients with SMA. In the FIREFISH trial, infants with SMA type 1 treated with Risdiplam exhibited substantial motor milestone achievements, such as sitting without support and improved survival (Baranello et al., 2021). The SUNFISH trial demonstrated that Risdiplam improved motor function in children and young adults with type 2 and 3 SMA (Mercuri et al., 2022).

These SMN2 splicing modifiers not only improve motor function and survival but also address some of the broader physiological aspects of SMA. For instance, improved respiratory function and reduced need for ventilatory support have been observed in patients treated with Nusinersen and Risdiplam. Additionally, these treatments have shown benefits in bulbar function, which affects swallowing and speech, further enhancing the quality of life for SMA patients (Chiriboga et al., 2020; Darras et al., 2019).

The safety profiles of Nusinersen and Risdiplam have been well-characterized in clinical trials. Common adverse events associated with Nusinersen include respiratory infections and post-lumbar puncture syndrome, whereas Risdiplam has been associated with mild to moderate gastrointestinal symptoms and fever (Finkel et al., 2017; Baranello et al., 2021). Continuous monitoring is essential to further understand the long-term safety and efficacy of these treatments.

6.0 Conclusion and Future Directions

As the understanding of Spinal Muscular Atrophy (SMA) continues to evolve, several promising avenues for future research and therapeutic development present themselves. While current treatments like gene therapy (Zolgensma) and SMN2 splicing modifiers (Nusinersen,

Risdiplam) have significantly improved patient outcomes, challenges remain in fully addressing the disease's complexity and heterogeneity.

Future research should focus on refining gene therapy strategies to address current limitations. While Onasemnogene Abeparvovec (Zolgensma) has demonstrated significant efficacy in treating SMA Type 1, optimizing vector delivery, reducing immunogenic responses, and increasing accessibility for different SMA types are crucial. Researchers should explore the use of alternative viral vectors or non-viral delivery methods to overcome immune barriers and enable repeated administrations if necessary. Additionally, investigating combination therapies that involve gene therapy and small molecule splicing modifiers could enhance therapeutic outcomes by targeting multiple aspects of SMA pathophysiology.

The role of modifier genes, such as NAIP and other genetic factors influencing disease severity, warrants further exploration. Identifying and understanding these genetic modifiers can lead to the development of personalized medicine approaches, where treatment regimens are tailored to the patient's specific genetic profile. Future studies should focus on the identification of additional modifier genes and their pathways, which could provide new targets for therapeutic intervention.

While current SMN2 splicing modifiers have shown promise, there is potential for developing next-generation small molecule therapies that offer greater efficacy, fewer side effects, and easier administration. Research should continue to identify compounds that can more effectively modulate splicing or stabilize the SMN protein, especially for patients with fewer copies of the SMN2 gene or those who do not respond optimally to current treatments.

Emerging research highlights the significance of cellular stress responses and neuroinflammation in SMA pathology. Future studies should explore therapies that target these pathways, such as antioxidants to mitigate oxidative stress or drugs that modulate the unfolded protein response (UPR). Investigating the role of neuroinflammation and developing anti-inflammatory treatments specifically designed for SMA could help slow disease progression and improve quality of life for patients.

Early diagnosis and intervention have proven critical in altering the disease course in SMA. However, more research is needed to understand the long-term outcomes of early treatment, particularly in gene therapy and splicing modifier contexts. Longitudinal studies should be conducted to assess the durability of these treatments, potential late-onset complications, and the overall impact on life expectancy and quality.

Despite significant advancements, gaps remain in our understanding of the precise mechanisms underlying motor neuron degeneration in SMA. Further research into the molecular and cellular mechanisms that contribute to SMA, including RNA processing defects, disrupted mRNA transport, and impaired autophagy, will be essential. This knowledge will not only aid in the development of new treatments but also enhance our ability to predict disease progression and response to therapy.

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The Effects of Offshoring on Political Party Dynamics in the U.S By Rohan Mehta

Abstract

The effects of globalization, specifically due to offshoring, have had profound effects on the American political mainstream. Previous studies on these effects have been conducted, including one before the Great Recession in Spain, where researchers found that Spanish voters punished incumbents for their stance on offshoring if they were counter to the voters' opinions. With another election cycle approaching in the U.S., and as economic issues take precedence in the American political mainstream, the question of the effects of offshoring on today's political scene becomes paramount. Our paper will use official election data from the New York Times as well as the Massachusetts Institute of Technology (MIT) Election Lab to collate information about recent trends in voting and see what, if any, relationships are present between offshoring and political party strength in the U.S. A positive correlation was found between levels of offshoring and Republican Party support, as well as a negative correlation between levels of offshoring by county and Democratic Party support. By exploring this essential question, we can hope to understand the strong emotions on both sides of the economic aisle that have shaped the political polarization in the U.S. and begin to bridge the gaps in knowledge between them.

Introduction

Three decades ago, states such as Ohio, North Carolina, and Iowa voted primarily Democratic, while New Jersey and New York were reliably Republican states; since then, these dynamics have been considered unrealistic by the majority of political analysts due to the states mentioned above being "safe" states for the opposite party. The state of political affairs in the United States has seen this marked shift in terms of voter share and party dynamics among the two main competing parties. Researchers attribute the main cause of these shifting party dynamics to globalization (World Trade Organization 2011), specifically the facet of offshoring, the concept of companies or governmental entities exporting jobs overseas in order to save costs and improve efficiency from a business perspective (NAPS 2016).

The use of offshoring is accepted in most modern American business circles but has seen a massive backlash among the American public, leading to its controversial debate. In fact, President Trump's victory in 2016 coincided with a 27% decline in the number of Republicans who felt favorably upon trade agreements (Cato Institute 2018). President Trump especially struck a chord with rural, working-class voters who felt left out by the burgeoning global economy and enjoyed hearing Trump's vision for an America that was once again a primarily manufacturing economy (Economic Policy Institute 2020); President Trump went on to secure what is considered the greatest upset in American political history in the 2016 election and won millions of votes in the 2020 election (USA Today 2018). In a Pew Research Center analysis conducted in 2018, shortly after the 2016 election cycle, about 64% of white, non-college graduated individuals voted for Donald Trump; in 2020, over 60% of rural voters voted for Trump (PRC and Marketwatch). The Center for Strategic International Studies (CSIS) conducted

a study on the decline of manufacturing jobs between 1990 and 2018, and the highest occurrence of job loss occurred in counties in the Central Midwest and the Southern Piedmont region—areas that voted for Trump heavily in 2016 and 2020 but voted for Obama in 2008 and 2012.

The number of college-educated Republican voters has declined in recent years (Reuters), while only 69% of Republicans without a college degree believe that free trade benefits Americans, down from 79% a few years earlier. Concurrently, since 1980, the number of Republicans in the high-income bracket who are usually urban voters has changed from a 10-point advantage among Republicans to a 60-point advantage for Democrats, a substantial swing (Cambridge Press 2023). These voting trends are not random; they are a pattern that is connected to the rise of globalization and offshoring as a norm in federal economic policy.

Previous studies on the possible connections between offshoring and its effects on political party dynamics have been conducted, such as one in the British Journal of Political Science discussing the impact of offshoring on regional party dynamics in Catalonia (Rickard 2021), which found that in a multiparty system, regardless of the party's policies, the dominant party was blamed by the majority of voters in the general election. A paper discussing the impact of trade liberalization on voting stances in the 107-109th US Congress from Texas A&M University is especially important, as it shows that Democrats and Republicans, despite being at odds economically, actually voted together on several free-trade bills under the Bush administration (Owen 2017). This means that the polarization of both parties on economic issues has a more recent origin. A comparative analysis of offshoring on European party dynamics was conducted in 2018 (Rommel and Walter 2018). One was conducted between the Great Recession and the Trump era, which is considered a shift in populist rhetoric, which fills in many of the gaps between 2009 and 2017 (Mansfield and Mutz 2013). A key finding from the paper was that President Trump cannot be solely attributed to the populist shift in economic rhetoric in the Republican Party; rather, the decline in faith in traditional institutions after the Great Recession fomented the Tea Party Movement, which set up for President Trump's eventual rise.

As such, we thought of conducting a similar analysis along the lines of finding connections between the effects of offshoring and political party dynamics in the U.S. using the most recent data, building off of the studies mentioned above; additionally, we hope to explore the specific regional trends that have occurred in this political transition, including the shift in urban voters toward the Democratic Party as well as the gain in blue-collar support among Republican politicians; these regional dynamics have become extremely pertinent to address for both politicians and for citizens to know about in order to make sense of modern American trends.

In modern American politics, it is known that the two main political parties have “flipped” their stances on economic policy following the Tea Party Movement in the Republican Party in the aftermath of the Great Recession compounded by the rise of President Donald Trump as a major political figure in the Republican Party; the Democratic Party has adopted the liberal market stance, whereas the Republican Party has become more isolationist and populist in their economic policy compared to recent decades. As such, I postulate that 1) areas with larger

levels of offshored jobs will intuitively vote Republican, and 2) areas with lower levels of offshored jobs and benefit from offshoring will vote Democrat.

Methodology

The methods outlined below will serve to test the hypothesis above. Offshoring is primarily defined as the practice of companies and/or governments moving jobs from the home nation (U.S.) to less developed countries to save costs or for other economic reasons (Brittanica). An offshoreable job is one which where the worker follows a set of predetermined rules and processes, making the reproducibility of the quality universal across a number of geographical locations. Many American companies saw this fact during the late 20th century when the majority of offshoring in the U.S. took place between 1958-2002 (CSIS). Using CSIS and U.S Census data, we will identify counties where the most manufacturing jobs were lost between 1958-2002 using the CSIS study; by doing so, it can be measured which counties offshoring has had the greatest impact. In addition, this data will provide insight into the counties that have grown the most in recent decades following the shift of the U.S. economy from a chiefly manufacturing economy to a services economy. Studies from the USDA also show how the second wave of offshoring coupled with the Great Recession in the early to late 2000s has also affected the dynamics of political parties in the U.S. The counties with the highest number of jobs lost to offshoring will be selected to measure the change in voter share from the 2000 to 2020 presidential elections. Using the official New York Times/Siena College Map in concurrence with Cornell's Dave Leip Election Data, which gives voting data by precinct over time and measures the change from the last election, our goal is to measure the change in official party voting share in these counties over the allotted period, both where offshoring was high and where economic growth was higher. By measuring the change in voter share, it can be observed whether there is a pattern emerging and what that pattern is if it exists.

Offshoring has been a prevalent practice among businesses since the early 1980s, becoming an economic cause for concern during the early 21st century (Barbe and Riker 2018). Many developed nations are adopting the various methods associated with it. In the long supply chain, the upstream productions are outsourced to cheap labor countries while downstream productions remain home, hiring legally unprotected contract foreign workers to perform more dangerous jobs. The reasons for this are primarily economic; in the game of comparative advantage, which is defined as a nation's ability to supply a good that the other person cannot get at a lower cost (Cato Institute 2023), developing nations such as China and India have a larger youth population as well as lower wages to compete with U.S. labor standards and their aging domestic population, making these countries prime investment targets for American companies (Jensen and Kletzer 2008). In addition, it is widely accepted that low-skill, blue-collar jobs are at a higher risk of being offshored since many jobs in the field follow a list of rules and procedures that can be applied to a number of geographical locations; white-collar industries such as healthcare and information technology are relatively safer (Harper 2003). These jobs are local and need to be proximal to the customer in order for the services to be performed, so

offshorability is impractical in many settings; in fact, white-collar workers tend to benefit from offshoring practices (Riker 2018).

Offshoring in the U.S has been one of the most divisive issues in modern political thought; the first signs of the fracture among political parties on it were evident in an analysis of congressional talking points from 2001-2005, where Republicans predominantly talked in favor of trade liberalization, which inadvertently led to offshoring, and Democrats advocated for a more protectionist stance, even if both agreed on many trade liberalization bills such as the North American Free Trade Agreement (NAFTA), the Trans-Pacific Partnership (TPP), and many others (Owen 2017). This marks an interesting change from classical American conservatism, which calls for free-market economics as well as trade liberalization; many Republican administrations, such as Reagan and both Bushes, were firm believers in them. After conducting a pan-European study, researchers concluded that parties that are in favor of more liberal-market policies are assumed to be pro-offshoring and receive less support from those with offshorable jobs, and parties with more isolationist policies are assumed to be against trade liberalization and offshoring and receive more support from those with offshorable jobs (Rommel and Walter 2018). In the U.S., studies conducted after the Great Recession showed that these fractures began to rupture even further, as many Americans adopted a more protectionist stance after the Great Recession of 2007-2009 (Mansfield, Mutz, and Brackbill 2016). The researchers above attribute the main cause of this shifting stance to the general distrust that many Americans felt toward the free market system, in addition to the failure of reputable financial institutions such as the Federal Reserve to avert such a crisis.

The Great Recession combined with the post-industrial economy shifted political party dynamics, where a retroactive study concluded that Donald Trump was responsible for the right-wing populist shift within the Republican Party (Arfin and Stockemer 2023). Populism is defined as “a political approach that strives to appeal to ordinary people who feel that their concerns are disregarded by established elite groups” (Oxford Languages). Interestingly, many political scientists also emphasize the importance of “populism's adversarial identity is claimed by a representative leader, who mobilizes the media to convince the audience that he embodies the people's many forms of discontent against traditional parties' spineless mainstreamism”—a “striking parallel to many populist leaders of today, including President Trump and Jeremy Corbyn (Urbanati 2019). Research shows that a primary cause of President Trump's unparalleled dominance within his own party during his rise in 2016 was economic discontent among certain groups, especially in locations where Chinese imports are prevalent; these regions rejected centrist legislators for those with a more protectionist stance (David Autor *et. al* 2017). Additionally, a deep analysis of the voters behind Trump's astronomical rise attributes it to 1) the Tea Party Movement, which led to the Republican Party's susceptibility toward right-wing populism, and 2) the general distrust among large swaths of the American public of financial and cultural elites (Lempinen 2020).

Researchers have also noted that there has been a pronounced shift in the blue-collar demographic of voters from primarily Democratic voters toward the Republican Party (Newman

and Skocpol 2023). This is especially interesting, as according to the same study, up to 60% of American union workers voted Democratic in previous elections, indicating that a mass exodus has occurred within the Democratic Party. In 2020, President Trump did lose the election, but actually expanded his margins in rural counties; the researchers state that the sole variable leading to President Biden's victory was the shift in margins among primarily urban voters (Albrecht 2022). However, studies have shown that during the same period, urban, educated voters shifted primarily toward the Democratic Party, virtually erasing the "country club" Republican vote (Brown and Mettler 2023). What has been found is that during the period of mass offshoring of blue-collar jobs from the U.S. to other, developing nations coincides with the change in political party dynamics, with white-collar, wealthy individuals flocking to the Democratic Party, while blue-collar, working-class workers flocked to the Republican Party. In addition, other developing nations where jobs have been previously offshore have had a profound influence in the areas where President Trump won by large margins in key states. The reason why this is essential to understanding the connections between offshoring and political party dynamics is that for most of the 20th century, voters had what is known as "cross-cutting affiliations," where both Democrats and Republicans, despite having opposing policy positions attempted to work things out and come to a collective consensus on local matters. However, in recent decades, the decay of rural institutions such as union halls and the Church has led to the widespread polarization present in American politics; researchers attribute the main cause of this decay to the rapid offshoring of blue-collar jobs in rural areas (Mettler 2022). To conclude, there are some blatant connections between offshoring and the shift in political party dynamics that have taken center-stage over the past three decades, and while numerous previous studies have been conducted, we hope to find the explicit effects of offshoring on each political party and the changes within them over 21st-century American federal elections.

Theoretical Framework

My paper draws upon modern American political theory as well as macroeconomic theories such as supply shocks, labor economics, and exchange rates to effectively formulate the arguments that will be used to test the hypothesis given below and to see if there is a relationship between the effects of offshoring and political party dynamics in the U.S.

Part 1: Economic Theory Behind Offshoring

Offshoring has recently become salient in American politics and elsewhere with a twist. In 1950, the global production of raw steel had the bulk of it sourced from the U.S. at around 47% (World Steel 2007), with traditional Rust Belt states such as Pennsylvania, Ohio, and Kentucky forming the bulk of the U.S. steel exports. At the time, many developing countries still did not have independence in Latin America, Africa, and Asia. Europe was still recovering from WWII and did not have the functional capacity that the U.S. did, such as factories, and strong business institutions, and what money was present was being poured into post-war rebuilding rather than the manufacturing industries of European nations. The American manufacturing

monolith faced little competition post WWII, and American companies enjoyed a large and highly skilled domestic labor pool.

A few decades before, U.S. labor laws were quite lenient. The 40-hour work week did not exist, and worker safety standards through the Occupational Safety and Health Administration (OSHA) did not exist until 1934, allowing companies to get away with skirting labor standards. Many free-market Republicans advocated in Congress and in the White House for a laissez-faire economy, which allowed for little government intervention in economic affairs (University of Virginia Miller Center 2024). That changed in the 1920s and 1930s when President Roosevelt began to pass a number of pro-worker laws such as the Wagner Act of 1935 (private workers can organize unions), the Fair Labor Standards Act of 1938 (establishes a federal minimum wage), and many other New Deal-esque provisions (e.g. the establishment of the TVA and FDIC). These laws made working in blue-collar occupations an advantage for many Americans, as a college degree was not necessary and certain working conditions and benefits were guaranteed. From this point forward, a two-pronged attack on the safety of blue-collar jobs in the U.S. occurred: 1) the U.S began to shift towards a predominantly services economy (e.g., restaurants, hotels, IT, and healthcare), and 2) the former European colonies began to assert themselves economically on the global stage as they gained independence and became sovereign states.

Up until this point, the U.S. economy was known to export goods such as steel, iron, coal, and other raw and polished goods across the world, with its manufacturing industry being a key asset in WWII (Department of Defense 2020). However, during this time many service industries began to make their way into the economy; many reasons contributed to the change, including the passing of the G.I Bill, which allowed the millions of American soldiers coming home after WWII to enroll in college. With the initiation of the Cold War, the American education system placed great emphasis on math and science jobs to beat the USSR in the Space Race, passing the National Defense Education Act (NDEA) in 1958, which changed the way Americans view college (SUNY Buffalo State University 2021). The Republican-majority U.S Congress under the Truman administration on the rights of U.S blue-collar workers by passing the Taft-Hartley Act of 1947, which placed limitations on the power of unions to organize, a law which is still in place today. The heavily Republican Congress under Truman passed said law and other anti-union bills with Truman's veto.

Over the next decade, white-collar jobs began to take over the job market; in 1970, blue-collar jobs made a large plurality at 40% and were the dominant type of worker historically; today that number is about 15%. Easy access to college education coupled with the growth of American industries outside traditional blue-collar jobs such as healthcare, information technology (IT), and others shadowed those of a manufacturing nature like General Motors and U.S. Steel. At the same time, developing nations across the globe began to move into the post-colonial economy. The first wave of deindustrialization, or the concept of Western nations outsourcing traditional blue-collar jobs to developing nations (International Monetary Fund 1997), happened in the 1970s and 1980s with primarily Asian nations. The Economic Policy

Institute states that a primary cause of deindustrialization for low-level blue-collar jobs in the U.S. to China, for example, was the fact that the Chinese government did not have stringent labor standards at the time and did not enforce them.

This point is essential since a large amount of operating costs in companies come from the cost of labor; the labor protections passed in the U.S. contributed to the rising costs of labor domestically, meaning that American companies looked favorably on the lack of these protections abroad. The liberalization of many now-robust economies such as China and India, with their burgeoning populations, allowed U.S. companies to shift production to these nations in order to save on labor costs. Since laborers did not have the rights guaranteed by U.S. labor laws elsewhere, companies were not subject to legal scrutiny; as a result, GM and other auto companies in the 1980s moved their main manufacturing plants from Detroit to China and other developing countries. In addition, blue-collar jobs usually had a set number of rules and processes that can be applied to a number of geographical settings, unlike white-collar jobs, which performed services within a certain area and needed to stay in the given area to perform them; a doctor cannot perform surgery in America while living in China. However, steel manufactured in China is the same as in the U.S., meaning that traditional blue-collar jobs could be shipped abroad for lower prices and higher efficiency. This had an astounding effect on the population size of the Detroit metropolitan area, which went from 1,849, 568 in 1995 to 713,777 in 2010, the largest decline of any major U.S. city in that time period.

At the same time, high-skilled blue-collar jobs emigrated to countries such as Japan and South Korea, where policies such as the *keiretsu*, where companies made alliances with suppliers and bought shares in either company (Harvard Business Review 2013), and heavy government intervention from the 1950s to 1970s helped the emergence of technology conglomerates such as Sony in Japan and Samsung in South Korea to dominate the tech landscape, as well as Taiwan becoming a major player in the semiconductor industry. These two factors created a general decline in the manufacturing sector in the U.S. economy, as companies shifted their production to other countries and as working Americans joined the white-collar workforce and left the blue-collar one.

The second wave of these industries vanishing from the U.S. economy occurred in the 1990s to the early 2010s, when the era of free-trade agreements as well as the Great Recession permanently caused a change in the working demographics of Americans. In the Bush and Clinton administrations, great effort was made to inculcate nations into the American economic fold that were previously under Soviet influence. Trade deals such as the Trans-Pacific Partnership (TPP) and NAFTA were signed. The North American Free Trade Agreement was signed into effect on January 1, 1994, and since then has been a controversial act; President Trump had the repeal of NAFTA as a main argument of his in the 2016 election. NAFTA led to a decline of over 350,000 auto jobs in the past 30 years and solidified the practice of businesses moving to more cost-effective nations such as Mexico for industrial purposes. Many automobile manufacturers as well as industrial plants shifted to Mexico, in a concept known as near-shoring, where offshoring happens within a geographically proximal region. While these trends

continued, the blue-collar job market took another hit in the Great Recession of 2007-2009, when the Hamilton Project concluded that middle-skill, blue-collar workers were the most hit by the economic disaster. Seven years later, President Trump ran on a populist economic platform and won.

Part 2: Political Party Dynamics

According to a recent Statista poll conducted in July of 2023, over 35% of voters listed either inflation or other economic issues as the most important issue going into the 2024 election. Despite other pressing issues on the ballot such as climate change, social issues, and recently COVID-19, the economy has been a primary concern for American voters since the American Revolution, given the reasons why the U.S. emerged as a country in the first place (i.e., steep British taxation without representation). While both parties' stances on social issues have shifted over the past several decades, their economic positions have not. Since the presidency of Franklin Delano Roosevelt (FDR), the Democratic Party has espoused primarily economic progressive policies, with some examples being the protection of labor unions, the favoring of welfare systems such as Medicare and Obamacare, and placing checks on large corporations in an effort to curb corruption. The Republican Party was known to be the "party of the rich," according to the Cambridge University Press. Rich and wealthy industrialists such as Andrew Carnegie and Cornelius Vanderbilt were known friends of the Republican Party.

That began to change in the late 1970s to the late 1980s when President Ronald Reagan took advantage of Nixon's Southern Strategy. The Southern Strategy was an idea created by President Richard Nixon in order to shift the balance of power in the South to the Republicans. The Democratic administrations of Kennedy and Johnson led to sweeping civil rights reforms and protections for civil liberties, such as Roe v. Wade. Many cultural conservatives, especially in the South, did not appreciate this, and Ronald Reagan successfully inculcated many previously Democratic voters into the Republican fold for rising sociocultural resentment. For example, many counties in Kentucky voted exclusively Democrat for centuries up until that point; in fact, Muhlenberg County voted Republican for the first time in 144 years in 2020. Ohio and Indiana voted for President Obama in 2008 and 2012, and Indiana did so in 2008. These states now vote primarily Republican.

There seems to be mounting evidence that there is a shift in economic stances among parties that are influenced by voter sentiment. When asked why rural voters turned their backs on the Democratic Party, a primary answer was their handling of the economy and how the party was partially responsible for the destruction of manufacturing jobs as well as agricultural ones in many rural communities. In Tennessee, New Deal-era organizations such as the Tennessee Valley Authority (TVA) have lost funding, and the institutions that the Democratic Party put up to grow rural industry were lost. Democrats were also known to protect unions and their right to assemble; over 22% of American workers were in a union in 1983, a large percentage of blue-collar workers. In 2023, that number has declined to less than 10% of all American workers. Many rural voters feel that the Democratic Party has failed them time and time again, from

deindustrialization to NAFTA to the Great Recession. These events have led to a dynamic shift in rural voting patterns toward the Republican Party, and I argue that this is not a coincidence. Simultaneously, Democrats have received more wealthy, suburban voters than in years past due to the Republican Party's trend toward right-wing populism. From this, I argue that the hypothesis I make is two-fold.

H1: As a result of deindustrialization and the offshoring of jobs, counties with high levels of offshored jobs will trend Republican.

H2: Areas that have lower levels of offshored jobs will trend primarily Democrat.

A key note is that urban in this context does not apply to large metropolitan areas such as Chicago, New York, Miami, and other large U.S. cities; rather, counties with one large small town are considered urban. Using this framework, I will use an empirical approach to test these hypotheses and see if there are some significant correlations between offshoring and political party dynamics in the U.S.

Methodology

The methodology for the experiment is as follows: The goal of the study is to find possible relationships between the effects of offshoring on political party dynamics over the past two decades of presidential elections at the county level since our hypothesis predicts that the Republican voter share change is most evident in the 21st century. In order to do so, I chose to use Dave Leip's Cornell Election Data, which compares party voter share by county over the past 6 presidential election cycles. In order to measure if offshoring has a correlation with political party dynamics, I chose to test the differences between counties with high levels of offshoring compared to lower levels of offshoring. A county with higher levels of offshoring is defined as a county where according to official CSIS data, the level of manufacturing is Low, where low is the official subjective measure that the CSIS data set uses. Counties with lower levels of offshoring are the opposite of the definition above. Using Cornell data, the goal will be to see how voter trends have changed over time in these selected counties; the Cornell data set has data from 1972-2020, while the CSIS data set has it from 1990-2018, with both sets solely having information at the county level.

The counties will be matched on both data sets, and temporal trend analysis using longitudinal data will be used with a regional emphasis on Appalachia and New England. If in the counties defined by Definition 1 show a Republican trend of more than 10% in the change of voter share in the direction of the GOP over the past 4 elections, then the conclusion can be drawn that offshoring has affected voter share and in turn, political party dynamics. In addition, if in counties with low levels of offshoring the swing toward the Democratic Party in voter percentage over the past election cycles is more than 10%, then the effect is also true. If the opposite in both cases is true, a conclusion can be drawn that there is not a statistically significant relationship between offshoring and political party dynamics in the U.S.

Results and Analyses

The statistical analysis was conducted in the Midwestern and Eastern regions of the U.S, with over 28 counties in six states analyzed; Pennsylvania, New York, Indiana, Wisconsin, Michigan, and North Carolina. The classification of each county of rural vs. urban was found using each state government's official methodology, since Indiana classifies counties into three strata, while Pennsylvania adheres to the official U.S Census classifications. The CSIS data set structured the counties by the level of manufacturing jobs, an arbitrary and subjective classification of Low, Medium, or High. The data also indicates that the job loss was due to offshoring, allowing the set to be used to measure a decline in offshore levels. In the 2008 election, out of the 28 counties selected, 60.71% of the counties voted Republican, and 39.29% voted Democratic. In 2020, 89.29% of the counties were won by Republicans, while only 10.71% voted Democratic, a marked change in just three election cycles. 4 out of the 28 counties had election results under a margin of <5%, a measure for close elections on the county level according to the U.S. government. In 2008, two of these counties (Richmond and Lake) voted Democratic. The percentages were 50.3-48.8% for Lake and 49.5-48.6% for Richmond. In 2020, Richmond was won by the Republican Party 57-42.2%, as was Lake in 56-42.4%. The third county, Sheboygan, went Republican in 2008, but expanded its margins by over 8%. The Republican voter share increased in all 28 counties, including the 3 counties in 2020 won by President Biden.

Hypotheses 1 and 2 are disproved by the data; regardless of the level of manufacturing jobs in 1990 and in 2018, all 28 counties trended Republican. In counties that had Medium levels in 1990 and Low in 2018, the margins increased the most, in places such as over 17% in Trumbull County, Ohio. In the two counties that shifted up in the number of manufacturing jobs, indicating that offshoring did not affect these areas as much in Manitowoc and Madison Counties, the Republican voter share increased, countering the original hypothesis that areas with lower offshore levels will trend Democratic. An interesting county is Davidson County in North Carolina, where the manufacturing level went from low to high, indicating that offshoring had the opposite effect on this county. However, the Republican voter share margin went from 66.2% to 73% from 2008 to 2020, a substantial increase that disproves the contrapositive of H1. Regardless of the decline or increase in offshore levels the Republican Party has proven to be dominant in the 28 counties analyzed, and offshoring levels, regardless of strata, do not contribute to the GOP's vast margins. After analyzing the voting share and patterns between 2008 and 2020, 11 out of the 28 counties qualified for the >10% swing in favor of the Republican Party, while the other 17 did not. However, it is important to mention that the vast majority of these counties are rural, and 4 of the counties only swung Democratic in either election; the highest swing was 4 points, which is statistically inconsequential. Possible theories could be that 1) the 10 counties with medium and high levels of manufacturing in 2018 could not have been affected by offshoring and developed local manufacturing hubs in their county; 2) the sociotropic effects of counties around one county that do not feel the brunt of offshoring may be inclined to vote Republican due to these effects. The majority of counties, regardless of offshoring level, swung heavily toward the Republican Party, albeit to varying degrees.

Conclusions

The analysis above shows that regardless of offshoring level and manufacturing level, the Republican Party has won in 25 out of the 28 counties and expanded their margins in all 28 counties. The findings can help to explain why counties in many rural areas, which were once solidly Democrat have now swung Republican. Future research should expand on these findings, as well as test how many counties adapted to the effects of the offshoring. The CSIS study mentioned that the areas around Boston in New England were also heavily affected, but recovered quickly due to the immigration domestically and internationally of white-collar, highly-skilled workers to the region. The effects of offshoring on metropolitan areas (e.g., Boston, Chicago, New York) are definitely an area that could be looked into. Hopefully, using the knowledge gained above, we can gain insight into an important political trend that has shaped the present American climate and will have a substantial impact on the 2024 federal and state elections. The findings also demonstrate the importance of economic factors on political outcomes (offshoring on politics) and how both influence each other.

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The Effect of Waste Water on Red Onion (*Allium Cepa*) Root Growth By Abhitha Kumar

Abstract

Water scarcity has prompted the exploration of alternative water sources, including wastewater, for agricultural purposes. This study investigates the effect of various wastewater sources on the root growth of red onion (*Allium cepa*). Onion bulbs were exposed to cooking, air conditioning (AC), washing machines, swimming pool wastewater, and clean water (control) over 10 days. Root growth measurements were taken daily to compare the effects of each sample. Cooking wastewater consistently promoted the greatest root growth during the early stages, while swimming pool and AC wastewater exhibited the least growth. By the end of the experiment, control plants outperformed all others, indicating that long-term exposure to clean water fosters better growth. Phytotoxicity analysis revealed that swimming pool wastewater showed the highest root toxicity (16.625%) while washing machine wastewater had the lowest (8.37%). The findings highlight the potential of certain wastewater types, such as cooking wastewater, to support early plant development, but also the limitations of using untreated wastewater over prolonged periods. This study underscores the importance of assessing wastewater quality before its use in agriculture to ensure sustainable crop growth.

Keywords: *Allium cepa*, domestic wastewater, Phytotoxicity, swimming pool wastewater

Introduction

Good water quality is critical to everyone's well-being and health. Water quality is critical for human survival, animal welfare, the ecosystem, agriculture, and social and economic growth. Worldwide, more than 80% of household wastewater is dumped into waterways without getting enough treatment. Numerous contaminants can be found in domestic wastewater, such as fertilizers, oil and grease, detergents, bio waste, household chemicals, heavy metals, salts, pathogens, pharmaceutical ingredients, soluble and particulate organic matter, and cooking and bathing waste. By increasing biological oxygen demand (BOD) and chemical oxygen demand (COD), pollutants change the pH, hardness, inorganic component content, and pathogen load of water (Agarwal et al., 2022). Domestic wastewater that has not been treated poses a risk to aquatic and marine life, hinders crop productivity, and contributes to several diseases that water carries.

Wastewater is water that is discarded from households, workplaces, and industries. It was formerly known as sewage and originated from washing machines, toilets, sinks, showers, and industrial activities.

Types of wastewater	Sources
Greywater	Showers, baths, hand basins, washing machines, laundry troughs
Blackwater	Toilet units, dishwashing units, and kitchen sinks
Sewage	A combination of greywater, blackwater, and trade waste
Industrial wastewater	This includes all wastewater except sewage. Industrial wastewater varies in quality and quantity depending on the industry type or business size.

Table 1: Types of Wastewaters (Akcin et al., 2005)

Domestic wastewater includes waste from the kitchen, shower, washbasin, toilet, and laundry that is generated from human activity in a home.

The average strength of residential wastewater is determined by per capita water consumption, habits, diet, standard of living, and household lifestyle. Wastewater varies daily, hourly, and seasonally in strength and composition. The fundamental reason is that water usage varies in families. Compared to underdeveloped countries, households in developed countries consume more water.

Domestic wastewater typically has a solid content of around 0.1% and is physically described as having a musty odor and a grey color (Al-Mawla et al., 2023). The solid material comprises feces, food fragments, paper towels, oil, grease, detergent, salts, metals, soaps, sand, and grit. Physically, sludge formations and anaerobic conditions can arise from releasing suspended materials In the environment of Reception.

Chemically, domestic wastewater is composed of organic (70%) and inorganic (30%) chemicals and different gases. The main components of organic compounds are proteins (65%), lipids (10%), and carbohydrates (25%), and the people's diet influences these proportions. Inorganic components include heavy metals, phosphorus, nitrogen, pH, sulphur, chlorides, alkalinity, and toxic substances. However, ~ 85-90% of the total inorganic and ~ 55-60% of the total organic components are dissolved in wastewater because they comprise more dissolved solids than suspended.

Accelerated urbanization and higher living standards have resulted in large volumes of wastewater, making disposal a major concern. Additionally, the lack of high-quality groundwater for farming has forced farmers to use these wastewater. Although the wastewater has all the nutrients needed for plants to develop, it also contains a lot of heavy metals, which are harmful to plants and humans. The chemical composition and characteristics of wastewater, which vary based on sources like population density, industrial activities, and agricultural practices, significantly impact plant growth either positively or negatively (ul Ain et al., 2019). Studies suggest that using wastewater in agriculture can enhance crop yields and growth. However, the pollution stress from wastewater, especially at higher concentrations, has been found to reduce seedling fresh weight, negatively affecting crop development. Additionally, root crops such as potatoes, carrots, turnips, and radishes generally absorb fewer pollutants compared to leafy

vegetables like spinach, fenugreek, and mint, which are more prone to contamination due to greater surface area exposure (ul Ain et al., 2019). The use of treated and untreated wastewater for irrigation increased the levels of Cd, Pb, and Ni in the edible section of vegetables, posing a long-term health risk (Balkhair et al., 2016).

According to Hussain et al. (2002), the predominance of domestic wastewater may result in high salinity levels that may affect the yield of salt-sensitive crops. Research has also shown that different plants and species within a genus have different rates of pollution uptake and accumulation.

Allium cepa is a herbaceous, perennial plant (typically produced as an annual or biannual in cultivation) with 4 - 10 leaves approximately 30 cm long and a blooming scape that can reach 100 cm tall from an underground bulb. In due course, the plant divides and forms a cluster of plants (Flora of China, 1994). The onion was one of the first plants to be grown for food and medicine (Phillips. R. & Foy. N. (1990). It is one of the most extensively produced and farmed plants on Earth. It is mostly grown for its edible bulb but also for its leaves. The onion, or *Allium cepa L.*, has been a widely grown and consumed vegetable for 4,000 years. The genus Allium is most diversified in the Mediterranean region, while China and India produce the most onions globally. The unique flavor and pungency of onions are attributed to a range of sulphur compounds, the composition of which changes according to the variety, production season, and storage life (Lawande, K. E. (2012). Given the diverse impacts of effluents, the current study aimed to assess the influence of domestic wastewater on *Allium Cepa* growth.

Methodology

Materials

1. Plant sample used: 15 Medium-sized red onions.
2. 15 Wide-mouthed Paper cups (2.75 cm radius)
3. Water samples used: swimming pool wastewater, cooking wastewater, AC outlet wastewater, washing machine wastewater, and tap water (control).
4. Thread & Ruler
5. Measuring cylinder (100ml)
6. Kitchen Knife

Sample Collection

Five clean plastic bottles of 500 ml were used for the wastewater sample collection. Each bottle was labeled with essential information, including the type of wastewater (viz., Swimming pool wastewater, cooking wastewater, AC outlet wastewater, washing machine wastewater, and tap water (control)), date, time, and location. All the samples were stored at room temperature.

Procedure

The Red onions (2 Kg) used in this experiment were bought online from the Amazon website on the 1st of January 2024, and the experiment was initiated on the 3rd of January 2024. Fifteen medium-sized onion bulbs were selected for the experiment.

The dry roots at the base of the onion were gently scraped, leaving a damp, exposed area. Five paper cups (labeled), each with a radius of 2.75cm, were filled with approximately $\frac{1}{4}$ cup or 60ml of wastewater, respectively. The onion bulbs were carefully placed on each cup so that the stem portion of the bulb (basal part) just touched the water. The entire experiment was run in triplicates to avoid errors (Set of 3 for each wastewater sample). The growth of the roots was monitored for ten days, and root length was measured daily using a centimeter scale. The data was tabulated in an Excel spreadsheet.



Fig 1:Experimental Setup

Formula & Calculation

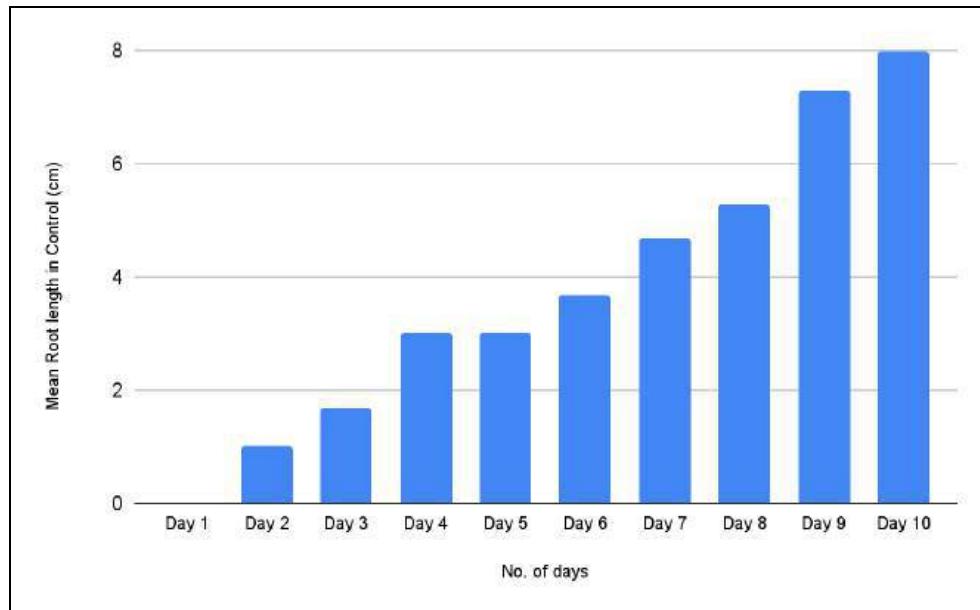
- % Phytotoxicity for the root of the onion bulb was calculated by the following formula given by **Chou and Lin (1976)**.

$$\% \text{ Phytotoxicity of Root} = \frac{\text{Root length of control} - \text{Root length of treatment}}{\text{Root length of control}} \times 100$$

Results and Discussion

Root Growth (cm)										
Sample	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Control A	0	0	0	3	3	4	5	6	7	7
Control B	0	1	2	2	2	3	4	5	7	7
Control C	0	2	3	4	4	4	5	5	7.5	8
Mean	0	1	1.67	3	3	3.67	4.67	5.33	7.3	8.0

Table 2: Root growth of *Allium Cepa* in the control water sample

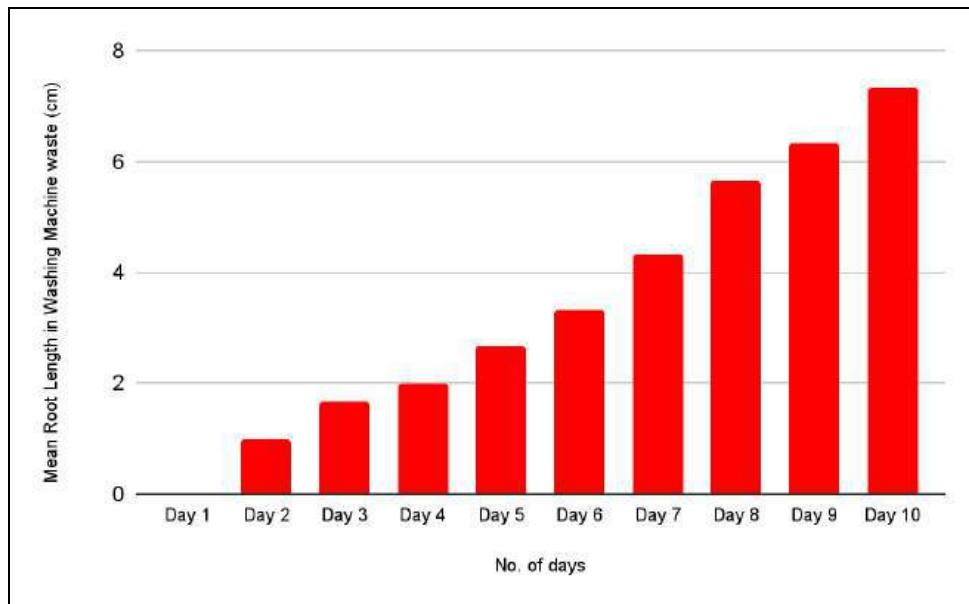


Graph 1: Mean root length of *Allium Cepa* in the control water sample

The composition of tap water can vary significantly depending on its source, treatment processes, and local environmental factors. However, tap water typically contains various dissolved minerals (Calcium, Magnesium, Sodium, Potassium, etc.), gases (Oxygen and carbon dioxide), trace elements (Iron, copper, Zinc, etc.), organic compounds, and microorganisms. From Table 2, it can be seen that the root growth was initiated on day 2. The onion root length has grown from 1cm to 8cm over ten days. The growth of the onion root was exponential during the entire study session. This could be likely due to the nutrients present in the tap water, thereby providing all the essential nutrients required for the growth of the onion plant.

Root Growth (cm)										
Sample	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Washing A	0	0	1	2	3	3	4	6	6	7
Washing B	0	1	2	2	2	3	4	5	6	7
Washing C	0	2	2	2	3	4	5	6	7	8
Mean	0	1	1.66	2	2.66	3.33	4.33	5.66	6.33	7.33

Table 3: Root growth of *Allium Cepa* in Washing Machine Wastewater

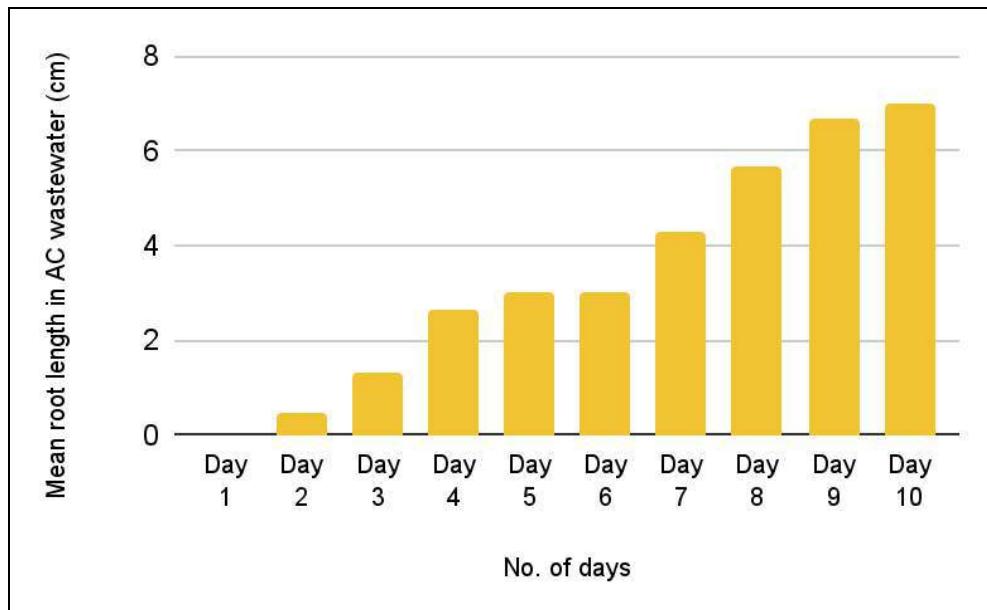


Graph 2: Mean Root Length of *Allium Cepa* in Washing Machine Wastewater

Soap, detergents, and surfactants are all present in the wastewater from washing machines and laundry. Soaps contain salts, fats, and oils of sodium and potassium treated chemically with a strong alkali (**Jegathambal et al., 2021**). From Table 3, it can be seen that the root growth was initiated on day 2. The onion root length had increased from 1.0 cm to 7.33 cm over ten days. Graph 2 shows that the plants exposed to washing machine wastewater had preferably a good root length growth compared to the control. The detergents and strong alkali salts (Sodium and potassium) present in the water sample could have acted as nutrients for the plant growth.

Root Growth (cm)										
Sample	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Ac A	0	0	0	2	2	2	3	4	6	7
Ac B	0	1.5	2	3	3	3	5	6	7	7
Ac C	0	0	2	3	4	4	5	7	7	7
Mean	0	0.5	1.33	2.66	3	3	4.33	5.66	6.66	7

Table 4: Root growth of *Allium Cepa* in AC outlet wastewater

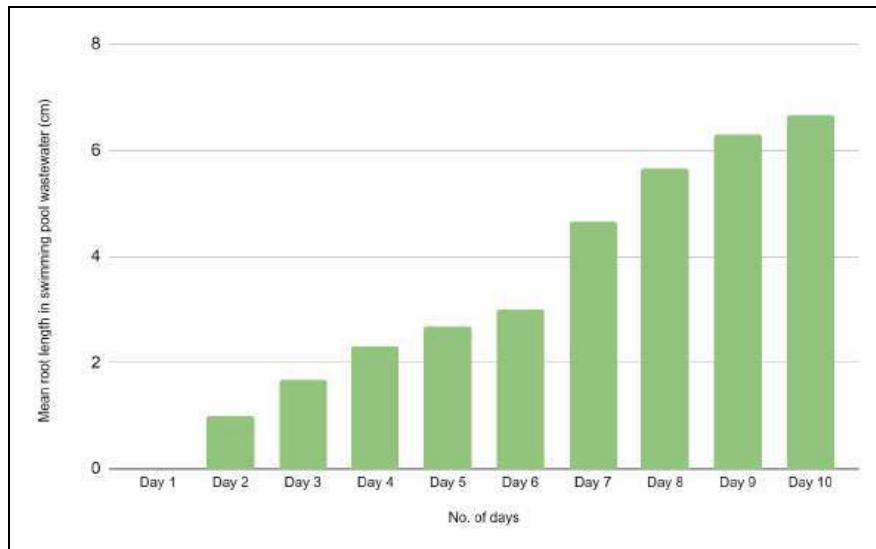


Graph 3: Mean Root Length of *Allium Cepa* in AC Outlet Wastewater

Condensate from air conditioners or AC is essentially distilled water and is low in mineral content (calcium, magnesium, and potassium). The onion root length had increased from 0.5 cm to 7cm over ten days. Graph 3 shows that the plants exposed to AC outlet wastewater had a slower growth rate of the roots than the control. This could probably be because the AC water had a lower concentration of all the essential nutrients required for the growth of the plants.

Root Growth (cm)										
Sample	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Swimming pool	0	0	2	2	2	2	4	5	6	6
Swimming pool	0	2	0	3	3	3	5	6	6	6
Swimming pool	0	3	1	2	3	4	5	6	7	8
Mean	0	1.66	1	2.33	2.66	3	4.66	5.667	6.33	6.67

Table 5: Root growth of *Allium Cepa* in swimming pool wastewater

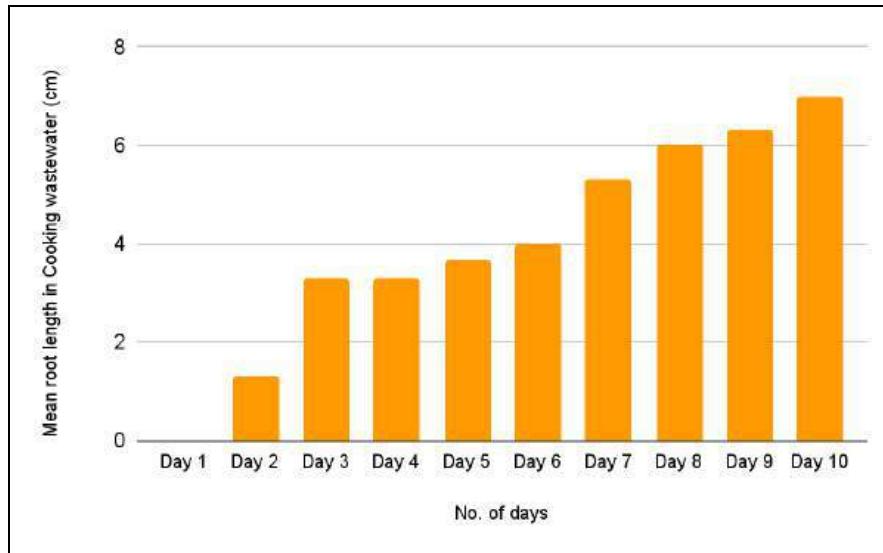


Graph 4: Mean Root length of *Allium Cepa* in swimming pool wastewater

There are a lot of suspended solids in the swimming pool wastewater, and the backwash has a high concentration of chlorine compounds (Reißmann, 2005). The onion root length had increased from 1.6 cm to 6.67cm over ten days. From graph 4. it can be seen that the initial growth was rapid; however, the root growth was restricted over a period of time. This could be due to the high chlorine content of the swimming pool water, which could have restricted the root growth of the onion plant.

Root Growth (cm)										
Sample	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Cooking A	0	4	4	4	4	4	6	7	7	8
Cooking B	0	0	3	3	4	4	5	6	6	6
Cooking C	0	0	3	3	3	4	5	5	6	7
Mean	0	1.33	3.33	3.33	3.66	4	5.33	6	6.33	7

Table 6: Root growth of *Allium Cepa* in cooking wastewater

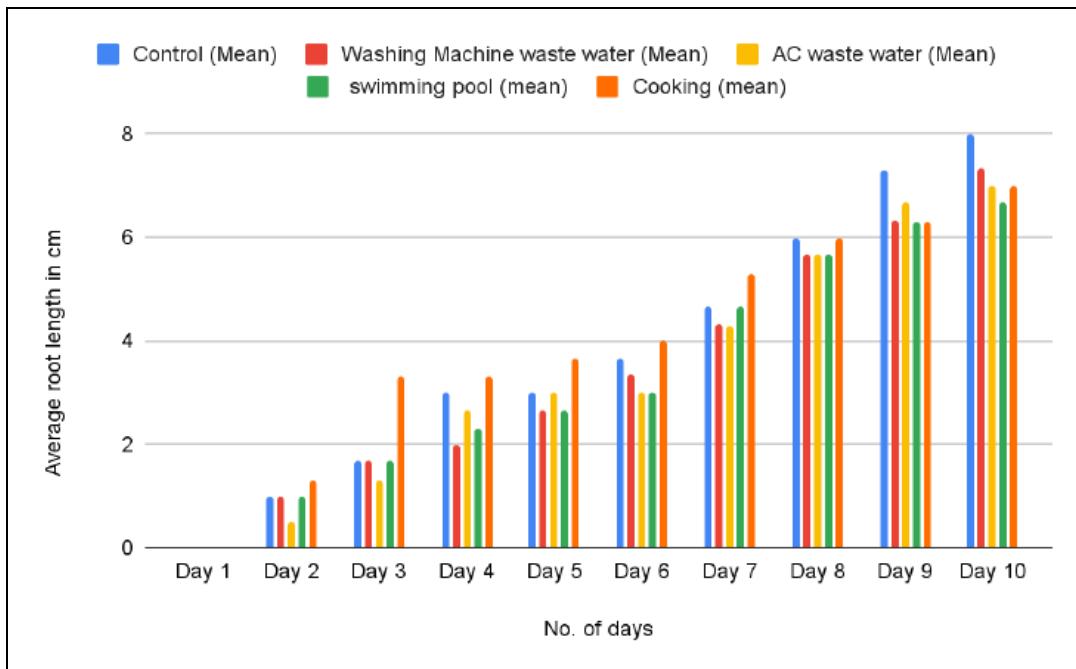


Graph 5: Mean Root Length of *Allium Cepa* in Cooking Wastewater

The composition of cooking wastewater can vary depending on factors such as the types of food prepared, cooking methods used, and kitchen practices. However, typical wastewater comprises Organic matter, Nutrients like Nitrogen, Phosphorus, and Potassium, Grease and Oil, Chemical Additives such as detergents, sanitizers, cleaning agents, and Microbial Contaminants. From Table 6, it can be seen that the root growth was initiated on day 2. The onion root length had increased from 1.3 cm to 7.0 cm over ten days. Graph 2 shows that the plants exposed to cooking wastewater had relatively good root length growth compared to the control. The nutrients and organic matter present in the cooking wastewater sample could have acted as nutrients for the plant growth.

Average Root length (cm)										
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Control (Mean)	0	1	1.67	3	3	3.67	4.67	6	7.3	8
Washing Machine wastewater (Mean)	0	1	1.67	2	2.67	3.33	4.33	5.67	6.33	7.33
AC wastewater (Mean)	0	0.5	1.3	2.67	3	3	4.3	5.67	6.67	7
Swimming pool (mean)	0	1	1.67	2.3	2.67	3	4.67	5.67	6.3	6.67
Cooking (mean)	0	1.3	3.3	3.3	3.67	4	5.3	6	6.3	7

Table 7: Average root length of *Allium Cepa* growing in different wastewater over 10 days.



Graph 6: Comparison of Mean root length of *Allium Cepa* growing in different wastewater for 10 days.

From Graph 6. it can be observed that:

1. On Day 1 none of the onion plants showed root growth.
2. On days 2 & 3 the cooking wastewater showed maximum root length growth, whereas Ac wastewater showed the least growth.
3. However, on day 4, the cooking wastewater showed maximum root length growth, whereas washing machine wastewater showed the least growth.
4. On day 5 the cooking wastewater showed maximum root length growth, whereas swimming pool & washing machine wastewater showed the least growth.
5. On day 6 the cooking wastewater showed maximum root length growth, whereas swimming pool & AC wastewater showed the least growth.
6. On day 7 the cooking wastewater showed maximum root length growth, whereas AC & washing machine wastewater showed the least growth.
7. On day 8 the cooking wastewater & control showed maximum root length growth, whereas swimming pool, AC & washing machine wastewater showed the least growth.
8. On day 9 the Control showed maximum root length growth, whereas swimming pool & cooking wastewater showed the least growth.
9. On day 10 the control showed maximum root length growth, whereas swimming pool wastewater showed the least growth.

Sample	Mean root length on Day (cm)	% Phytotoxicity of root
Control	8.0	—
Washing Machine wastewater	7.33	8.37
AC wastewater	7.0	12.5
Swimming pool outlet wastewater	6.67	16.625
Cooking wastewater	7.0	12.5

Table 8: Effect of Wastewater on the *Allium Cepa* root length (% phytotoxicity)

When specific chemical compounds inhibit plant growth and development, this is referred to as percent phytotoxicity (%) (Hyder et al., 2023). Table 8. represents the % root Phytotoxicity in Onion plants exposed to different wastewater samples. The % root Phytotoxicity ranged from 8.37-16.625%, wherein washing machine wastewater exhibited the least phytotoxicity, whereas swimming pool waste showed maximum phytotoxicity.

Conclusion

The primary objective of this study was to assess the effects of various types of domestic wastewater on plant growth and agriculture. The findings indicate that while initial plant growth showed rapid progress, the growth rate eventually declined, halting altogether. This suggests that certain minerals present in wastewater may support early-stage plant growth but could later hinder development due to potential toxicity or nutrient imbalances.

Among the tested wastewater types, the control group exhibited the most vigorous growth, followed by plants irrigated with washing machine water, air conditioning condensate, cooking water, and lastly, swimming pool water. The diminished growth observed with swimming pool water can likely be attributed to the chlorine content, which may have negatively affected the plants' health.

The study's limitations include a relatively short experimental duration (10 days) and a narrow range of wastewater types, predominantly greywater. Extending the experiment over a longer period and testing a broader range of wastewater types could yield more comprehensive insights. Nonetheless, the results indicate that treated domestic wastewater can positively influence plant growth and could be a viable alternative for garden irrigation, contributing to water conservation efforts.

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Advancing VLCAD Treatment: The Future Role of Targeted CRISPR-Cas9 Therapy

By Arjun Patel

Abstract

VLCAD deficiency is a rare genetic disorder of a fatty acid metabolism that currently has many symptom management options but no cure. CRISPR-Cas9 is emerging as a possible treatment plan for this deficiency. Given the rise in CRISPR-Cas9 technology for treating genetic diseases, this paper will delve further into how it could be used to correct the VLCAD enzyme deficiency. CRISPR-Cas9 is a technology that can already target specific genes and has the possibility to change the lives of many patients affected by this disease. Despite the fact that CRISPR-Cas9 has many limitations and has still not been used to treat VLCAD in humans, it is still a viable tool that could be used to treat the VLCAD disease.

Discussion

Very long-chain acyl-coenzyme A dehydrogenase (“VLCAD”) deficiency or very long-chain acyl-CoA dehydrogenase deficiency (“VLCADD”) is a rare genetic disorder of a fatty acid metabolism (Mp). VLCADD is quite rare and estimated to affect 1:40,000 patients.

VLCADD is defined as a health condition where the enzyme that starts the initial step in the process of turning food into energy of very long-chain fatty acids is missing or not working properly (Leslie and Saenz-Ayala). The breakdown of fatty acids takes place in well-defined structures in each cell, called the mitochondria, that are located in the cytoplasm of cells where energy is produced during the breakdown of complex substances into simpler ones (Nord). This condition prevents the body from being able to turn very long chain fats into energy due to the missing enzyme. Patients with VLCADD present with the following types of symptoms: lack of energy, muscle weakness, and low blood sugar. It is very common for these patients to experience muscle pains due to the breakdown of muscle tissue, particularly if fasting, being sick, exercising extensively or exposing themselves to extreme temperatures (Mp). These patients also have a propensity for having serious heart or liver problems. There is no cure for VLCADD at this time; however, there are several medical treatments that help patients prevent, manage or otherwise control their symptoms.

The predominant treatment plan for VLCADD focuses on keeping periods of fasting at a minimum (Leslie and Saenz-Ayala). For example, care for newborns who are diagnosed with VLCADD requires feeding frequently to avoid fasting, even during the night. Additional treatments are geared towards nutrition and diet, such as eating low-fat, high-carbohydrate foods with frequent feeding intervals. Beyond lifestyle changes, medications can also be used to manage this disease. Patients may also take supplements of carnitine if there is evidence of a carnitine deficiency, but this has not been widely studied, so it remains controversial among metabolic physicians (Nord). Riboflavin was often recommended but has recently not been shown to be beneficial and thus, has not been very prevalent. In addition, Bezaibrate is an

experimental medication originally developed to lower blood cholesterol but also shown to increase the amount of VLCAD protein in cells; however, limited clinical studies have been published to show its efficacy in use for treating VLCAD and no active clinical trial is currently in progress. One additional recommendation includes supplementing with medium chain triglycerides, commonly ingested as MCT oil (Leslie and Saenz-Ayala). In June 2020, the United States Food and Drug Administration (“FDA”) approved Triheptanoin for the treatment of long chain fatty acid oxidation disorders, including VLCADD because it was shown to improve long term effects of the disease as compared to similar doses of MCT oil (Shirley). Given that all the current treatments are only for the purpose of reducing any symptoms, it is important to find a cure for VLCADD to improve the lives of such patients, and new gene-editing technologies may be a possible solution.

CRISPR is a cutting-edge gene editing technology, having the potential to cure rare genetic diseases because it can edit DNA. CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats, and Cas9 is a CRISPR associated protein (Doudna). Together, the CRISPR-Cas9 system is a method of locating precise gene sequences, making a break in the DNA at the specific location, and allowing for the opportunity to edit such sequences by modifying the gene it is targeting. Because CRISPR-Cas9 can edit DNA, mutations can be entirely erased or replaced in a patient. The CRISPR-Cas9 system has the ability to treat infectious diseases, autoimmune disorders, cancers, and rare genetic disorders. Many recent clinical trials using cells edited with CRISPR-Cas9 have been approved for treating cancer (Liu et al.). There are a growing number of preclinical studies based on rodents showing the potential for this treatment plan to work well. To date, the CRISPR-Cas9 system is widely used to correct genetic variants with the hope of treating many human genetic diseases. An example of which are inherited diseases, which are generally diseases that do not currently have any cure, including without limitation sickle cell disease, β-thalassemia, and hemophilia. On December 8, 2023, the FDA approved two milestone treatments, Casgevy and Lyfgenia, which are both gene therapies for the treatment of sickle cell disease in patients 12 years and older (Fda). This is a signal that gene therapy is advancing in modern science and can be successfully used for the treatment of genetic disorders. This research paper will investigate how CRISPR-Cas9 technology could be used to correct a VLCAD enzyme deficiency at the genetic level.

VLCADD is a rare genetic disorder that is inherited when both parents have a copy of the recessive gene causing the disorder (Nord). The parents of an individual with an autosomal recessive gene each carry one copy of the gene mutation, but usually do not show any signs or symptoms (Mp). Mutations in the ACADVL gene cause VLCADD because this gene provides the instructions for making an enzyme called very long-chain acyl-CoA dehydrogenase, which is required to break down very long chain fatty acids found in foods and the body's fat tissues. Variants in the ACADVL gene lead to a shortage or deficiency of the VLCAD enzyme within cells, leading to the symptoms previously discussed (Leslie and Saenz-Ayala).

Gene therapy using an adeno-associated virus has been shown to help treat VLCADD based on improved laboratory test results within the first two (2) weeks of treatment on mice

who were challenged to fast yet maintain glycemic values (Kosak). Given that the blood glucose levels improved in the mice that went through this gene therapy, and the confirmation of the VLCAD protein in targeted tissues, the ability for gene therapy to work to treat VLCADD seems hopeful. One of the reasons why VLCADD is a potential candidate for treatment using the CRISPR-Cas9 system is because the genetic cause of this disorder is known. The protein encoded by the ACADVL gene can be targeted because it is the first step of the fatty acid oxidation process, which may be missing or working improperly (Ncbi). In fact, the ACADVL gene could be targeted by the CRISPR-Cas9 system such that the gene could be identified, cut and replaced in an affected patient. Then, that patient's cells could produce the previously missing enzyme and properly break down very long-chain fatty acids (Nord). VLCADD is a rare genetic disorder where the enzyme to break down very long-chain fatty acids is missing and although there are some treatment options, there is no cure. Because VLCADD has a known gene sequence, the CRISPR-Cas9 system could help provide a cure because of its capability to edit the ACADVL gene.

VLCADD is typically tested during routine newborn screening, so the mutations in the ACADVL gene associated with VLCADD are known (D'Annibale et al.). In fact, newborn screening does often find different variations in the ACADVL gene, creating uncertainty in diagnosis and treatment. Currently, ACADVL has more than three hundred identified variants. That said, the CRISPR-Cas9 system has already been used to recognize the ACADVL gene. CRISPR-Cas9 system was used to knock out ACADVL in HEK293T cells, and this targeted deletion was subsequently confirmed using laboratory testing. This shows that the CRISPR-Cas9 system can properly target and delete the ACADVL gene associated with causing VLCADD. Knowing that the CRISPR-Cas9 system can identify the ACADVL gene means that the CRISPR-Cas9 system can likely also be used to edit or modify such ACADVL gene (Bi). The CRISPR-Cas9 system can be used for diagnostic purposes such as identifying specific stretches of genetic code on the ACADVL gene and can be further tested for gene editing in such precise locations. There are many clinical trials in progress with the use of CRISPR-Cas9 (Henderson). The approval of the gene editing technology for the use to cure sickle-cell disease was one of the major landmarks for this technology. The Casgevy drug approved by the FDA can also cure transfusion-dependent beta thalassemia. The CRISPR-Cas9 system has been used to treat patients with cancer (Regaldo). In the pipeline now, there are other diseases that are being tested for treatment using the CRISPR-Cas9 system, such as autoimmunity. CRISPR based treatments may also be extrapolated for different disease causing mutations within the same gene because scientists can standardize part of the treatment plan such as the Cas protein, the method of delivery to the cells, how treatment is administered and what is given to patients (Henderson). Treatments could be customized by modifying the specific guide RNA sequence and any gene editing differences. So, treating new conditions can be scaled based upon the knowledge discovered by treating existing conditions. To date, gene therapy shows a lot of promise but still needs more testing for VLCADD. For example, gene therapy and mRNA have been used to help treat VLCADD but have only been tested on mice, not humans (Kosak). Despite the promise for

the applications of CRISPR-Cas9, there are some challenges to be addressed in clinical treatments in patients with different diseases using CRISPR-Cas technologies (Liu et al.).

The reason CRISPR-Cas9 has not yet been used for the treatment of VLCADD has been due to its current limitations. One major concern is the possibility for off-target effects, this is when the CRISPR-Cas9 accidentally edits other locations in the genome. Reducing this risk likely requires increasing specificity for the target or reducing the timeline for the Cas9 activity to take place (Yang et al.). For example, shortening the half-life for the Cas9 system delivery method has worked better as well as increasing the specificity of where the DNA is cut. In addition, since the discovery has been made through newborn screening that there are many different variants of the ACADVL gene, there is a concern about the heterogeneity amongst patients, as also seen in a study related to another similar fatty oxidation disorder called MCADD (Odendaal, Christoff, et al.). Despite these risks, scientists in the field are working to overcome these limitations, and have made some recent breakthroughs with the approval of Casgenvy (Henderson). While the issue of cost still remains an issue, since the Casgenvy treatment has a \$2MM price tag, the use of CRISPR-Cas9 continues to be an exciting technology that offers the promise of finding cures to so many rare diseases that have baffled scientists to date. In 2022, the U.S. Congress passed legislation directing the FDA to create a platform technology designation to help reduce costs and break the barriers for both producing and offering life-changing therapies such as gene editing using the CRISPR-Cas9 system. It is likely that a combination of government support and personalized treatment will be needed for a breakthrough treatment for VLCADD using the CRISPR-Cas9 system (Mathur and Sutton).

In summary, VLCADD is a rare genetic disorder, caused by a known recessive gene called ACADVL that currently has no cure and the symptoms can only be managed (Nord). The CRISPR-Cas9 system for gene editing has the potential to cure VLCADD upon further clinical testing because the gene and several known variants have already been identified, and the gene editing therapies have been tested in mice (Zhao et al.). Furthermore, the CRISPR-Cas9 system was recently approved by the FDA to cure a rare disease, paving the way for approval of similar treatments (Henderson). Despite any limitations with respect to clinical treatment development, the CRISPR-Cas9 system likely remains a viable option to explore for the future treatment of VLCADD.

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How does the Use of AI Tools and Technologies By Small and Medium Enterprises in Peru's Retail Sector Affect Their Revenue Growth and Competitiveness Compared to Larger Companies By German Gabriel Kruger Lishner

I. Introduction

The adoption of artificial intelligence (AI) is rapidly transforming industries worldwide, with the retail sector experiencing significant advancements in operational efficiency, customer service, and data-driven decision-making (Rashid & Kausik, 2024). While AI adoption is predominantly observed in large corporations, its potential to enhance competitiveness and drive revenue growth among small and medium enterprises (SMEs) is increasingly recognized (Soni, 2023). In Peru, SMEs represent a crucial component of the economy, contributing significantly to employment and economic activity (INEI. (s/f). Instituto Nacional de Estadistica e Informatica. Gob.pe. Recuperado el 12 de diciembre de, 2024). However, their ability to leverage AI effectively remains limited due to challenges such as financial constraints, lack of technical expertise, and infrastructural deficiencies. In Peru, SMEs represent a crucial component of the economy, contributing significantly to employment and economic activity. However, their ability to leverage AI effectively remains limited due to challenges such as financial constraints, lack of technical expertise, and infrastructural deficiencies. These barriers hinder SMEs' capacity to adopt and integrate AI-driven solutions, limiting their potential for growth, competitiveness, and innovation in an increasingly technology-driven market.

AI technologies, such as machine learning algorithms, chatbots, and predictive analytics, hold immense promise for SMEs, particularly in Peru's retail sector. These tools can optimize supply chain operations, personalize customer interactions, and improve decision-making. However, the gap in AI adoption between SMEs and large corporations raises critical questions about competitiveness and revenue generation in an increasingly digitized market.

Despite the growing accessibility of AI tools and their demonstrated benefits, many Peruvian retail SMEs struggle to adopt these technologies effectively. Limited financial resources, insufficient technical knowledge, and inadequate government support hinder their ability to compete with larger corporations that are better positioned to implement and capitalize on AI-driven innovations. This disparity creates a pressing need to understand how AI adoption influences the revenue growth competitiveness of SMEs in Peru's retail sector, as well as the factors that facilitate or hinder its effective implementation.

This study aims to examine the impact of AI adoption on the revenue growth and market competitiveness of retail SMEs in Peru. It seeks to identify the primary enablers and barriers to AI implementation among these businesses, such as access to funding, technical expertise, and regulatory support. Additionally, the study will propose actionable recommendations for policymakers and stakeholders to promote AI adoption and ensure its equitable benefits within the retail SME sector.

This research holds significant implications for the Peruvian economy, as SMEs account for a substantial portion of business activity and employment. By analyzing the potential of AI

technologies to enhance the efficiency and competitiveness of these enterprises, this study seeks to provide insights into how SMEs can bridge the technological gap with larger corporations. Furthermore, the findings aim to inform policymakers about the importance of fostering an environment that supports AI adoption, particularly through targeted incentives, training programs, and infrastructure development. Ultimately, this research contributes to the broader goal of leveraging technology to drive inclusive economic growth in Peru.

Methodology Overview

This study employed a mixed-methods approach to investigate the impact of AI adoption on the revenue growth and competitiveness of retail SMEs in Peru. Quantitative data were collected through structured surveys targeting retail SME owners and managers, focusing on AI utilization, perceived barriers, and performance metrics. Additionally, qualitative insights were gathered through interviews with industry experts and policymakers to contextualize the findings and identify enabling factors. Data analysis involved statistical techniques to evaluate trends and relationships, complemented by thematic analysis of qualitative responses to uncover deeper insights.

Scope and Limitations

The study focuses on retail SMEs in Peru, examining their adoption of AI technologies, such as chatbots, predictive analytics, and inventory management systems, and its impact on business outcomes. It excludes larger enterprises and other sectors to maintain a targeted exploration of SMEs in retail. Key limitations include potential biases in self-reported data from survey respondents and limited access to comprehensive financial records for analysis. Additionally, the findings may not fully capture regional disparities within Peru or the influence of informal sector dynamics. Resource constraints and the nascent state of AI adoption in the region further restrict the generalizability of results.

II. Literature Review

The emergence of Artificial Intelligence (AI) technologies has profoundly transformed various sectors, with the retail industry being one of the most significantly impacted. AI enhances operational efficiency, improves customer service, and facilitates advanced analytics, creating a paradigm shift in how businesses function. This revolution is particularly evident among small and medium enterprises (SMEs) in developing countries, where the adoption of AI brings both unique opportunities and significant challenges. This literature review delves into the current state of AI use among retail SMEs in third-world countries, examining the benefits, barriers, and implications that come with its implementation.

The integration of AI technologies in retail has been both extensive and impactful. Applications of AI range widely, encompassing inventory management, personalized marketing, and enhanced customer engagement. Research conducted by Maxime C. Cohen and Christopher S. Tang (The role of AI in Developing Resilient Supply Chains | GJIA. Georgetown Journal of

International Affairs, 2024) reveals that AI-driven systems can optimize supply chains, predict consumer behavior, and improve customer interactions. These capabilities are crucial for retail SMEs in developing nations, where resource constraints can severely limit operational efficiency.

One of the primary opportunities presented by AI is enhanced decision-making.

Advanced AI analytics tools equip retailers with the capacity to make informed, data-driven decisions by analyzing consumer behavior and market trends. According to Mhlongo, N. N. Z., Falaiye, N. T., Daraojimba, N. a. I., Olubusola, N. O., & Ajayi-Nifise, N. a. O. (2024)., (Mhlongo et. al., 2024) This leads to improved stock management and reduced wastage—an essential advantage for retailers operating in regions plagued by logistical challenges.

Furthermore, AI technologies, such as chatbots and virtual assistants, have significantly improved customer experiences by offering immediate support and personalized recommendations. Moreover, the implementation of AI can lead to substantial cost efficiency. As noted by Asmaa Alhashimy (2024) (Alhashimy, 2024) Automating routine tasks through AI can markedly reduce labor costs, which is particularly advantageous for SMEs in third-world countries where financial margins are often minimal.

However, despite the promising advantages of AI adoption, several barriers impede its widespread implementation among retail SMEs in developing countries. A primary obstacle is the lack of technical skills. A study by Ernestine Siu (2024) (Siu, 2024) points out that many SMEs face significant shortages of skilled personnel necessary for the effective implementation and management of AI technologies. This skill gap not only hampers adoption but also limits the effective utilization of AI tools. Additionally, financial constraints frequently pose a significant challenge. Many retail SMEs contend with strict budget limitations that complicate investments in advanced AI technologies. Research by Tania Babina, Anastassia Fedyk, Alex He, James Hodson, (2024) (Babina, 2023) indicates that the substantial initial costs associated with AI adoption and deployment can dissuade smaller businesses from pursuing such advancements. Furthermore, infrastructure challenges, including unstable internet connectivity and inadequate hardware, present considerable roadblocks to effective AI implementation. Tania Babina, Anastassia Fedyk, Alex He, James Hodson, (2024) Also argue that without a robust technological infrastructure, the full benefits of AI technologies cannot be realized.

Several empirical case studies shed light on successful AI integration within SMEs in developing countries. For instance, a report detailing retail SMEs use of AI for inventory management revealed remarkable outcomes, including that AI-driven inventory management has shown a 20% reduction in excess stock and improved inventory accuracy, which contributes to minimizing stock-related discrepancies, Michael Abramov (2024). Similarly, a research that employed AI-driven marketing tools experienced increases in customer engagement and sales performance, underscoring the potential for AI to enhance even modest operational frameworks. Mitra Madanchian, (2024) (Madanchian, 2024). While existing literature provides valuable insights into the benefits and barriers of AI adoption in retail SMEs, further research is necessary to deepen our understanding of these phenomena. Suggested areas for future investigation include longitudinal studies that assess the long-term impacts of AI implementation on SME

performance, providing insights into sustainability and growth. Furthermore, sector-specific studies focusing on the distinct challenges and opportunities faced by retail SMEs in individual countries could foster tailored solutions for AI adoption. Lastly, analyzing the impact of government policies on promoting AI integration in SMEs will be crucial for maximizing the technological benefits within developing economies.

III. Peruvian business background

Adoption and Application of Artificial Intelligence in the Peruvian Business Environment: General Perspectives and Focus on SMEs

The adoption of artificial intelligence (AI) is gaining momentum in Peru, particularly among larger companies, where the current adoption rate stands at 34%. This positions Peru as the fourth leading country in AI adoption within Latin America, with advancements most notable in sectors such as financial services, insurance, and telecommunications. Such rapid growth can be attributed to the increasing accessibility of digital tools and the pressures exerted by global competition, which prompt companies to modernize their operational frameworks. Bibiana Guardamino Soto (2024) (Soto, 2024). In Peru SMEs play a significant role in the economy, accounting for approximately 99.6% of formal businesses and employing around 60% of the economically active population. This includes a variety of sectors and regions across the country. However, a significant portion of these enterprises operate informally, with reports indicating that 8 out of 10 SMEs are informal, apart from that, the retail sector is a significant contributor to the SMEs landscape. As of recent reports, retail constitutes around 40% of SMEs in the country, reflecting its critical role in local economies. Infobae (2022) (Perú: Mypes representan el 99.6% del sector empresarial, pero aún el 86% son informales, 2022).

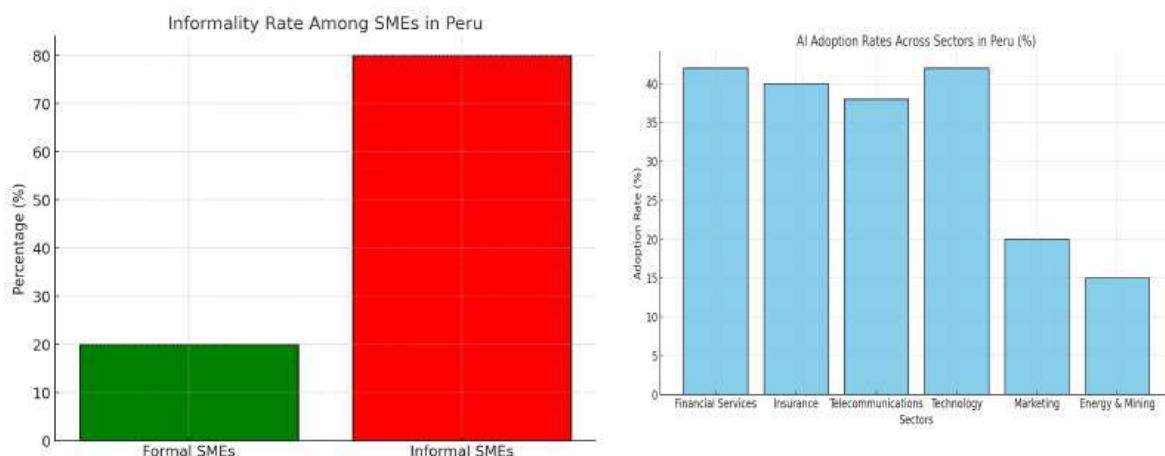
In the realm of AI implementation, specific sectors have emerged as leaders. Financial services and insurance are at the forefront, with adoption rates of 42% and 40%, respectively. Perú Retail (2024) (El 34% de empresas en Perú ya utiliza inteligencia artificial: ¿qué sectores lo usan más, 2024). In these industries, AI is employed for various purposes including predictive analysis, customer segmentation, fraud prevention, and automated customer service, all of which enhance response times and reduce operational costs. Petr Stros (2024) (Stros, 2024). The telecommunications and media sectors also exhibit notable adoption, with a rate of 31%. Here, AI is utilized for data analysis, campaign personalization, and fostering customer retention while adeptly managing vast amounts of user-generated data Infobae (2024) (Soto, 2024). Although the energy and mining sectors demonstrate a more limited current adoption, there are projections for increased usage aimed at optimizing processes and elevating workplace safety in the future.

Automation driven by AI is reshaping operational efficiency across multiple business functions, with the technology sector leading the charge at an impressive rate of 42%. Following closely are finance and sales areas. According to a study by McKinsey, AI-driven automation has the potential to boost efficiency by 30-40%, allowing employees to concentrate on strategic functions. Moreover, in the marketing domain, AI's contribution has improved campaign personalization and led to cost reductions of up to 20% McKinsey & Company (2024) (Singla et al., 2024).

Despite these advancements, the proliferation of AI in Peru is not without its challenges. A significant barrier to widespread adoption is the lack of necessary infrastructure and a shortage of specialized AI talent. Statistics indicate that 46% of companies remain in the early stages of AI exploration or testing, with many lacking a structured plan for comprehensive implementation. La república (2021) (Lr & Lr, 2021). Small and medium-sized enterprises (SMEs) face escalated challenges due to their limited resources, but government and industry associations are initiating programs to bridge this skill gap through targeted training efforts. International Labour organization (2021) (SMEs in Peru transform to become more productive and competitive. International Labour Organization, 2024).

Future projections indicate a continued upward trend in AI adoption within businesses, particularly in manufacturing, retail, and logistics. A report predicts that 70% of non-SME companies will increase their investment in AI within the next two years. Adam zaki (2024) (Zaki, 2024). In the retail sector, AI is poised to enhance customer experiences through personalized recommendations and improved inventory management. Emizentech (2024) (Samsukha, 2024). Similarly, in mining, AI is expected to increase operational efficiency by enabling real-time monitoring of machinery, potentially resulting in annual operating cost savings of up to 20% Picterra (2023) (Rushton, 2024)

AI adoption among Peruvian SMEs remains significantly lower than among larger firms, with many small and medium enterprises perceiving AI as an inaccessible luxury due to high initial costs and inadequate infrastructure. Nonetheless, AI has the potential to provide substantial advantages to these SMEs, particularly in enhancing sales and customer service via technologies such as chatbots and behavioral analysis. These innovations could facilitate a higher degree of personalization and customer satisfaction. Maha Yassin (2024) (Yassin, 2024). Additionally, operational implications of AI could translate into process transformations within sectors like retail, manufacturing, and logistics, optimizing inventory management and supply chains.



Source: El comercio (El 86,3% de mypes son informales y aún no recuperan niveles de ventas o empleo prepandemia. El Comercio Perú, 2022)

Source: Perú Retail (El 34% de empresas en Perú ya utiliza inteligencia artificial: ¿qué sectores lo usan más, 2024)

Difficulty to adapt

The adoption of artificial intelligence (AI) technologies offers significant potential to transform business operations by enhancing efficiency, improving decision-making, and fostering customer engagement. However, for small and medium-sized enterprises (SMEs) in Peru, the road to embracing AI is fraught with substantial challenges. These difficulties stem from a combination of financial constraints, technical skill gaps, and infrastructural inadequacies, creating a landscape where the benefits of AI remain largely inaccessible to smaller businesses.

One of the most significant obstacles to AI adoption among Peruvian SMEs is the financial burden associated with its implementation. Unlike large corporations that can allocate substantial resources toward technological advancements, SMEs often operate with tight budgets and limited financial flexibility. The upfront costs of acquiring AI tools, upgrading existing infrastructure, and providing necessary training for employees can be prohibitive for many smaller businesses. While larger firms in Peru, particularly in sectors like finance and telecommunications, are leveraging AI for advanced applications such as predictive analytics and customer segmentation, SMEs in the retail sector frequently struggle to afford even basic AI-driven solutions like automated inventory management systems. The predominance of informal enterprises—approximately 80% of SMEs in Peru—further exacerbates this challenge, as these businesses often lack access to formal financing mechanisms that could facilitate technological investments. Perú Reports (2016) (Post, 2016).

Another major hurdle is the scarcity of technical expertise required for effective AI integration. Many SMEs lack the in-house knowledge or access to affordable external consultants needed to deploy and maintain AI systems. This shortage of skilled professionals poses a significant barrier, as AI technologies often require specialized training for proper implementation and management. Without adequate technical support, SMEs risk implementing solutions that fail to align with their operational needs, leading to suboptimal outcomes or even wasted investments. The technical skill gap is particularly pronounced in Peru, where educational and vocational training programs tailored to emerging technologies are still in their nascent stages. This leaves many SMEs ill-prepared to navigate the complexities of AI adoption.

Infrastructure challenges also play a crucial role in hindering the adaptation of AI technologies among Peruvian SMEs. Reliable internet connectivity, robust hardware, and advanced digital platforms are essential for leveraging AI effectively. However, many SMEs, particularly those operating in rural or underdeveloped regions of Peru, face infrastructural deficits that make such requirements difficult to meet. In these areas, inconsistent connectivity and outdated equipment limit the ability to implement and sustain AI-driven operations. Even in urban centers, where infrastructure is more developed, smaller businesses often prioritize immediate operational needs over long-term technological upgrades, further delaying the adoption of AI.

Cultural and organizational factors also contribute to the difficulty of AI adaptation. Many SMEs in Peru perceive AI as a luxury reserved for large corporations rather than a feasible investment for their scale of operations. This perception is compounded by a lack of awareness

about the tangible benefits of AI, such as improved customer experiences and operational efficiencies. Additionally, resistance to change within organizations, stemming from fear of job displacement or skepticism about technological reliability, further slows the pace of AI adoption.

Despite these barriers, efforts are being made to address the challenges faced by Peruvian SMEs in adopting AI technologies. Government initiatives and industry associations are beginning to promote programs aimed at enhancing access to digital tools and providing targeted training for business owners and employees. However, these efforts remain in their infancy and require greater scalability to have a meaningful impact across the SME sector.

IV. Discussion

Cost of implementation

The high cost of implementing AI technologies represents a substantial obstacle for small and medium enterprises (SMEs) in Peru. While large corporations often allocate significant budgets for technological advancements, SMEs typically operate with tighter financial margins, making it challenging to justify the initial investment in AI. The expenses include not only purchasing software and hardware but also the ongoing costs of maintenance, training staff, and integrating AI solutions with existing business systems.

For many SMEs, these costs can represent a significant portion of their annual budget, especially in a country like Peru, where economic disparities and regional inequalities further complicate access to technology. Unlike larger firms that can spread these costs across extensive operations and benefit from economies of scale, SMEs often lack the operational capacity to absorb such expenditures without risking financial strain.

Additionally, many SMEs face difficulties accessing external financing to support AI adoption. High-interest rates, stringent lending requirements, and limited government support further exacerbate the situation. To address this, the government and private sector could explore alternative financing options, such as low-interest loans, leasing programs for AI technologies, or public-private partnerships that subsidize the cost of AI adoption.

Comparison with Large Corporations

Large corporations in Peru have been at the forefront of AI adoption, especially in sectors like finance, telecommunications, and retail. These firms are better positioned to implement AI because they have access to superior resources, including financial capital, skilled technical personnel, and advanced digital infrastructure. For example, companies in the financial sector use AI for fraud detection, customer segmentation, and predictive analytics, enabling them to offer personalized services while reducing operational risks.

In contrast, SMEs lag significantly due to a combination of financial constraints, lack of expertise, and inadequate infrastructure. This disparity is particularly evident in the retail sector, where larger companies leverage AI for sophisticated inventory management, customer insights, and marketing strategies, leaving SMEs to rely on manual processes or outdated technologies.

Consequently, SMEs find it increasingly difficult to compete on efficiency, cost-effectiveness, and customer engagement.

The gap is further widened by the rapid pace of digital transformation among larger corporations, which increasingly adopt cutting-edge AI tools such as machine learning and natural language processing. SMEs, on the other hand, often lack even the basic digital tools required to initiate AI adoption. This growing technological divide threatens the long-term sustainability of SMEs unless targeted interventions are made to democratize access to AI technologies.

Implications for Policy and Business Strategy

The widespread implementation of AI among SMEs in Peru has the potential to drive significant economic benefits, including enhanced productivity, job creation, and competitiveness. However, realizing these benefits requires coordinated efforts by policymakers, industry leaders, and the SMEs themselves.

Policy Implications: Policymakers have a critical role in addressing the systemic barriers that hinder AI adoption among SMEs. Key recommendations include:

Financial Support Programs: Establish grants, tax incentives, or subsidized loan programs specifically tailored to SMEs for purchasing AI technologies.

Infrastructure Development: Invest in improving digital infrastructure, such as broadband connectivity, particularly in rural and underserved regions where many SMEs operate.

Capacity Building: Create programs to train SME employees in AI-related skills, ensuring that businesses can effectively utilize the technologies they adopt.

Public-Private Partnerships: Foster collaborations between government, universities, and tech companies to develop affordable, scalable AI solutions designed for SMEs.

Business Strategy Implications: From a strategic perspective, SMEs should adopt a phased approach to AI implementation, beginning with low-cost, high-impact solutions such as chatbots for customer service or inventory management software. These technologies provide immediate benefits, such as cost savings and improved operational efficiency, while laying the groundwork for more advanced AI adoption in the future.

Additionally, SMEs could explore collaborative models, such as forming consortia to share AI resources or collectively negotiate better terms with technology providers. Such alliances could enable SMEs to access technologies that might otherwise be beyond their reach.

Global Comparisons: Lessons for Peru

The global adoption of artificial intelligence (AI) among small and medium enterprises (SMEs) showcases a stark contrast in the readiness and success of nations in leveraging technology for economic growth. Countries like Vietnam, Kenya, and India stand out for their ability to integrate AI into SME operations, driving significant advancements in productivity, competitiveness, and market growth. These nations have implemented targeted strategies that have enabled their SMEs to not only adopt AI but also reap substantial benefits from its use, offering a benchmark for Peru.

Vietnam has emerged as a leader in fostering AI adoption among SMEs, largely due to its government's proactive initiatives. Programs such as the National Digital Transformation Program provide subsidies and training to help SMEs access AI tools tailored to their specific needs. Public-private partnerships have also played a vital role, with tech companies collaborating with government agencies to offer affordable, localized AI solutions. This approach has significantly improved the operational efficiency of Vietnamese SMEs, particularly in sectors like retail and agriculture. For instance, many SMEs have reported a 25% increase in revenue after adopting AI-driven customer analytics tools, which help predict consumer behavior and personalize marketing strategies. Mckinsey & Company (2023) (Deveau et. al., 2023).

Kenya, often referred to as "Silicon Savannah," has similarly positioned itself as a hub for AI innovation in Africa. The country's focus on creating accessible and affordable AI technologies has enabled even resource-constrained SMEs to benefit from automation and analytics. Innovation hubs in Nairobi provide SMEs with access to mentorship, training, and technology, fostering a vibrant ecosystem for AI adoption. FWAMBA (2024) (Kenya's Silicon Savannah: strategic leap into future of global innovation, 2024). Moreover, government programs offering grants and low-interest loans specifically for technology upgrades have further accelerated adoption. In the retail sector, AI has transformed inventory management, with many SMEs achieving up to a 20% reduction in stock wastage through predictive analytics and enhanced supply chain coordination.

India's extensive IT infrastructure and large talent pool have propelled its SMEs to the forefront of AI adoption. Government initiatives such as "Digital India" and "Startup India" have provided financial incentives and technical support for SMEs to integrate AI into their operations. Indian SMEs have embraced AI to optimize supply chains, personalize customer interactions, and streamline marketing efforts. For example, an Indian SME implementing AI-based customer engagement platforms reported a 30% increase in sales within six months, illustrating the transformative potential of these technologies.

In comparison, Peru faces significant challenges in replicating these success stories. While SMEs account for 99.6% of formal businesses in Peru and employ approximately 60% of the workforce, their ability to adopt AI remains limited. One of the primary barriers is the underdeveloped digital infrastructure, particularly in rural areas where many SMEs operate. Unlike Vietnam or India, where reliable internet connectivity supports widespread AI use, Peruvian SMEs often struggle with unstable and costly internet services, making cloud-based AI solutions inaccessible.

Another major hurdle is the lack of technical expertise. Countries like India benefit from a robust educational system that produces a steady supply of tech professionals, while Peru faces a significant shortage of AI specialists. Many SMEs lack the in-house knowledge needed to implement and manage AI tools effectively, further widening the technology gap. This skill deficit is compounded by insufficient training programs, as current initiatives to upskill workers in Peru remain sporadic and limited in scope.

Financial constraints also hinder AI adoption among Peruvian SMEs. Unlike Kenya, where targeted grants and low-interest loans have made AI technologies affordable, most Peruvian SMEs struggle to secure funding for technology upgrades. High initial costs, combined with limited access to credit, make AI seem like an unattainable luxury for many small businesses. Additionally, Peru's policy framework has primarily focused on fostering AI adoption among large corporations, with little attention to the specific needs of SMEs. This lack of targeted support exacerbates the challenges faced by smaller enterprises, leaving them at a disadvantage in an increasingly competitive market.

Despite these barriers, Peru has significant potential to enhance AI adoption among its SMEs. The country can draw valuable lessons from global leaders like Vietnam, Kenya, and India. For instance, establishing regional innovation hubs could provide SMEs with access to affordable AI tools and training, similar to Kenya's approach. Expanding digital infrastructure, particularly in underserved areas, would ensure that SMEs across the country can leverage AI technologies effectively. Additionally, implementing workforce training programs and offering financial incentives, such as grants and low-interest loans, could help SMEs overcome cost and skill barriers.

By addressing these challenges and adopting best practices from other nations, Peru has the opportunity to position itself as a regional leader in AI adoption among SMEs. With strategic investments in infrastructure, skills development, and policy support, Peruvian SMEs could bridge the technological gap with larger corporations and compete more effectively in both domestic and international markets. This would not only enhance the competitiveness of the retail sector but also drive inclusive economic growth, ensuring that the benefits of AI are accessible to all segments of the economy.

V. Findings and Analysis

Data and Methodology

This analysis is based on a combination of case studies, primary data sources, and a review of relevant reports from organizations such as McKinsey & Company, El Comercio, La Republica and Infobae

The research design combines quantitative and qualitative methods to explore the current state of AI adoption among SMEs in Peru. Quantitative data is gathered from industry reports that track AI usage, revenue growth, and market competitiveness. Qualitative data is derived from case studies, policy analyses, and expert interviews that provide deeper insights into the challenges and opportunities of AI integration. The study's analytical framework includes a focus on financial constraints, infrastructure limitations, the availability of skilled labor, and the regulatory environment, all of which are critical to understanding the dynamics of AI adoption in SMEs.

Case studies

Case studies were drawn from SMEs in Peru's retail sector, with comparative insights drawn from countries like Vietnam, Kenya, and India. These nations have seen varying degrees of success in implementing AI in their SME sectors, providing valuable lessons for Peru. The study also examines global trends in AI adoption and how these practices can be adapted to the Peruvian context.

Research design

The study employs a mixed-methods approach:

Quantitative analysis of AI adoption rates, impacts on revenue, and competitiveness using statistical trends.

Qualitative insights derived from case studies, policy evaluations, and industry reports.

This combined methodology ensures both depth and breadth in addressing the adoption challenges and opportunities.

Analytical Framework

The analysis focuses on the interplay between four key factors:

Financial Barriers (cost of implementation).

Technical Expertise (availability of skilled labor).

Infrastructure (digital and technological readiness).

Regulatory and Collaborative Efforts (policy support and partnerships).

Adoption Rates

Approximately 46% of SMEs in Peru are in the exploratory phase of AI implementation, with adoption concentrated among medium-sized enterprises in urban areas. Informal and rural SMEs face the most significant barriers, resulting in low adoption rates compared to global benchmarks.

Impact on Revenue Growth

Short-term AI investments, such as implementing predictive analytics and chatbots, have been shown to generate immediate returns, with reported sales increases of up to 30% in other regions like India. However, most Peruvian SMEs have yet to realize these benefits due to underutilization of AI capabilities.

Impact on Market Competitiveness

SMEs leveraging AI solutions gain advantages in efficiency, customer engagement, and operational scalability. However, the technological divide between SMEs and larger corporations in Peru exacerbates market disparities, particularly in the retail sector.

Factors Facilitating AI Implementation

Key facilitators include

- Access to affordable and localized AI tools (as seen in Vietnam).
- Training programs tailored to SME needs (as observed in Kenya).
- Government-backed financial incentives like grants or subsidized loans.

Regulatory Support

Existing policy frameworks in Peru primarily cater to larger corporations. However, international comparisons suggest that targeted SME policies—such as Vietnam's National Digital Transformation Program—could significantly improve adoption rates.

Collaboration

Collaborative models, such as public-private partnerships and regional innovation hubs, have proven successful in countries like Kenya and India. Peru could replicate these by fostering partnerships between government, tech firms, and universities to offer SMEs affordable tools and skills training.

VI. Conclusion

Summary of Findings

The study examines the adoption of artificial intelligence (AI) among small and medium enterprises (SMEs) in Peru's retail sector, highlighting its potential benefits and significant challenges. AI technologies offer promising opportunities for SMEs, including improved customer engagement, optimized inventory management, and revenue growth. However, adoption remains limited, with only 46% of SMEs exploring AI solutions, compared to the more extensive use by larger corporations. Financial constraints, such as high initial costs and limited access to funding, significantly hinder SME adoption. Informal SMEs face even greater challenges, as they lack access to resources and formal financing mechanisms.

Additionally, a lack of digital infrastructure, especially in rural areas, and a shortage of technical expertise further impede AI integration. Without skilled personnel or reliable digital tools, many SMEs are unable to utilize AI effectively, widening the technological and competitive gap with larger corporations. Larger firms leverage advanced AI solutions to streamline operations and dominate the market, leaving SMEs struggling to keep pace.

Despite these challenges, case studies from other countries like Vietnam, Kenya, and India demonstrate that targeted policies, affordable AI tools, and workforce training can significantly enhance SME adoption. The study suggests a phased approach, starting with low-cost AI tools to achieve immediate gains, while investing in infrastructure, training, and policy support for long-term growth. Addressing these barriers is critical for enabling Peruvian SMEs to compete in an increasingly digital economy.

Long-Term Investment or Short-Term Investment

For many SMEs in Peru, financial constraints and resource limitations often make short-term investments in AI appear more feasible. A short-term approach typically involves

adopting low-cost, scalable AI solutions that deliver immediate results. These may include implementing chatbots to improve customer service, utilizing AI-based marketing tools for quick sales boosts, or employing predictive analytics to optimize inventory management for the next sales cycle.

The advantages of this approach lie in its ability to generate rapid returns on investment. For example, integrating AI tools to streamline supply chain processes can immediately reduce overhead costs, while implementing automated customer support systems often enhances customer satisfaction and retention. According to a study by Automation Anywhere, businesses that adopt AI for process automation can see efficiency improvements of up to 30% and cost reductions of 20%. Peruvian SMEs operating in the retail sector can particularly benefit from such measures, as retail accounts for approximately 29% of AI usage in Peru, addressing critical pain points like inefficiencies in stock management or delays in customer response times.

However, the short-term focus comes with inherent limitations. While these measures may provide immediate relief and benefits, they do not necessarily address the underlying structural challenges that inhibit long-term growth. For instance, a chatbot may reduce the workload on customer service staff, but without broader investments in data infrastructure and workforce training, its functionality may remain underutilized. Moreover, over-reliance on short-term solutions can lead to a fragmented technological framework, creating inefficiencies in integrating various AI tools over time.

In contrast, viewing AI adoption as a long-term investment enables SMEs to lay the groundwork for sustainable growth and adaptability. This approach involves committing resources to comprehensive strategies that include upgrading digital infrastructure, developing in-house technical expertise, and aligning AI tools with the overall business model. Long-term investments focus not only on immediate operational benefits but also on creating a resilient ecosystem that allows businesses to scale and innovate over time.

For example, Peruvian SMEs that invest in advanced analytics systems integrated with their customer relationship management platforms can gain deeper insights into consumer behavior. These insights inform more strategic decision-making, from product development to market expansion. A McKinsey report indicates that AI-driven insights can increase sales revenue by 10-20% by optimizing marketing and sales strategies. Similarly, investing in cloud-based AI infrastructure ensures scalability, enabling businesses to handle increasing data volumes as they grow. Training programs for staff to understand and manage AI systems further bolster long-term competitiveness by fostering a workforce capable of navigating technological shifts.

The long-term approach is particularly critical given the dynamic nature of the retail market in Peru, where customer preferences and market conditions evolve rapidly. By embedding AI capabilities into their core operations, SMEs position themselves to adapt to these changes proactively, rather than reacting to them as they arise. Additionally, such investments align SMEs with global trends, ensuring their relevance in an increasingly digitized economy. The International Data Corporation (IDC) predicts that global AI spending will reach \$154

billion by 2024, underscoring the importance of staying competitive in a rapidly advancing field (IDC, 2023).

Balancing Immediate Gains with Long-Term Growth

While the benefits of long-term investment in AI are substantial, the financial realities of Peruvian SMEs cannot be ignored. Approximately 46% of businesses in Peru are still in the exploratory phase of AI implementation due to resource constraints and lack of skilled personnel. Many SMEs lack the capital to undertake significant technological overhauls. Thus, a balanced approach that combines short-term and long-term strategies may be most effective.

For instance, SMEs can begin with cost-effective AI tools that address immediate needs, such as predictive analytics for inventory management, while simultaneously planning for larger investments in infrastructure and training over time. Incremental implementation allows businesses to achieve quick wins while building a foundation for sustainable growth. A combined strategy ensures that businesses benefit from short-term ROI while positioning themselves for long-term success in a competitive market.

Limitations and Future Research

While existing research offers valuable insights into AI adoption among SMEs, significant gaps remain in understanding its long-term impacts, sector-specific challenges, and policy effectiveness. Current studies often emphasize the short-term benefits of AI adoption, such as cost savings, but fail to address issues of long-term sustainability and scalability. Additionally, SMEs are frequently treated as a homogenous group, overlooking the distinct challenges and opportunities faced by businesses in different sectors or regions. The lack of comparative studies examining AI adoption in Peru relative to other developing countries further limits the contextual understanding needed to develop effective strategies.

Addressing these limitations requires a more nuanced approach to research. Longitudinal studies could provide valuable insights into the long-term effects of AI on SME performance, including revenue growth, market competitiveness, and job creation. Research should also explore the sector-specific challenges faced by retail SMEs in Peru, which differ from those encountered in manufacturing, logistics, or agriculture. Moreover, a stronger focus on contextual analysis would enable a deeper understanding of the unique factors shaping AI adoption in Peru compared to other nations.

Future research should prioritize the evaluation of existing government initiatives aimed at supporting AI adoption among SMEs. Investigating the effectiveness of these policies could reveal areas for improvement and inform the development of more targeted support measures. Comparative studies with other countries could help benchmark Peru's progress, identify best practices, and facilitate the transfer of successful strategies. By addressing these research gaps, policymakers and stakeholders can better support the equitable and sustainable adoption of AI within the SME sector.

Closing Remarks

The integration of AI technologies into Peru's SME sector presents a transformative opportunity to enhance the competitiveness of small businesses in the retail industry. Despite significant challenges, including financial limitations, skill shortages, and infrastructural deficits, the potential benefits of AI are substantial. With targeted support from policymakers, industry leaders, and educational institutions, Peruvian SMEs can overcome these barriers.

Drawing lessons from global success stories, Peru has the opportunity to create an enabling environment that fosters equitable AI adoption. Investments in digital infrastructure, tailored training programs, and affordable AI solutions are crucial for bridging the gap between SMEs and larger corporations. By embracing both short-term and long-term strategies, Peruvian SMEs can build resilience, improve operational efficiency, and thrive in an increasingly digital economy.

This research underscores the importance of a collective effort to empower SMEs with the tools and skills necessary for sustainable growth. Policymakers, business leaders, and technology providers must collaborate to ensure that the benefits of AI adoption extend across the SME sector, driving inclusive economic growth and securing Peru's position in a competitive global market.

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Alternate Minerals for Photovoltaics By Khanh Truong

Abstract

Photovoltaics are one of the leading renewable energy sources to help combat climate change since sunlight is widely accessible in many areas. However, photovoltaics can negatively impact the environment due to the destruction of habitats, land use, and depletion of critical minerals. This literature review paper uses Google Scholar to extract 11 papers. Keywords used to search these papers are: Solar materials U.S., U.S. photovoltaic industry, U.S. photovoltaics, Advancements in photovoltaics, and Environmental Impact of photovoltaics. One of the most common minerals used as a semiconductor for photovoltaic cells is silicon. Many alternatives include Gallium Arsenide, Perovskites, and quantum dots. Nanoparticles can be applied to photovoltaics to improve efficiency and reduce cost per watt. Gallium Arsenide and nanoparticles stand out as outstanding semiconductors for photovoltaics to improve efficiency and scalability. More research on reducing the environmental impact of photovoltaics is required. The paper concludes with key findings from the results and discussion section.

Keywords photovoltaic materials, alternate photovoltaic minerals, photovoltaic efficiency, photovoltaic sustainability, photovoltaic scalability.

Introduction

Background

Photovoltaics are one of the leading sources of renewable energy since sunlight is widely accessible in many areas. Photovoltaic cells convert sunlight into electrical or thermal energy. A variety of materials can be used to make the electron transport layer, a layer in photovoltaic cells that converts input power into output power, such as silicon, gallium arsenide, copper indium gallium selenide (Machín & Márquez). Silicon is one of the most used materials in photovoltaic cells due to its abundance in the Earth's crust (Machín & Márquez).

In 2021, the U.S. had 108.7 gigawatts (GW) of direct current photovoltaics, which can power 18.9 million American houses and offset more than 110 million metric tons of CO₂ emissions (Tabassum et al.). According to Tabassum et al., many federal policies have helped the growth of the solar industry, such as the Investment Tax Credit (ITC), Modified Accelerated Cost Recovery System (MACRS), and the Sunshot Initiative. In addition, the Inflation Reduction Act played a significant role in decreasing the production costs and installation costs of solar modules, which would boost the industry as well (Min et al.). Photovoltaics stands to be a promising renewable energy source to comply with the Paris Agreement.

Challenges

However, photovoltaics have many challenges that need to be solved, as the demand for renewable energies increases to combat climate change. These challenges include the efficiency of the solar cells, scalability, and environmental impact on the manufacturing process. The efficiency of the solar cells needs to increase to meet future energy demands. The current efficiency for commercial photovoltaic cells is around 20% to 25% (Dada and Popoola). Installing photovoltaics will negatively affect the surrounding soil, the ecosystem, displace fauna, and reduce farmable land (Sebestyén). In addition, acquiring materials to produce photovoltaics will deplete natural resources, especially rare earth minerals, as demand and production increase (Sebestyén).

The goal of this Paper

This paper aims to answer the research question: what roles do minerals play in photovoltaics and how can we make them more energy efficient, cheaper to make, and more eco-friendly in the construction process through material composition? We will review alternative materials that can be used to help alleviate those challenges. Furthermore, we will evaluate the system surrounding photovoltaics, working to improve their use, impact, and efficiency.

Methodology

In this review paper, papers were retrieved from databases and used to acquire information. The main database from which the papers were retrieved is Google Scholar. The search was limited to papers published between 2020 and 2024 to focus on the most recent advancements and findings in photovoltaic technology. Papers that have experimental data included are the main subjects used in this review. 10 papers will be used for this review. The review process includes summarizing the papers' contents, analyzing such content, and concluding by proposing the best materials for either of the three challenges: efficiency, scalability, and environmental impact.

Results

Efficiency

Silicon, the current most common material to be used in photovoltaic cells, has the highest power conversion rate for silicon at 25% under controlled conditions, but industrially produced silicon cells have efficiencies of 15% to 18% (Dada and Popoola). Singh et al. stated that monocrystalline silicon achieves power conversion efficiency of 24.4%, and polycrystalline silicon of 19.9%. They predicted the maximum power conversion efficiency for crystalline-based silicon photovoltaic cells is 30%. Gallium arsenide (GA) can absorb a wide range of light wavelengths, operating at higher temperatures, and absorbing light under low-light conditions than Silicon photovoltaic cells, allowing GA photovoltaic cells to achieve efficiencies above 29% (Machín & Márquez).

Halide perovskites are emerging as a high-performance mineral for photovoltaic cells due to their exceptional abilities including high power conversion rates and tunable bandgaps (Machín & Márquez). In addition, the perovskite crystal structure allows for a high degree of tunability, which can be used to tune the photovoltaic cell for a set condition to maximize efficiency (Mishra et al.). There are other promising forms of perovskites as well. According to Maziviero et al., hybrid perovskites, made from lead halide and methylammonium, have a high absorption rate in the visible solar spectrum, have a direct and tunable bandgap, can transport both positive and negative charges and high mobility of excitons. Maziviero et al. suggested that the structural organization of the perovskite layer in photovoltaic cells can increase power conversion efficiencies. The authors suggested the Ruddlesen-Popper arrangement, which consists of alternating layers of face-centered cubic structures and perovskite layers placed on the crystallographic z-axis. Another structure that the authors suggested was the multi-junction (tandem) cells, which consisted of two or more subcells stacked either in series or parallel and achieved power conversion efficiencies of over 44%.

Quantum dots can be used to increase efficiency due to their tunability of size and shape to adjust to a desired frequency of light (Dambhare et al.). According to Dambhare et al., quantum dot-sensitized solar cells can theoretically achieve efficiencies of up to 44%. In their paper, Singh et al. recorded that quantum dots currently achieve efficiencies between 11% and 17%.

Nanomaterials can be applied to photovoltaic cells to improve power conversion efficiency. Graphene is a promising nanomaterial to be applied in photovoltaic cells to increase their efficiency. For example, incorporating Graphene as an electrode to dye-sensitized solar cells using Zinc Oxide would increase the cell's performance by 36% (Jain et al.). For perovskite photovoltaic cells, indium sulfide is a promising nanomaterial to be used with the specific structure of perovskites due to its efficient light absorption of various wavelengths, high charge carrier mobility, and it is affordable (Mishra et al.).

Organic photovoltaic cells face power conversion efficiency deficiencies relative to inorganic photovoltaic cells such as polycrystalline silicon. As a way to improve efficiency, Kothari et al. suggested the addition of metal nanoparticles such as silver or gold to the commonly used conducting polymer in organic photovoltaic cells known as PEDOT:PSS. The authors stated that silver nano prisms used with the duel interface doping technique on organic photovoltaics using poly (PIDTT.DFBT): PC71BM have power conversion efficiencies raised from 7.70% to 9%. Gold nanoparticles applied to PEDOT: PSS have shown an improvement in efficiencies from 8.31% to 9.19%.

Scalability

Silicon is the second-most common material in the Earth's crust, making it a popular option as the mineral to be used for mass-producing photovoltaic cells (Machín & Márquez). It was the most common mineral being used in photovoltaic cells with 80% of the commercial solar market comprising single crystalline silicon cells (Dambhare et al.). The cost for a

photovoltaic system that converts sunlight into electricity (excluding inverter) is \$0.2 per watts direct current (W_{DC}) after the enactment of the Inflation Reduction Act (Min et al.). In organic solar cells, the current minerals being used as the electrode are indium-doped tin oxide (ITO) and fluorine-doped tin oxide (Jain et al.). According to Jain et al., ITOs already available on the market have a recorded transmittance rate of 80%, fluorine-doped tin oxide has similar properties; however, these materials have many drawbacks, including high cost, low flexibility, and difficulty to manufacture. The authors proposed graphene as a substitute instead since it has outperformed ITOs both as anode and cathode; and it can be used in a cost-effective fabrication process for organic solar cells, allowing for mass production. Cadmium Telluride (CT) is a promising semiconductor material for photovoltaic cells due to its high power conversion rate, which would allow for the manufacturing of solar cells with significantly thinner layers of CT than traditional cells (Machín & Márquez). This can allow for the production of CT cells at a competitive price, allowing for mass production. Singh et al. stated that thin film photovoltaics that use semiconductors such as Gallium Arsenide, Cadmium Telluride, and Copper Indium Gallium Selenide would allow for the manufacture of thinner layers of the semiconductor material, thus making thin films more cost-effective than that of traditional silicon cells. Perovskite photovoltaic cells can be manufactured using simpler and cheaper processes than silicon cells, and they can be applied to flexible, lightweight, and semi-transparent solar modules (Mishra et al.).

In addition to applying scalable materials, other measures can be taken to accelerate installments of photovoltaic panels. Such methods include utilizing community solar, where multiple users can purchase electricity from an –in most cases– off-site solar power installation (Hangen et al. 6). Hangen et al. claimed that utilizing community solar can lower the cost per watt for each user than rooftop installations, and the users can buy a portion of the energy output instead of the entire installation, which allows for greater accessibility of this renewable energy. The authors proposed a national renewable energy credits program to provide a supporting baseline for renewable energy sources like solar, developing pools of government and philanthropic support to fund solar installation projects and removing utility barriers to increase the accessibility of solar power to a variety of communities.

Environmental Impact

For Dye-Sensitized Solar Cells (DSC), high-efficiency dyes that were commonly used included ruthenium complex dyes and organic solubles such as N719, N3, and black dye (Dada and Popoola). According to Dada and Popoola, these dyes are poisonous, volatile, and explosive, and thus can harm the environment if not contained. To have low-cost and non-poisonous alternatives, the authors propose water and plant-based dyes like the TiO₂ nanorod (NR)-based hibiscus dye combined with electrodes like carbon, graphite, or gold. Shetwi recorded that the average predicted greenhouse gas emission rate from different photovoltaic systems is 36.75 Carbon Dioxide equivalent emissions per kilowatt-hour (CO₂eq/kWh) of electricity generated during the production phase. The authors release that Cadmium Telluride photovoltaic cells have

been shown to release the least air pollution and power consumption during manufacturing for photovoltaic cells.

There are positive and negative environmental effects that come with solar power (including photovoltaics). According to Shetwi, adding 60 GW of renewable energy to California could reduce the CO₂ production rate by 72%. Shetwi also claimed that 60 GW of renewable energy applied to Texas could result in a 54% reduction in emissions. Negative environmental effects from installed solar power systems (including photovoltaics) can be observed as well. According to Sebestyén, these systems can cause environmental issues such as soil erosion, releasing soilborne pathogens, the depletion of natural minerals, reducing farmable land, and negative effects on the ecosystem around the site. The author claimed that the environmental impact of the installed system also depends on its power conversion efficiency. Shetwi agreed with the statements provided by Sebestyén and also stated that hazardous compounds used in photovoltaic manufacture, including sulfuric acid, hydrochloric acid, and nitric acid, have negative environmental impacts if not contained properly.

Some solutions can be used to mitigate the negative environmental effects of photovoltaics. To reduce land use, Tawalbeh et al. proposed using floating photovoltaics, which are photovoltaics placed on top of a buoyant structure and then placed on a body of water, reducing land use significantly. The authors also mentioned that due to the constant cooling provided by the evaporation of water surrounding the floating photovoltaics, floating photovoltaics are expected to generate more electricity than in-land photovoltaics.

Discussion

Photovoltaics can contribute significantly to the renewable energy mix, accelerating our progress in replacing non-renewable energy sources with renewable energy sources. However, there are many challenges facing the mass installation of photovoltaics, including efficiency problems, costs, and negative environmental impacts. To improve efficiency in photovoltaic cells, these alternate materials were discussed: Gallium Arsenide, Halide Perovskites, Hybrid Perovskites, Quantum Dots, and nanomaterials. Alternate materials can improve scalability: Cadmium Telluride, Gallium Arsenide, Perovskites, and graphene. Organic dyes and Cadmium Telluride can be used to lower the environmental impact of photovoltaic cells. Gallium Arsenide is a promising semiconductor for photovoltaics. Its qualities include absorbing a wide range of wavelengths, operating at higher temperatures, and better absorbing under low light conditions than traditional silicon cells (Machín & Márquez). In addition, it can be applied to thin-film photovoltaics, which decreases the cost per module, allowing for Gallium Arsenide photovoltaics to be a competitive choice in the market compared to silicon cells (Singh et al. 2844).

Nanoparticles can increase the performance of photovoltaic cells. For example, in organic photovoltaic cells, graphene has outperformed ITOs as both an anode and cathode, and it can be used in a cost-effective fabrication process for mass production (Jain et al.). Nanoparticles can be applied to different types of photovoltaics and increase power conversion efficiencies. The

application of nanotechnology in photovoltaic cells should be further researched since they are versatile and could decrease the cost per module for photovoltaics.

The environmental impact of installed photovoltaic cells is an issue that needs to be addressed to increase the adoption of the technology. A solution is to install photovoltaics on already degraded land such as landfills, spent mines, or contaminated sites; this will reduce the photovoltaic's impact on natural habitats and fertile soil (Tawalbeh et al. 4). Another solution is to install floating photovoltaics, which would not require land use and could be more efficient than in-land systems due to the constant cooling from the evaporation of water (Tawalbeh et al. 4). In addition, research should also focus on finding alternative materials and processes that are non-toxic to the environment. According to Tawalbeh et al., numerous chemicals that were used in the separation, extraction, purification, and cleaning process of different types of photovoltaic cells including hydrogen, hydrochloric acid, and nitric acid are flammable, corrosive, toxic, and carcinogenic. To increase the safety of the workers and to reduce negative environmental impact, further research on non-toxic alternatives is necessary. Processes involving the recycling of used photovoltaics should be further researched to increase the practicality of recycling, which would decrease mining for new materials needed.

Conclusion

This paper introduces alternative minerals to be used in photovoltaics and other solutions to either increase or decrease aspects of the technology in the three main areas of focus: Efficiency, Scalability, and Environmental Impact. Gallium arsenide, Halide perovskites, Hybrid perovskites, Quantum dots, and nanomaterials were discussed to improve efficiency. Cadmium Telluride, Gallium Arsenide, Perovskites, and Graphene were discussed to improve Scalability. Organic dyes and Cadmium Telluride can be used to lower the environmental impact of photovoltaic cells. Nanoparticles are cost-effective and have been shown to improve the efficiencies of the photovoltaic cells applied, thus being a promising material to be incorporated into photovoltaic cells. Gallium Arsenide is a promising semiconductor mineral that has been shown to have high power conversion efficiencies compared to other current photovoltaics and can be applied in thin films, which is scalable because less material is required to create a module. In addition to introducing alternative minerals, the paper also introduces and discusses alternative solutions to solve some of the issues presented in the three main areas of focus and fields of research that need to be worked on.

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Assessing the Efficacy of CNN Model Size in Diagnosing Knee Osteoarthritis

By Aayush Balaji

Abstract

Knee osteoarthritis is a condition commonly occurring among the elderly, and is a natural joint disease caused by repetitive motion, and the loss of articular cartilage in proximity to the knee. The early identification and diagnosis of knee osteoarthritis is crucial in terms of successful treatment and the initiation of assistful exercises that are capable of hampering the knee osteoarthritis development process. The current methods of diagnosis, which include plain radiography and hyaluronic acid injections, are very prone to human error and inaccuracies. We hypothesize that larger pre-trained models with a greater number of parameters will outperform smaller models in accurately classifying knee osteoarthritis from radiographic x-ray images into three categories of Healthy, Mild and Severe. Specifically, we expect that the increased capacity of these larger models enables them to capture intricate patterns and features within the complex medical imagery. To test this hypothesis, we will evaluate the performance of three models of varying sizes on the task, analyzing their accuracy and ability to generalize across different levels of osteoarthritis severity. MobilenetV2, ResNet50 and VGG16 models with 3.5, 25.6 and 138.4 million parameters respectively were chosen to conduct the experiments. Experiments were conducted with different hyperparameters for each of the three algorithms keeping the underlying data consistent across all experiments. The test accuracy of the algorithms MobilenetV2, ResNet50, and VGG16 averaged 46.49%, 52.96%, and 53.57% respectively. These results support our hypothesis that a model with a larger quantity of parameters is capable of recognizing the patterns better for a complex dataset used throughout this study for recognition of knee osteoarthritis severity.

Introduction

Knee osteoarthritis is characterized as the gradual, progressive process in terms of the loss of articular cartilage. Specifically for adults of older age, it is an issue throughout the world in many areas. For example, approximately 25% of people 55 years of age or older have had knee pain on most days in a month for the past year, and about half of them have radiographic osteoarthritis in the knee, a group considered to have symptomatic osteoarthritis(1). In epidemiology, half of the world's population aged 65 years or older has OA, which is the most prevalent disorder of articulating joints in humans(2). Furthermore, approximately 654 million individuals aged 40 years and older were affected by knee osteoarthritis globally in 2020, highlighting the significant burden this condition imposes(3).

The definition of knee osteoarthritis, as well as the identification of risk factors and pathophysiological mechanisms, are being improved and developed as researchers investigate curatives of the condition(4). Radiographic evidence of knee osteoarthritis increased with age, from 27% in subjects younger than age 70, to 44% in subjects of age 80 or older(5). Through analysis, we can clearly recognize that this implies that as humans age, they are at higher risk for

symptoms linking to knee osteoarthritis. Various risk factors in relation to knee osteoarthritis include age, gender, obesity, injury, joint abnormalities, diet, excessive physical activity, physical inactivity, and genetic factors(2,6). The early detection and diagnosis of knee osteoarthritis is crucial in terms of the initiation of exercises that are known for hampering the osteoarthritis process, which may include activities such as weight reduction because of the irreversible damage that knee osteoarthritis opposes. Total knee replacement (TKR) would have to be done without the assistance of identifying osteoarthritis beforehand(7). Therefore, the development of an automated system for the analysis and detection of knee osteoarthritis could offer substantial benefits, not only to medical associations, but also to local communities worldwide, and it is the objective of this study. Both patient-reported and performance-based outcome measures have been used to assess physical function but currently there is no gold standard assessment in people with osteoarthritis(8). Many of these tests are approximate, but inaccurate.

The process of detecting knee osteoarthritis through visuals is very time consuming, however, deep learning models have the potential to automate this process and save time. This automated system could assist doctors and medical professionals in terms of diagnosing the condition faster since their time is very precious and limited. The flowchart in Figure 1 facilitates the process of creating training and experimenting with convolutional neural network algorithms as well as the methodology of this experiment. Specifically throughout the varying deep learning neural networks, after in-depth research, we found that Convolutional Neural Network(CNN) algorithms are more efficient due to various factors such as the capability in terms of extracting higher representations. Neural Networks can be used in a variety of problems such as pattern/image recognition, classification, clustering, natural language processing (NLP), regression, and other alternative methods(9). The major objective of this experiment is to identify the severity of knee osteoarthritis in an x-ray image utilizing machine learning and convolutional neural network(CNN) image processing algorithms. Essentially, we believe that experimenting and tinkering with the hyperparameters given to CNN algorithms would result in an efficient, machine learning-based model that is capable of identifying potential signs and the severity of knee osteoarthritis in an x-ray.

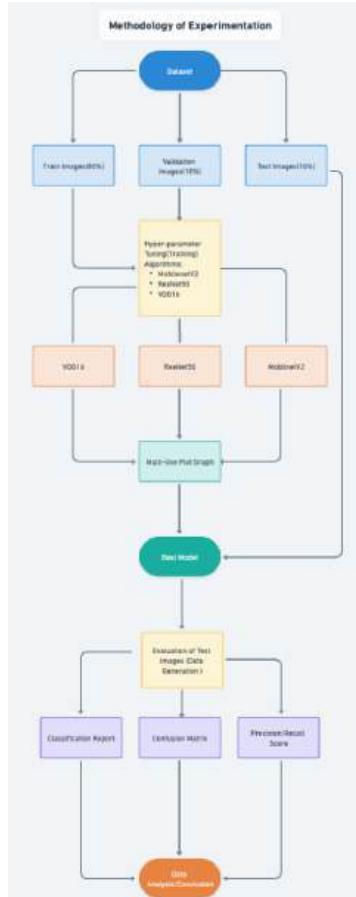


Figure 1. Experiment Flowchart. The following flow chart demonstrates the experimental process as well as the general methodology through this experiment. This process eventually resulted in the optimal performance model of each corresponding algorithm, and was also principally utilized for progression in terms of the machine supervised learning workflow.

Various related works have been conducted encompassing the medical concept of knee osteoarthritis, as well as technical concepts. Furthermore, alternative convolutional neural network approaches sustain a core around hyperparameters and fine tuning in terms of various algorithms. However, a minimal quantity of research papers suggest evaluation in terms of the amount of parameters corresponding towards each model, and few are outperformed throughout various factors as well.

We hypothesize that in the task of classifying knee osteoarthritis from radiographic x-rays, larger pre-trained models with a greater number of parameters will achieve higher accuracy than smaller models, due to their ability to capture more detailed as well as complex patterns and features within the images. We utilize three pre-trained architectures (a) MobileNetV2, (b) ResNet50, and (c) VGG16 to test our hypothesis. These models have the number of parameters ranging from 3.5 to 138.4 million parameters which makes them good candidates for testing the hypothesis. Additionally, they represent a range of model complexities and parameter counts—MobileNetV2 is a lightweight model designed for efficiency, ResNet50

offers a balance between depth and computational cost, and VGG16 is a deeper, more complex model known for its strong performance in image classification tasks.

Results

The experiments in this study were conducted to identify the impact of increasing model complexity and number of parameters in the task of classifying knee osteoarthritis from radiographic x-ray images, which is a crucial task for early diagnosis and treatment of the disease. Given the advancements in deep learning, pre-trained convolutional neural networks (CNNs) have shown promise in medical image classification tasks. However, there is a gap in understanding how the size and complexity of these models impact their performance specifically in the context of knee osteoarthritis detection. By evaluating models of varying sizes - MobilenetV2, Resnet50 and VGG16 - this experiment seeks to determine whether larger models with more parameters offer a higher accuracy in capturing the intricate details within x-ray images.

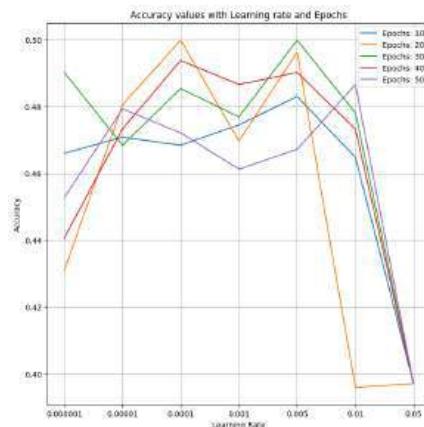


Figure 2. MobilenetV2 Multi-line Plot Graph. The following multi-line plot graph was generated utilizing the matplotlib programming library. This is assisting in terms of further analysis, evaluation, and interpretation of the data. Specifically, this graph depicts the various points represented as values from the corresponding model training data tables. This specific multi-line plot graph demonstrates the data trend as well as the accuracy points corresponding to the algorithm of MobilenetV2.

The experiment was conducted by creating disjoint sets of train, validation and test subsets of the original dataset, followed by hyperparameter tuning in which all algorithms varied among hyperparameter combinations. I utilized accuracy as the principal form of performance evaluation. Accuracy is defined as the percentage of correct predictions for the test/validation data.

Validation results as well as further evaluation of the test images results for MobilenetV2, ResNet50, and VGG16 are shown in Table 1 and Table 2 respectively. The highest validation accuracy in the case of MobileNetV2 was obtained with a learning rate of 0.005 and epochs value of 30, as well as an alternative, equivalent score consisting of an epoch value of 20 and base learning rate value of 0.0001. In contrast, RestNet50 achieved the highest validation

accuracy across all three algorithms of 0.6295(62.95%) with a learning rate of 0.0001 and an intriguing epoch value of 50. VGG16 achieved the highest model validation accuracy of 0.5932(59.32%) with hyperparameters of 0.0001 as a learning rate, and an epoch value 30.

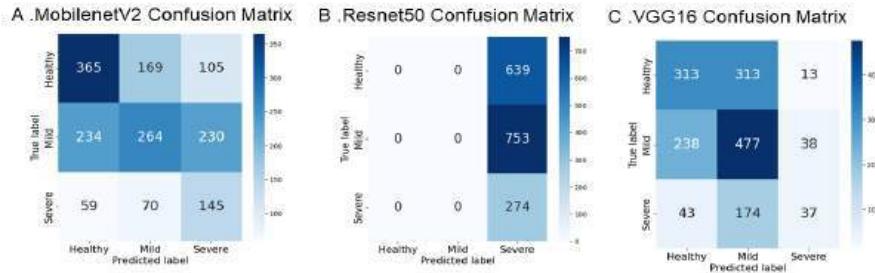


Figure 3: The confusion matrices for the analysis of the spectrum of obtained accuracies corresponding to the optimal model of **A) MobilenetV2 Algorithm** **B) Resnet50 Algorithm**. **C) VGG16 Algorithm**. This exemplifies not only a visual representation of the data, but a data balance clarification as well. The correctly and incorrectly predicted number of images for each classification(Healthy, Mild, Severe) in terms of the highest reached accuracy with each algorithm individually is shown as well. Confusion matrices show how accurate the model distinguishes between different severity levels of knee osteoarthritis.

The models with the highest validation accuracy were ultimately utilized for evaluating their performance on the test subset. This process, simply referred to as the evaluation of the test images, was considered as the concluding result in which the optimal algorithm is concluded. Furthermore, alternative depictions as well as interpretations of data are also generated such as a confusion matrix, and classification report. The accuracies obtained by the algorithms of MobilenetV2, ResNet50, and VGG16 throughout this process were 0.4298(42.98%), 0.4479(44.79%), and 0.4782(47.82%) respectively.

In summary, The MobilenetV2 algorithm had an accuracy of 50% in terms of the model training process, and 42.98% throughout the evaluation of the test images. The convolutional neural network algorithm of mobilenetV2 provides classification capabilities under computing constraints in devices storing minimal amounts of data, such as smartphones. This implementation leverages training and transfer learning from ImageNet to the dataset(10,11). The algorithm of ResNet50 possessed an accuracy of 62.95% and 44.79% corresponding to the same processes. This versatile, renowned convolutional neural network algorithm is popularly known for training through supervised learning as well as affect detection, image processing and recognition, and more(12). Finally, the algorithm of VGG16 was consistently performing similar to the others in terms of prediction balance, and prediction accuracy as well. It performed with an accuracy of 59.32% throughout the model training process, and an accuracy of 47.82% throughout the process of analysis and the evaluation of the test images.

The hyperparameters, as the principal independent variables of this experiment, had great significance. The hyperparameters, such as epochs, learning rate, and batch size, control various aspects of the training process. For example, epochs determine the number of times the entire dataset is passed through the model, the learning rate controls the size of the updates to the

model's weights, and the batch size specifies the number of samples processed before the model is updated, however, this specific hyperparameter remained constant throughout this experiment. Tuning, tinkering with, and modifying these hyperparameters helps in finding the optimal settings for the best model performance.

The hyperparameter tuning process data was recorded on a matrix exemplifying the hyperparameter combinations as well as acting essentially as a crucial factor in terms of the input of the generated multi-line plot graph. The data for the algorithms of MobileNetV2, ResNet50, and VGG16 are exemplified as decimals, which is the representation of the corresponding output of the model training code as shown through table 1. In this program, the train(80%) and validation(10%) images are used to further evaluate the remaining 10% of images. After all hyperparameter combinations have been recorded and the data table is downloaded into .csv format, a graph is generated utilizing a python programming library renowned for statistics and plotting specifically for programming: matplotlib. The multi-line plot graph displayed in the contents of Figure 2 provides an alternative visualization exemplifying the various points of data on a graph indicating accuracy.

After the evaluation of the test images, various accuracy depictions are generated such as a confusion matrix, precision/recall score, and classification report. These three accuracy depictions of the optimal performing model are utilized for each of the three algorithms, and they facilitate the process of forming conclusions in further analysis and discussion. Figure 3 demonstrates the confusion matrices for every corresponding algorithm. Specifically, this demonstrates the accuracy balance among varying volumes of data. Therefore, the diagonals of this matrix would indicate accurate predictions, and the classification quantity/categorization is listed on the left border and bottom border. In this experiment the categorization of healthy, mild, and severe would apply to the severity of an x-ray image provided from the test images.

Table 1: Example of the hyperparameter tuning process data. This exemplifies the accuracies of various hyperparameter combinations of different neural network algorithms, along with the overall accuracy of the best model through a process known as the evaluation of the test images. For example, in this specific instance, the top most table displaying data initially from the MobilenetV2 algorithm hyperparameter tuning process, is being judged within an approximation of 0.5 as the optimal accuracy. In each of the corresponding tables the columns are categorized in terms of base learning rate($10^{-6}, 10^{-5}, 10^{-4}, 10^{-3}, 5*10^{-3}, 10^{-3}, 5*10^{-2}$), whereas the rows imply the discussion of the epochs hyperparameter(10,20,30,40,50).

MobilenetV2							
Epochs/ Learning Rate	0.000001	0.00001	0.0001	0.001	0.005	0.01	0.05
10	0.4661	0.4709	0.4685	0.4746	0.4831	0.4649	0.3971
20	0.431	0.4806	0.5	0.4697	0.4964	0.3959	0.3971
30	0.4903	0.4685	0.4855	0.477	0.5	0.4782	0.3971
40	0.4407	0.4734	0.4939	0.4867	0.4903	0.4734	0.3971
50	0.4528	0.4794	0.4722	0.4613	0.4673	0.4867	0.3971

Evaluation of Test Images: 0.4298							
Resnet50							
Epochs/ Learning Rate	0.000001	0.00001	0.0001	0.001	0.005	0.01	0.05
10	0.4153	0.5811	0.5993	0.6199	0.5569	0.5787	0.3971
20	0.4976	0.5896	0.6186	0.6053	0.6174	0.6041	0.3983
30	0.523	0.5956	0.6138	0.6041	0.6065	0.5896	0.3983
40	0.5254	0.609	0.6053	0.6174	0.6102	0.6029	0.3971
50	0.5327	0.6041	0.6295	0.6223	0.5811	0.5896	0.3981
Evaluation of Test Images: 0.4479							

The precision/recall score generated in the evaluation of the test images is another significant visual in terms of further discussion. Recall is a performance metric utilized in terms of classification that measures and evaluates the proportion of true positive predictions out of all actual positive samples. In this case, for all x-ray images that consisted of severe knee osteoarthritis, recall would imply the quantity in which the algorithm accurately predicted as severe. Mathematically, this is represented as True Positive/Positive. The precision metric statistically measures the ratio between the True Positives and all of the Positives(13). Throughout this experiment, the precision metric of each categorization in each algorithm would be the quantity of accurate guesses/(accurate guesses+inaccurate guesses). For example, hypothetically, if the precision metric for the severe classification in the MobilenetV2 algorithm analysis was 0.9245, the algorithm is accurate when predicting severe 92.45% of the time in the test images. Notice how, although similar to accuracy, it is still an alternative performance metric. Overall, the visual representations generated from the evaluation of the test images would be of the most significant forms of data, because they judge the optimal model due to the model training process.

Table 2: Example of the hyperparameter tuning process data. This exemplifies the accuracies of various hyperparameter combinations of VGG16

VGG16							
Epochs/ Learning Rate	0.000001	0.00001	0.0001	0.001	0.005	0.01	0.05
10	0.3547	0.4843	0.569	0.5714	0.5823	0.5823	0.3971
20	0.4528	0.5206	0.5872	0.5872	0.569	0.5738	0.3971

30	0.4358	0.5787	0.5932	0.5545	0.5787	0.5908	0.3971
40	0.46	0.5763	0.5799	0.5339	0.5278	0.5751	0.3971
50	0.4709	0.5726	0.5835	0.5327	0.5799	0.5678	0.3971
Evaluation of Test Images:							
0.4782							

Discussion

Several crucial interesting trends were observed from the validation results obtained during hyper-parameter tuning in all three pre-trained models. In the case of MobileNetV2, at low learning rates of 0.000001 and 0.00001, the models were relatively stable, but had low accuracies across most epochs. Increasing the number of epochs impacted the accuracy slightly which shows that very low learning rates slowed down the learning process, preventing models from making significant progress in optimizing their weights. In case of mid range learning rates of 0.0001 to 0.005, the results were more promising. At a learning rate of 0.0001, the accuracy of the algorithm improved steadily reaching 0.49 at 40 epochs. With a learning rate of 0.005, there was a noticeable increase in accuracy peaking at 0.5 for 20 and 30 epochs. This suggests that moderate learning rates allowed the models to learn more effectively without overshooting the optimal weight configurations. Very high learning rates of 0.01 and 0.05 resulted in a low accuracy. The accuracy stayed constant as 0.3971 in case of the learning rate of 0.05 showing that the model did not converge at all. Best results were obtained at moderate learning rates and epoch values of 20-40. Very low learning rates require a very large number of epochs to make progress. On the other hand, very large learning rates result in overshooting of the optional value and not converging as a result of it.

ResNet50 displayed a very high accuracy in comparison to the other models when depicted on the graph in terms of hyperparameters, with a best epochs as 50, best base learning rate as 0.0001, and a total accuracy of 0.6295. As the ResNet50 model proceeded to the evaluation of the test images, it began to have a sudden, unexpected downfall in the accuracy to the best model. It seemed to be only predicting the category of “Severe” as this is exemplified through confusion matrix data. However, several notable inferences as well as data trends can be observed. Similar to MobilenetV2, this algorithm sustained a moderate quantity of the learning rate hyperparameter value. However, throughout the iterative process of learning optimization, Resnet50 seemed to obtain optimization encompassing an epoch value of 50, which astoundingly did not seem to overfit the dataset. In terms of the learning rate hyperparameter, the same can be inferred as MobilnetV2. Alternatively, the 0.05 learning rate value was modified slightly as per epoch, but provided no significant difference. We still conclude that this implies that moderate learning rates optimize accuracy due to the fact that low learning rates may take too long to

converge resulting in instability, and higher learning rates may take a significant decrease in probability of finding the optimal solution.

Lastly, the algorithm of VGG16 contained results that were similar to the test image evaluation in comparison to the model training, consisting of hyperparameter trends similar to MobilenetV2. However, it seems to perform poorly corresponded with the best hyperparameters when faced with a non-severe image, which we have observed is a flowing pattern throughout the experiment. Its best hyperparameters are an epoch of 30, and a base learning rate of 0.0001 which support the consistent conclusion of moderate hyperparameters throughout a spectrum. The two extremes of hyperparameters experimented sustained a relatively constant value, showing major deficiencies, as a base learning rate value of 0.05 remained at a 0.3971 accuracy once more. Corresponding towards a learning rate of 0.001, the accuracy of the algorithm improved steadily reaching 0.5872 when the epoch value was 20. With a learning rate of 0.0001, a notable increase in accuracy was existent, optimizing at 0.5932 for 30 epochs. Generally, optimization was obtained principally with moderate hyperparameters. With a test image subset accuracy of 0.4782, this algorithm consists of the highest accuracy in terms of test images and in terms of the average of the hyperparameter tuning process data and test image results. Therefore, our hypothesis is proven that in the task of classifying knee osteoarthritis from radiographic x-rays, larger pre-trained models with a greater number of parameters will achieve higher accuracy in comparison to smaller models, due to their ability to capture more detailed as well as complex patterns and features within the images. This is due to the fact that the algorithm of VGG16 consists of the greatest quantity of parameters among all algorithms included in this experiment, 138 million. Therefore, as stated throughout the hypothesis, VGG16 would be more capable of capturing more complex image features and patterns.

All three algorithms along with the optimal model seemed to be confused in the midst of the categorizations of “Healthy”, and “Mild”, which was crucially notable throughout the confusion matrix analysis. This may be due to the fact that there is only a slight inconspicuous difference in which the knee extends from varying severities. This also may be concerning the proximity of the narrowing joint space in which these two categorizations impact. Alternatively, although MobilenetV2 did not consist of the optimal model, its performance was capable of reaching a maximum average similar in comparison to the optimal model algorithm, VGG16. This slight difference is still a notable discussion due to the fact that the algorithm of MobilenetV2 consists of the minimal amount of parameters among the models, exemplifying significant variation among parameter quantities. Furthermore, the MobilenetV2 algorithm consists of the optimal data variation and balance in terms of confusion matrices, and is renowned for being easily deployed in an excellent range of computational environments, which substantially impacts the experimental widespread, facilitating the process of the deployment of the model. ResNet50, although surpassing VGG16 throughout hyperparameter tuning, had a particularly significant decrease in comparison to VGG16 accuracy standards, implying that data arrangement and processing had a major malfunction, while the confusion matrix of Resnet50 does indeed suggest that It was not entirely due to the inaccuracy of Resnet50, but a system error

through image analysis, selecting the “Severe” categorization as default. It is also noteworthy that for all algorithms tested, their best model significantly decreased in terms of accuracy performance when tested with the test image data. This implies and suggests that the alternative test data images may have been more complex, which is a crucial experimental factor.

The dataset utilized is fairly complex and there have been many comments about it on its platform(14). Furthermore, it was first providing us with an accuracy below average each time we modified the hyperparameters. However, we considered experimentation to be still viable, and will give accurate results in terms of data and statistical comparison relatively. For future experimentation, a different database can be sample tested through algorithmic learning before experimentation. We drifted to utilizing various techniques such as data augmentation, different algorithms, and eventually making the data more concise and relying on categorizing the images into healthy, mild, and severe, because we were originally using the Kellgren-Lawrence grading scale for knee osteoarthritis classification. The Kellgren-Lawrence grading scale evaluates osteophytes and joint space narrowing to assign a score between 0 to 4 (15). It evaluates a specified skeletal image and provides it with a designated grade, a number ranging from 0 to 4, in order of severity. 0 would signify no sign of osteoarthritis, while 4 would indicate and represent a severe source of osteoarthritis in the x-ray. We originally planned on experimenting with this utilizing machine learning, however the inaccurate results caused us to revert to a generic categorization.

Performance could have been potentially benefited due to the sourcing of more data and using other architectures of the model which might result in a better ability to distinguish between various severity classifications of X-rays which would also be significantly more substantial and impactful. Furthermore, a larger spectrum of hyperparameters would be extremely effective in terms of precise experimentation, as it would offer more opportunities in terms of obtaining maximum perfection. Recently, researchers have started utilizing [optimization algorithms](#) for the automatic adjustment of the hyperparameters of CNNs(16). This would have facilitated the time consuming process of hyperparameter tuning, and lead to an efficient as well as more precise and accurate experiment in the future. Another method to be considered beneficial in terms of future experimentation is Generative Adversarial Networks. Generative Adversarial Networks are the specific classification of algorithms that are capable of creating new data instances that act as the experiment train data. This new data will be automated and modified by the models themselves, and we have found various medical applications that have utilized this categorization of image generation resulting in an outperforming accuracy. Other technological methods such as an elaborate utilization of data augmentation and Generative Adversarial Networks would benefit this experiment in the future.

These results are significantly impactful due to the fact that they exemplify the utilization of artificial intelligence for substantial benefits, specifically to the medical field in this instance. These results are excellent considering the minimal volume throughout the dataset. This also alludes to several research questions, as well as potential future experimentation such as the study of the machine learning effect on osteoporosis, sarcopenia, and various other

musculoskeletal disorders and conditions concerning arthritis. This would be substantial, as well as thought-provoking as we could potentially compare data, results, and individual analysis to form more conclusions.

Overall, our experiments support our hypothesis that larger models with complex architectures capture the patterns better in case of complex images like x-rays for knee osteoarthritis. VGG16, which has the largest number of parameters across the three models tested, shows the highest test accuracy of 47.82% for categories. This dataset and experimentation has also led to the conclusion that further research into architectures is needed to improve the accuracy to a value that is acceptable in a medical scenario.

Materials and Methods

Dataset

The data repository is from Mendeley and it was sourced from the OAI database. Osteoarthritis Initiative (OAI), is a multi-center, longitudinal, prospective observational study of knee osteoarthritis (OA). The OAI is sponsored by the National Institutes of Health (NIH), specifically the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and other partners. This database contains various types of data, including clinical evaluation data, radiographic (x-ray) images, and magnetic resonance imaging (MRI) data of the knee, which researchers can use to study knee osteoarthritis. It was capable of being uploaded on platforms such as google drive, and other filing platforms. The algorithm processed the images in this dataset throughout experimentation and the process of hyperparameter tuning. It was divided into randomized categorizations among the images: train data(80%), test data(10%), and validation data(10%). As it was necessary in our case, the algorithm output was modified and converted into a more generic as well as brief categorization to prevent major error with the Kellgren-Lawrence grading scale format. We originally planned on experimenting with this utilizing machine learning, however the inaccurate results caused us to revert to a generic categorization. The code ran throughout the experiments was not generated, and it was created on a python platform known as Google Colab, a software library known as Tensorflow was utilized principally in terms of the machine learning aspect. This code generated the data as well as the statistical depictions, and was the principal function of general experimentation. Google suite was utilized for the purpose of file and data storage, as well as documentation.

Experimental Process

As the advent of this experiment's model training, the Convolutional Neural Network algorithm of MobilenetV2 was experimented with first. However, this specified order is not necessarily essential in terms of the general experimental design. The hyperparameter tuning process is a model training process in which the accuracy of an algorithm is recorded on a spreadsheet, each slot corresponding to a hyperparameter combination. This data is utilized to depict A.I. generated multi-line plot graphs, confusion matrices, and other depictions as well as various alternative visual representations of data. These visuals assist in terms of the analysis as

well as evaluation of the data and statistics. The hyperparameter spectrum that was utilized throughout experimentation was fairly large, ranging from an epoch of 10-50, and a base learning rate ranging from 10^{-7} to 0.05. These experiments for each chosen algorithm were run with the Adam optimizer(17). However, various algorithm analysis hyperparameters remained constant such as batch size. Experimentation within a larger variety of hyperparameters would be substantial for more potential best models. However, this process would require an extensive duration of time, and can be extended for the optimal performance. Once all hyperparameter combinations have been recorded, a graph was generated utilizing a programming library known as matplotlib, renowned for statistics and plotting specifically for programming. This is assisting in terms of further analysis, evaluation, and interpretation of the data because it provides an alternative visualization exemplifying the various points of data on a graph indicating accuracy. For the optimal analysis of the data, additional visual representations were generated such as the confusion matrix known for facilitating the process of accuracy clarification and data volume balance, and a classification report as well as a precision/recall score, which are also essentially displaying accuracy as a metric.

Data/Additional Background

For valid, viable results, this experiment was conducted in two sections of algorithm analysis: The hyperparameter tuning process, used for data in the multi-line plot graph and the general spreadsheet, and the evaluation of the test images, utilized to generate the confusion matrix as well as various other accuracy depictions. As these images differentiate, the accuracy may vary, however, the two principal data points should presumably be in proximity. This can be simplified by simply calculating the average, or any other statistical measurement, which is the rationale behind the fact that only these two numerical values were displayed for each corresponding algorithm as the optimal performance. These substantial processes were then repeated with the remaining algorithms, VGG16 and ResNet50. Finally, a conclusion was statistically as well as theoretically formed due to the experimental data provided, and the best model among the various algorithms were converted into a format in which it is accessible, and the model was deployed as a REST API so that people globally with an internet connection had access. AWS lambda and AWS Gateway was used to achieve this.

Risks and Safety

This experiment is conducted entirely through a device, and does not include any experimentation in relation to chemically or physically dangerous activities. Therefore, there are no caution notices corresponding towards this experiment.

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Geopolitical Gambits: Oil Prosperity and Idiosyncratic Diplomacy in Gaddafi's Libya By Evan Chen

Throughout the latter half of the 1960s and 1970s, the international geopolitical landscape resembled a giant chessboard, with the United States and the Soviet Union maneuvering for hegemonic control. Within the context of the Cold War in which these competing superpowers were hesitant to involve themselves directly in open conflict, the pair fought indirectly by backing their respective sides whenever a nationalist movement arose in various regions around the globe. Before the Soviet Union established their interventionist policy in the continent of Africa by backing a Communist militia in Chad in 1974-75 as well as supporting Somalia's military coup with tanks and weapons, a singularly charismatic leader named Muammar Gaddafi rose from humble beginnings to organize an overthrow of the weak Libyan monarchy in 1969. Gaddafi's timing was impeccable, as the previously poor nation leveraged a rapid rise in oil prosperity, which provided fertile ground for Gaddafi to impose a socialist authoritarian government to meet the nationalistic fervor of the Libyan public. This paper will analyze Gaddafi's positioning Libya as a major exporter, which stimulated Gaddafi's ambitions in expanding Libya's influence in both Arab and African nations; then, it will demonstrate how his irrational decision-making due to his failure in maintaining stable relationships with both Pan-Arab nations and Sub-Saharan Africa; finally, this paper will assess the effects of Gaddafi's isolation and condemnation from global superpowers. While tactically skilled with a keen understanding of tribal politics and enriched by an oil economy, Gaddafi failed to grasp how his nation fit within the broader context of foreign diplomacy, which led to his isolation as a leader.

Before Muammar Gaddafi's rise to power in 1969, Libya was a monarchy characterized by its decentralized governance and large socio-economic disparities between the King's Court and the masses, which set the stage for a revolutionary change. In the latter half of the 1950s, the country was overwhelmed by significant regional inequalities and a lack of cohesive national governance; King Idris's attempt to rule through the "United Kingdom of Libya" federal system, which sought to balance power among the three distinct regions of Cyrenaica, Tripolitania, and Fezzan, began to fail. His ability to maintain power relied heavily on close patronage with influential political networks, including the Sanusi-aligned tribes, and was further sustained largely due to his dependence on "the British and American military protection and financial aid" (Bell 16). This dependence on foreign support illustrated the weaknesses of his regime and fueled growing resentment among young Libyan nationalists, including Gaddafi. However, the anger amongst the Libyan population was significantly intensified by King Idris's consolidation of wealth following the discovery of oil.

King Idris's push to position Libya as a major oil exporter in 1959 centralized governmental power for economic development, which, while drastically increasing the nation's

wealth, also heightened regional conflicts. The discovery of oil brought substantial revenue to the country as the annual income per capita went from \$25 in 1959 to \$2000 a decade later (Pargeter 41). The overall revenues from petroleum exports increased rapidly as well, growing more than “fifteen fold from \$40 million in 1962 to \$625 million in 1967” (St John 76). Within eight years of its first shipment, Libya was the world's fourth largest exporter of crude oil, a rate of expansion previously unknown anywhere in the industry's history. However, this rapid economic growth brought uneven distribution of the resulting wealth, seeing that the newfound development heavily favored Cyrenaica, where the Sanusi monarchy had its stronghold. This centralization of economic control and the inequity exacerbated the already existing regional disparities in Tripolitania and Fezzan. The existing federalist government failed to modernize and was replaced by a more centralized state in 1963. The government had failed to stamp out corruption in the leaner times, as the oil money only increased its scale: the King's Court “failed to distinguish the public treasury from the privy purse” (Anderson 518). As the bureaucratic controls failed to curb wanton dishonesty, the stage was set for a revolution.

Muammar Gaddafi's rise to power was facilitated by widespread dissatisfaction with King Idris's regime and motivated by Libyan nationalist sentiments through the desire for a more equitable distribution of oil wealth. His education during his youth was marked by constant changes due to expulsions rooted in his fervent nationalist views. This transition eventually landed Gaddafi in a military academy in Benghazi during 1963, following a defiant confrontation with an English teacher in Libya: "You are the one who should leave for good, not just this room but the entire country" (Pargeter 49). Far from being daunted by his military training or his time in Britain in 1966, the young nationalist's resolve only deepened. Gaddafi notably resisted conforming to foreign influences by refusing to learn English, which symbolized his rejection of Western dominance and a commitment to Libyan sovereignty. His general disdain for their imperial colonizer laid the groundwork for his revolutionary ambitions, culminating in the Al Fateh Revolution on September 1, 1969. Emulating the views of Egyptian President Gamal Abdel Nasser, Gaddafi was “devoted to his goals of Arab unity, anti-imperialism, and Arab socialism, to which [he] added an explicitly political attachment to Islam” (Anderson 520). The establishment of Gaddafi's regime in an unofficial alliance with Nasser aligned his revolutionary ideology with broader pan-Arab and Islamic movements.

Under Gaddafi, Libya underwent significant economic transformations, including most significantly the nationalization of the oil industry, which aimed to redistribute wealth and reduce dependency on foreign aid for development. Immediately after the Free Unionist Officers seized power after the September Coup in 1969, the Revolutionary Command Council (RCC), headed by Gaddafi began to implement a socioeconomic and political revolution in Libya. Despite rapidly modifying from a capital-deficit state to a capital-surplus state, the extraction of oil in Libya was heavily constrained by foreign petroleum companies: “Libyan oil exports exceeded 3 million barrels per day (bpd); however, the revenue received per barrel of oil remained one of the lowest in the world” (St Jon 76). In response to foreign intervention, the RCC opened negotiations with the oil companies working in Libya, eventually gaining a majority control in

all of them through modified participation agreements or outright nationalization (St Jon 76). By 1973, despite Gaddafi's efforts that led to significant increases in revenue and greater control over oil production, the Libyan authorities assumed that similar aggressive tactics could be applied across other sectors with less inelastic demand like rangeland, pasture, and water: "the RCC misinterpreted the political lessons to be drawn from its confrontation with the oil industry to the detriment of economic policy in other areas" (St John 76). Such arrogant oversight eventually led to teetering diplomatic relations, as Gaddafi continuously assessed Libya's status above all.

Domestically, Gaddafi strengthened his rule in the 1970s through internal political reforms, transforming Libya into a "Jamahiriya" or "state of the masses." From the outset of his regime, Gaddafi's main ideology linked freedom, socialism, and unity. The RCC's approach to socialism was too strict, adhering too often to blunt theoretical doctrine instead of pragmatic implementation. Beginning in 1973, the government delivered basic socialist tenets like increased housing, improved health care, and greater access to education; however, this spending was curbed over time as expenditures on arms, cash flow problems, and the lack of economic growth took hold of the Libyan economy in the latter half of the 1970s (St. John 77). Despite socialist rhetoric, the old elites maintained cohesion through a system of patronage, spoils, and privileges distributed among urban interest groups and tribal elites (El-Kikhia 4). In this time, Gaddafi sought to brand himself as a political thought leader with the publication of his Green Book, a manifesto that outlined his political and economic beliefs. In spite of having been inspired by Mao's *Little Red Book*, the political philosophy throughout the book rejects capitalism, communism, and representative democracy. Instead, Gaddafi proposes direct democracy overseen by the General People's Committee that allows direct political participation for all adult citizens (St John 77). The widespread publication of the Green Book urged greater governmental management of private enterprise in the fall of 1978, as workers took control of 200 companies. The government also increased its redistribution of land over the next three years on the Jefara Plain west of Tripoli. By 1981, the socialist takeover was nearly complete, as the General People's Congress announced the state was nationalizing all import, export, and distribution functions (St. John 77). The Libyan approach to socialism became more radical than that of its neighboring states, but Gaddafi aspired to alter other African countries under the similar Islamic-socialist ideology.

Muammar Gaddafi's ambitious attempts to strengthen Libya's regional ties and unify Arab and African nations under his leadership ultimately backfired, leading to significant financial losses and increased diplomatic isolation. Gaddafi's efforts in unifying with Libya's closest Mashriqain neighbors to consolidate his political position and strengthen his influence on regional politics failed after his determination "to exceed his mentor [Nasser] by injecting uncompromising militancy into the ideology he had adopted" (Ronen 108). Gaddafi's increasing obsession with Arab unity soured Tripoli's relations with Egypt and damaged its prestige in other Mashriq countries, which were concerned about Gaddafi's increasing activism. Even his new attempt in creating a new union, known as the Federation of Arab Republics consisting of Libya,

Syria, and Egypt, soon collapsed after its formation in October 1971 (Ronen 108). To add insult to injury, the October 1973 War, launched by Egypt and Syria against Israel, excluded Gaddafi from the core of the Arab-Israeli conflict. After facing this humiliation, Gaddafi looked instead to Africa as an outlet for his political ambitions after a surge of oil wealth. In early 1971, after Ugandan ruler Idi Amin deposed the regime of Apollo Milton, Gaddafi saw an opportunity to extend his influence into Sub-Saharan Africa. He quickly formed an alliance with Amin, providing military support and financial aid to bolster Amin's regime after Amin expelled all Israelis from the country on March 27, 1972. However, due to Amin's propensity for fomenting domestic political strife and, indeed, his emerging reputation as a cruel despot, Libya paid a high price for its commitment to Amin's collapse in April 1979:

Libyan troops reportedly endured about 400 casualties and the loss of large quantities of military equipment. In addition, Libya was forced to pay Tanzania and the new regime in Uganda the sum of US\$60 million to ensure the safe withdrawal of its forces and secure the release of its captured troops. Libya also suffered a diplomatic backlash across the African continent (Ronen 153).

After Libya withdrew its forces from Uganda, Chad became more attractive to Libya, which needed an alternative foreign arena for rehabilitating the regime's prestige and the army's morale. By early 1979, Gaddafi became interested in the Aouzou Strip that was rich in uranium in Chad. However, the Libyan-supported coup to achieve unity and "integration and identity between the two countries in their political and social systems" (Ronen 163) triggered international condemnation from the Organization for African Unity (OAU), the US, and USSR. Pressure from abroad forced Gaddafi to retreat from Chad. In addition, Gaddafi failed to gain the necessary consensus to hold the OAU summit in Tripoli in August 1982, drastically minimizing his influence in the African continent.

Throughout Gaddafi's rule, Libya's international relations shifted between conflict and reconciliation in global Cold War politics, as it remained in a contentious stance against Western imperialism while failing to fully align with the Soviets. Relations with the United States deteriorated in 1975 when the US refused to deliver military transport planes that Libya had purchased (Anderson 530). This last minute repudiation was attributable to Gaddafi's participation in the oil boycott of the United States, which followed the Libyan-sponsored 1973 Arab-Israeli war. Additionally, Libya's growing ties with the Soviet Union during the Cold War era raised alarms in the U.S., leading to a reevaluation of military sales that might enhance Gaddafi's military capabilities. Tensions escalated even further as the US accused Libya of sponsoring terrorism, prompting Gaddafi to counter by accusing the US of imperialism and terrorism in its support for Israel. During the Iran Hostage Crisis in 1979, a government-backed mob stormed the American embassy in Tripoli (Anderson 530). Within the Cold War alignment between the USSR and the US, Libya received "an estimated 12 billion dollars' worth of equipment [that] had been transferred to Libya by the USSR since 1976, and there were

estimated to be about 2,000 Soviet military advisors, and an equal number of East German and Cuban technicians, in Libya” (Anderson 526). This alignment did not imply that Libya functioned as a Soviet satellite, as their diplomatic and military arrangement was more of a business relationship rather than ideological, as Libya refused to sign the “Treaty of Friendship” that was standard for Soviet business dealings (Anderson 526). Part of the problem was religious, as the secular Soviets referred to Gaddafi as a “fanatical” Muslim who would never fully align with the international Communist cause. In 1982, Gaddafi wrote the following memo to the heads of the embassies of the USSR, Bulgaria, Poland, Czechoslovakia, Hungary, and Romania:

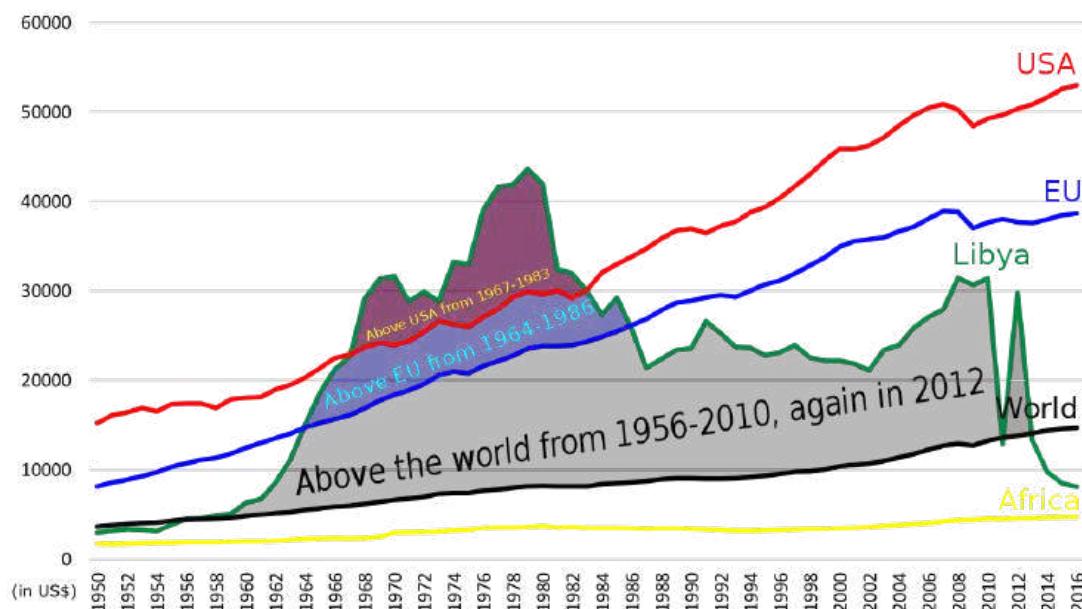
We have finally recognized that our relations are just of a commercial and not of a friendly nature. Your arms you are selling to us are looking to us like children’s toys... We have stopped all arms deals with you, since we do not have confidence any more in your missiles, tanks, and aircraft. The friendship and the relations between you and us are in serious danger. Israel is fighting against us together with America. However, we are facing Israel alone... We do regret the situation that has emerged and are asking for urgent transmission of this position to your governments. There is nothing else left to say (Schaefer 1).

Gaddafi’s erratic tone speaks to his broader errors in diplomacy, as he isolates himself by speaking in absolutes and issuing ultimatums that strain relationships even further. This approach left little room for nuanced diplomacy or compromise. His rhetoric not only alienated potential allies in the Eastern Bloc but also reduced the flexibility and support Libya might have garnered from other non-aligned or developing nations. Gaddafi’s confrontational style, combined with his ideological unpredictability, meant that Libya often found itself isolated on the global stage. Thus, operating between competing hegemonic networks, Gaddafi’s idiosyncratic diplomacy cut a singular path that defied easy categorization.

In the intricate choreography of geopolitics, Muammar Gaddafi’s Libya emerged as an unlikely player on the global stage, protected by oil prosperity that underwrote his irrational diplomatic maneuvers. As the Cold War influenced international affairs, Gaddafi navigated the turbulent waters of superpower rivalry with a blend of ambition and audacity. His ascent to power in 1969 marked a seismic shift in Libyan politics, fueled by nationalist fervor demanding equitable distribution of oil wealth long shackled by monarchy. Despite his successes in seizing power, his erratic decision-making and penchant for military posturing strained relationships with both regional allies and global superpowers, which left Libya increasingly isolated. Internally, Gaddafi’s socialist experiments sought to remake and modernize Libyan society, yet his dogmatic adherence to ideology often clashed with pragmatic realities, ultimately fostering discontent and increasing socio-economic disparities as a result of poor governance. His ambitious attempts at regional political consolidation faltered in both the Arab world and the African continent, which culminated in financial losses and diplomatic setbacks that indicated the limits of his grandiose vision. On the international stage, his confrontational rhetoric and

erratic behavior alienated potential allies and further isolated Libya. For proof, look at the evocative image of Gaddafi posing with other world leaders, including US President Barack Obama, in the Appendix. His costumed performance was underwritten by the graph above that shows the unprecedented spike in Libya GDP per capita growth that outpaced even the US during its oil boom. Ultimately, these two images in the Appendix are linked, as Gaddafi consolidated power at the exact right time to install himself as a dictator with little regulatory oversight. In cutting his own singular, highly performative path through 20th Century geopolitics, his iconic legacy is ultimately one of contradictions and missed opportunities.

APPENDIX



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- I have neither given nor received any unauthorized aid on this essay

The Human Brain: Anatomy, Evolution, and the Complex Systems of Pleasure

By Max Yu

Key Terms Human brain, neuroplasticity, evolution, pleasure, survival mesocorticolimbic circuitry, dopaminergic system

The brain might just be one of the most complex, amazing organs ever. It manages many physical operations while simultaneously controlling a plethora of emotions, thoughts, and feelings that either add to or take away from what it means to be human. The human brain occupies the center of a central nervous system, comprising billions of neurons connected by trillions of synaptic connections so that humans can perceive, react, and adjust to their environment. However, to get a better sense of the brain, one must delve into the brain's anatomy, its history of development over time, and how its nervous systems function to stabilize essential elements like enjoyment. Thus, this brief essay will discuss these elements from readings in *Psychological Science 7th Edition* by Elizabeth A. Phelps, *Direct Fit to Nature* by Uri Hasson, et al., and *Pleasure Systems in the Brain* by Kent C. Berridge and Morten L. Kringelbach.

The Anatomy of the Human Brain

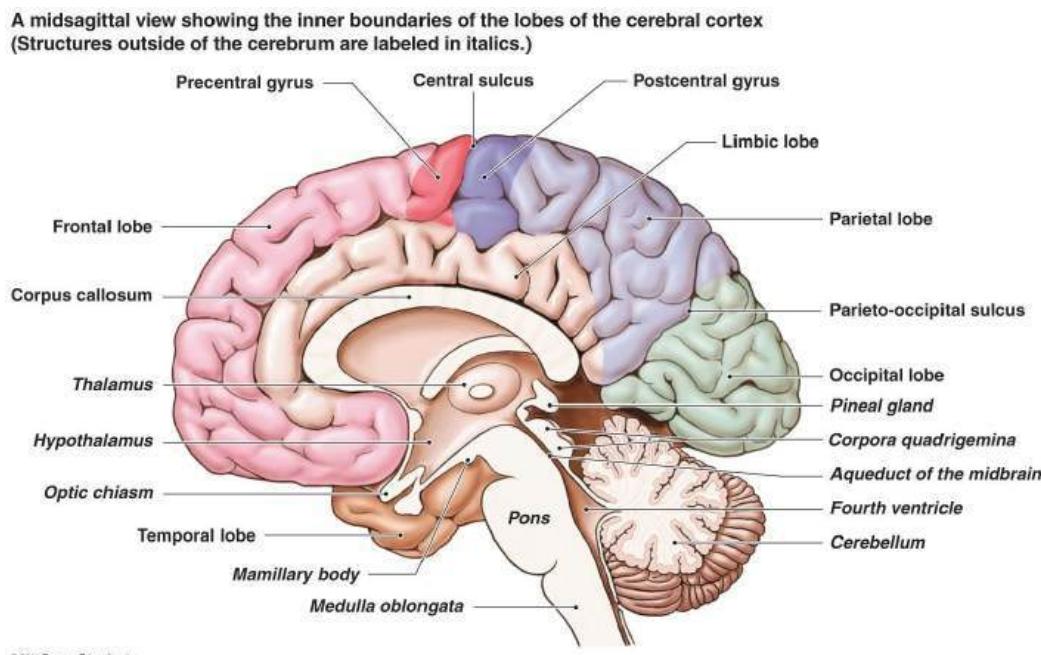


Figure 1

Humans can accomplish so much because the brain is divided into compartments. Distinct major regions of the brain regulate everything from basic functioning to advanced processing and problem-solving. For example, the largest region is known as the cerebrum, which itself has two hemispheres and four lobes: the frontal lobe, parietal lobe, temporal lobe, and occipital lobe.

The **frontal lobe** is responsible for higher-level thinking. It is involved in the processes of thinking—namely, decision-making and problem-solving—and includes parts of personality. In addition, the social control and executive function (*Psychological Science 7th Edition*) of the prefrontal cortex—which humans utilize to a greater extent than other animals—is found in this area of the brain. Thus, when this area is compromised—as in the case of Phineas Gage—it stands to reason that personality changes occur afterward because this area is what makes a person who they are and regulates what they do. Located toward the back of the brain, the **parietal lobe** corresponds to the processing of touch sensory information and body awareness and movement. For example, the somatosensory cortex is responsible for processing sensory information from touch. The **occipital lobe** is located at the back of the brain and corresponds to vision; for example, the primary visual cortex (V1) helps process basic visual features (*Psychological Science 7th Edition*). The **temporal lobe** is essential for hearing, understanding language, and memory. For example, the hippocampus is where long-term memories are created, and Wernicke's area is how we understand spoken and written language.

Furthermore, there are subcortical structures. For instance, the **corpus callosum** is a dense white matter tract that connects the two hemispheres together, allowing them to communicate with each other and connect. Another subcortical structure operates more as an under-the-radar device; this is the **basal ganglia**, which aids in motor control, procedural learning, and habit. The basal ganglia is a set of three nuclei: the caudate nucleus, putamen, and globus pallidus, which account for the learning of automatic, fluid, cohesive physical movement. Therefore, dysfunction in the areas that degenerate here is linked with such movement disorders as Parkinson's.

Of all the fascinating systems in the brain, none is more fascinating than the **limbic system** which regulates emotional functioning along with memory formation and retention. The limbic system is composed of the **amygdala**—which regulates emotions associated with fear and pleasure—and the **hippocampus**—which regulates spatial navigation and memory. Ultimately, all functioning in conjunction with the larger limbic system creates a superpower that assists in much processing of emotional and automatic/reactive behavior that people engage in without a second thought during daily life. (*Psychological Science 7th Edition*).

Along with these more general regions, many more notable autonomic actions are processed by brainstem components located in specific regions. For instance, the **midbrain** is responsible for reflexes to hear and see. The **pons** regulates the ability to sleep, wake, and breathe. The **medulla** assists with involuntary actions such as a beating heart and blood pressure. Thus, such areas keep the body in the expected range of operation without any voluntary activity

or involvement. Similarly, the **cerebellum**, underneath the occipital lobe, has the same type of function with general fine motor functioning, balance, and even attention and language.

Evolutionary Perspectives on Neural Networks

Understanding how and why the brain operates with such complexity but so efficiently has much to do with how it evolved over time. For example, much at present in neuroscience suggests a comparison between biological neural networks (BNNs) and artificial neural networks (ANNs), pitted against one another for optimization and learned adjustment. In *Direct Fit to Nature*, the concept of evolution itself is something that's much easier than it's implied—it's a "blind fitting process" where life forms and objects learn how to evolve, not from creation, but from death.

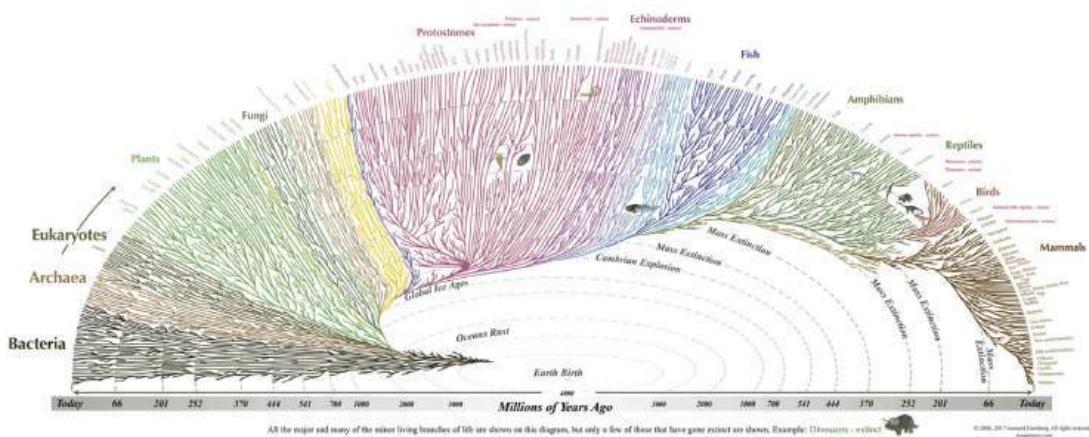


Figure 2

The human brain has adapted to specific evolutionary pressures over the past millions of years. For example, evidence exists of larger brain sizes in hominids as increasingly social hierarchies were engaged, increasingly complex webs of environmental opportunities and dangers were addressed, and tools—the present-day size of the prefrontal cortex increased (areas relative to intentional purposeful activity and lingual communication increased significantly) (*Direct Fit to Nature*). In addition, with the slowly increasing neocortex, the "social brain hypothesis" comes forth with the prevailing rationale for human intelligence being the capacity to regulate and maintain vast social networks.

Yet this was not a seamless, linear development. The course of these millions of years in a linear progression saw certain structures becoming exapted along the way. For instance, the basal ganglia was part of basic motor skills in the primary brain, but it, over time, became repurposed in the secondary brain, associated with decision-making and habits. This exaptation of old neural pathways illustrates how evolution fixes issues of natural dynamics (*Direct Fit to*

Nature). In addition, evolution demonstrates how plastic the brain is. Neuroplasticity is the formation of new neural pathways over a lifetime. This plasticity is behind the aspects of learning and memory and how the brain compensates for itself after trauma. Therefore, from an evolutionary perspective, neuroplasticity enables humankind to solve new challenges, whether more effective application of learned skills, adapting to a novel range of temperatures, or establishing new patterns of social engagement (*Direct Fit to Nature*). In addition, adults have a plastic brain well into adulthood.

Yet another vital yet nuanced comparison stemming from the neuroscience of BNNs and how ANNs operate today is the notion of generalization. Where ANNs generalize by adjusting their synaptic weights—learned associations—BNNs and humans alike possess similarly astounding amounts of generalization through cumulative sensory experience over time. The brain knows how to generalize from one experience, adjusting its pathways to anticipate or remember a second. Thus, where BNNs and ANNs are thought to be "over-parameterized" models (more connections than necessary because they can), humans also possess a plethora of redundant connections more than essential for proper functioning (*Direct Fit to Nature*). Thus, both systems can generalize from an exorbitant amount of data without anyone telling them how to do it or programming it to do so efficiently in a second sense; it's merely a "direct fit to nature." The elegance of BNNs and how they operate in real time with sensory input and feedback processing is akin to how the brain grew within a complicated, nonlinear, chaotic, and sometimes adverse world. Such an application is by far a reality from much of contemporary neuroscientific published literature which, through a reducible experimentalistic stance, infers a human-understandable brain function to then try to piece together what was actually going on in the brain. Yet natural learned and human-inspired creations show that the ultimate control for ultimate function comes from operating within the already established complex realities—not reduction (*Direct Fit to Nature*).

One interesting aspect about this direct fit model is the interpolation vs. extrapolation inference for what the neural training entails. Where statistical models would claim that to create the best generalization fit, one should extrapolate, it's the opposite for the brain. The brain learns to generalize from experience and only generalizes from what it knows—only generalizing from well-sampled (learned) information and learned over time. Thus, the over-parameterization of BNN and ANNs serves this purpose quite nicely. They become specialists and are great at interpolation since all their trained/exposed parameters tell them how to do things (e.g., face learning, language learning) extremely well based on previous experience (*Direct Fit to Nature*). But they fail at extrapolation—which suggests they cannot learn how to do anything beyond what they've learned before.

Pleasure Systems in the Brain



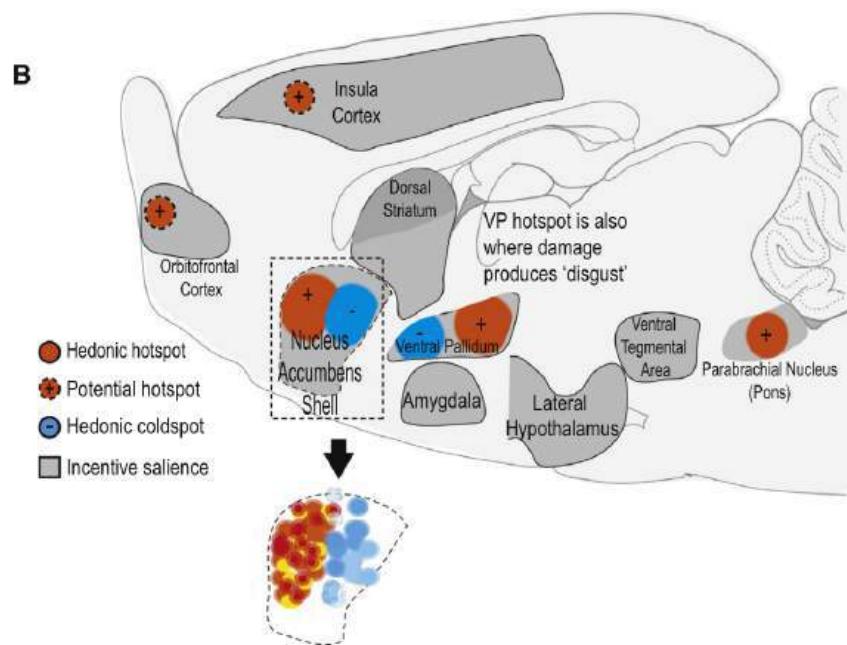
Figure 3

To study brain reward systems is to understand the varying neurocircuitry that renders pleasure, with incentive, motivation, and reward effects. They are all linked by the **mesocorticolimbic circuitry** that integrates the separate pathways for liking (hedonic impact), wanting (incentive motivation), and learning (associative/cognitive representations). Therefore, each component involves the brain in an active, proactive, and reactive process for empowered action and involvements with learned associations for the productive means of survival when pleasurable actions occur from eating, socializing, and reproduction (*Pleasure Systems in the Brain*).

Pleasure systems operate in specific, localized regions of the brain. The **nucleus accumbens (NAc)** is the center for pleasure, as a mediator of liking and wanting. The **ventral pallidum (VP)** acts as an intermediary in the pleasure pathway, making pleasure even more pleasurable through specific neuropeptides. Regions of the brain associated with pleasure include the **amygdala** and **orbitofrontal cortex (OFC)**, the latter having the mid-anterior OFC specifically associated with generating pleasure (*Pleasure Systems in the Brain*). Neuroimaging studies demonstrate that the same regions of the brain activated by food are also activated by music and socialization; in this way, a "common neural currency" exists across pleasurable activities. However, just because similar brain regions light up for similar pleasurable outcomes does not mean they are the causative factors for pleasurable effects. For instance, mesolimbic dopamine used to be classified as the pleasure neurotransmitter; more recently, it has been discovered that it has more to do with "wanting" (behavior) than "liking" (pleasure). This is an essential differentiation to make across a range of disorders relative to reward and motivation—for instance, addiction has too much wanting and not enough liking (*Pleasure Systems in the Brain*).

In fact, addiction is one of the better scenarios to explore when examining pleasure systems gone awry. For instance, when dopamine pathways become sensitized, that means that heightened arousal to stimuli is possible, giving our "wanting" a more delineated reward. Ironically, this is the heightened "wanting" (conditioned response) that occurs in the absence of increased (or decreased) hedonic response. Thus, more research on these pathways in the brain must be undertaken to better understand (1) the neural circuitry that supports "wanting" and (2) the neural circuitry that supports "liking" for better therapeutic solutions for addiction and any other disorders that plague compromised pleasure systems (*Pleasure Systems in the Brain*). But pleasure isn't merely "liking" and "wanting," either. The pleasure systems in the brain are rather

complicated. It's area-specific activation of certain sites and neurochemicals, the activation of the NAc by opioids and endocannabinoids, which is correlated with increases in "liking"—but only when activation occurs within a certain cascade and certain areas of the brain. Yet there are hedonic hotspots found in the NAc and VP that permit stimulation to create increases in "liking"—but only to create "liking" based upon their connected circuitry (*Pleasure Systems in the Brain*). Thus, finding such hedonic hotspots indicates an understanding of another layer of functioning relative to how pleasure is experienced on a neurochemical and systemic level.



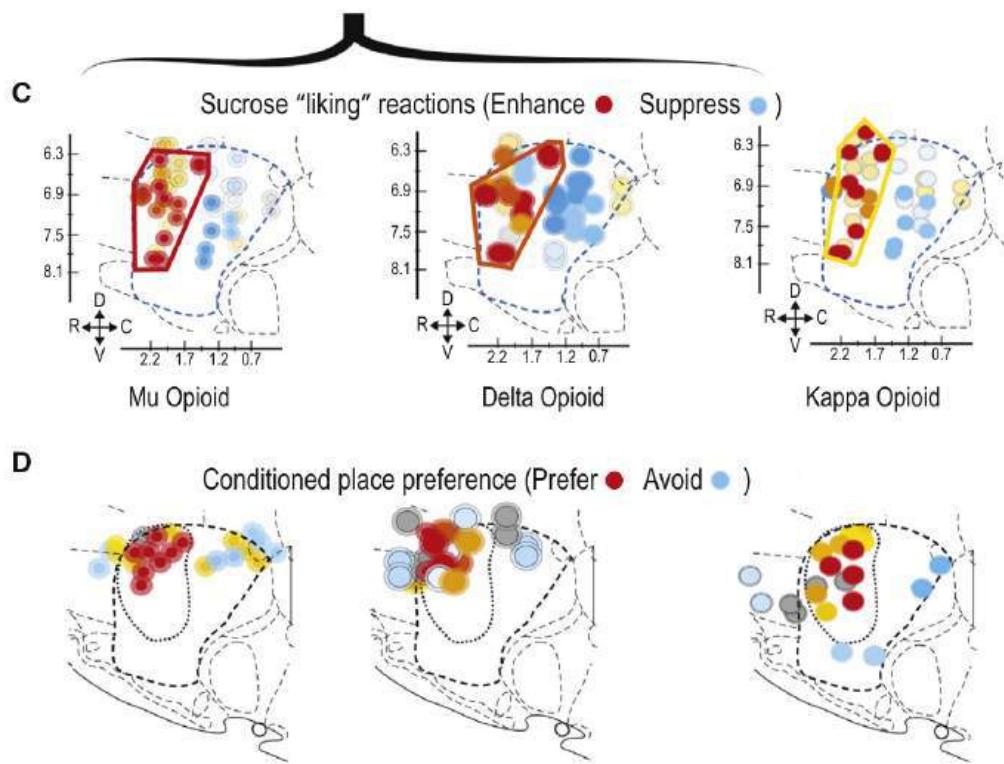


Figure 4

The **dopaminergic system** impacts reward and pleasure. Dopamine is the neurotransmitter linked to "feeling good." It exists within the brain's reward pathways; however, it does not make someone feel good—this neurotransmitter regulates how people assess the motivational valence of the reward—which neuroscientists call "incentive salience." The urge for something to become a powerful want/nagging hunger—or heroin—and subsequently, more sought after. Thus, the population of dopaminergic neurons located in the **ventral tegmental area (VTA)** generates dopamine, projecting to the **nucleus accumbens (NAc)** and **prefrontal cortex**, among other executive function/emotionally evaluated regions (*Pleasure Systems in the Brain*). Thus, this neuropathway is activated via performance endeavors or illicit psychoactive use—and it's strong because it makes people want to do it again.

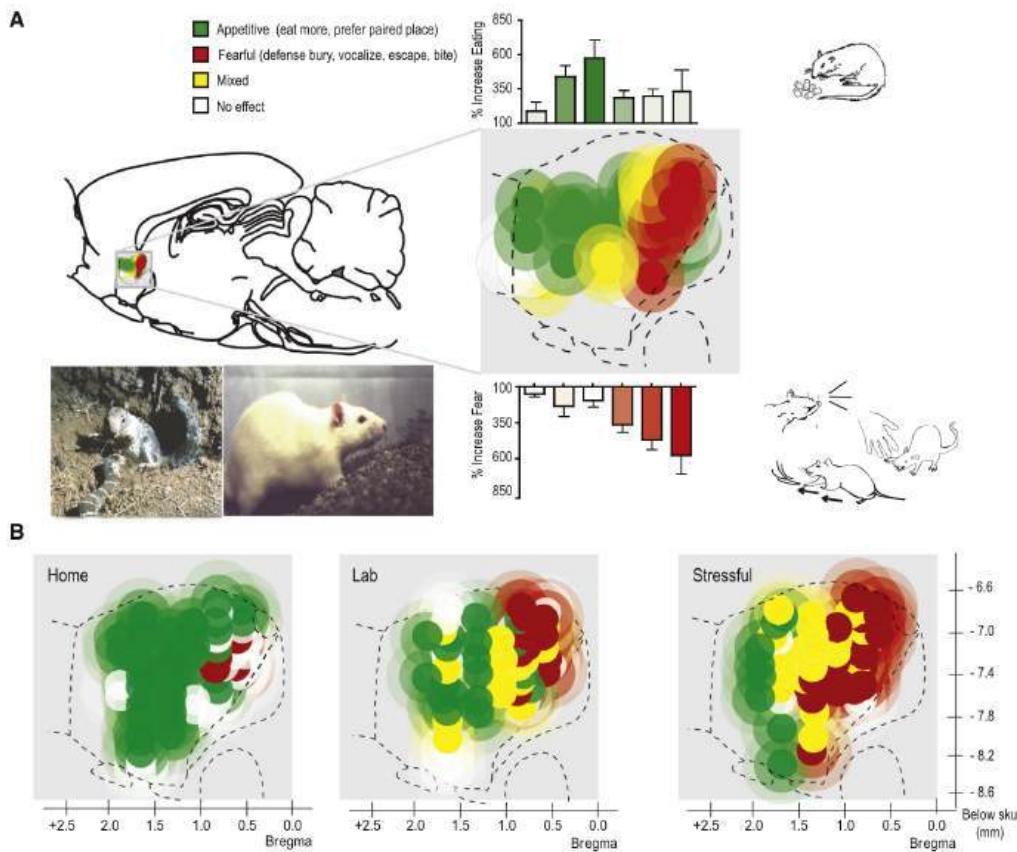


Figure 5

Furthermore, studies in animals and humans suggest that when humans eat, when they drink, when they have sex—these are biological reinforcers—dopamine flows through this pathway. However, when humans eat, when they take opiates and stimulants—cocaine, heroin—this process is hijacked; these substances create a greater quantity of dopaminergic activity to the brain's pleasure centers than any biological reinforcer—and more than the brain can withstand, leading to prolonged and increased reactions compared to any biological reinforcer. Thus, getting high is experiencing that false dopaminergic discharge. However, when the brain recognizes it feels good, the reaction begs for more. And more. Thus, drug seekers have such a reaction. In addition, as drugs are used more often, the brain accommodates in the long term to downregulate natural dopamine, making biological reinforcers difficult to enjoy—this is the symptom of the addict (*Pleasure Systems in the Brain*). However, when it comes to reward, the **opioid system** is involved to a much higher degree. The body's natural opiates are called endorphins, and they bind to opiate receptors found in the pleasure centers of the brain—the **nucleus accumbens** and **ventral pallidum**—which induce euphoria and satisfaction. In other words, when someone wants something and they get it, it's not necessarily because of the dopaminergic system that they're happy about getting it; it's more so that the second they have it,

their body becomes flooded with endorphins. Therefore, the relative interplay of reward via the opioid and dopaminergic systems gives a fuller understanding of reward and why it's pleasurable.

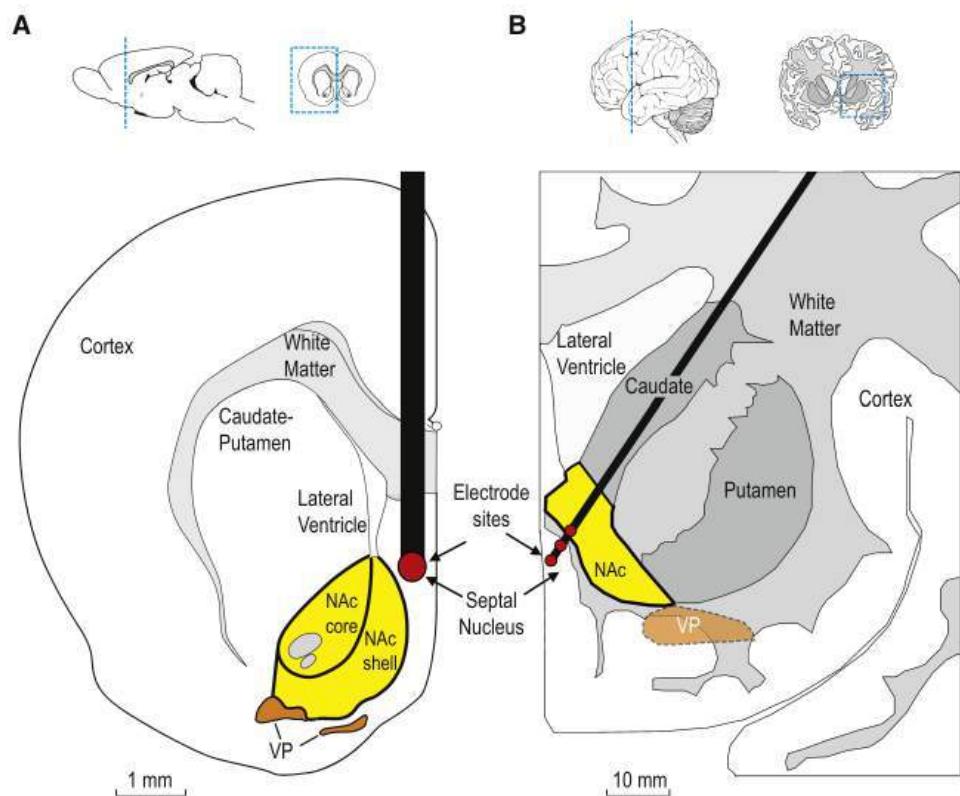


Figure 6

But these pathways are also essential for learning in addition to what just feels good. **Learning** feels good, after all, and it is stimulus-reinforcement based. The mesolimbic pathway teaches creatures what they enjoy and what they will be inclined to do to ensure a situation concludes with a pleasurable outcome. For example, learning via the stimulus of tasting really good, sugary fruit, an organism remembers that taste and seeks it out at another time. Likewise, being part of a social group from which a rewarding outcome occurs helps ingratiate loyalty to the group, something critically important for the survival of social species.

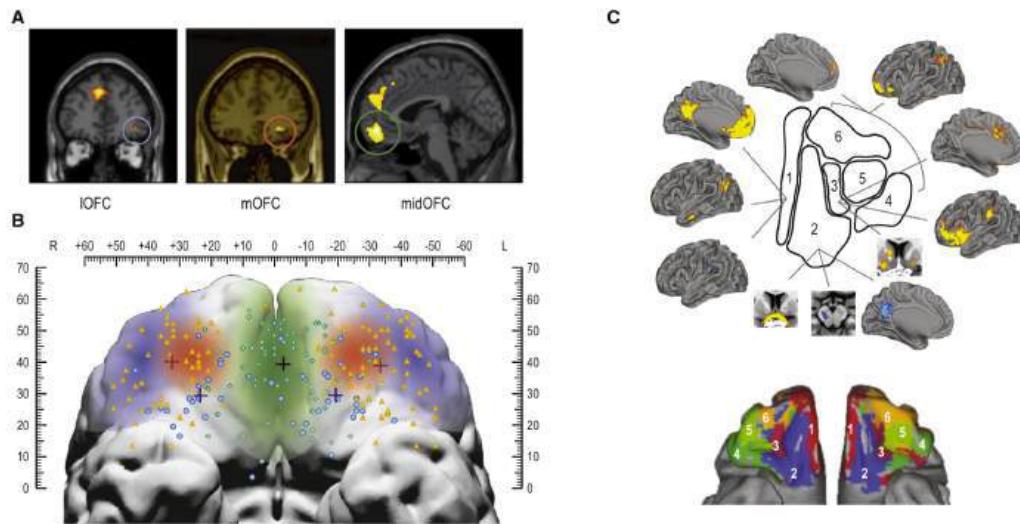


Figure 7

Yet importantly, the reward system doesn't always function as intended. It's inverted; it's exploited. Through no one at fault or by accident, something gets to be desired, and when in possession, the amount of reward for having such is exponentially greater. Drugs, alcohol, even certain processed foods exploit these systems and start generating exponentially higher rewards. It's this maladaptive system that creates addiction, as what once was a good time is desired and desired again when the brain realizes that goal-directed behavior produces those quick hits of feel-good—even over time, existing becomes more important than eating, talking, or any other goal-directed behavior that gives such high levels of reward and satisfaction. People want more, and they enjoy less. (*Pleasure Systems in the Brain*).

Pleasure and Evolution

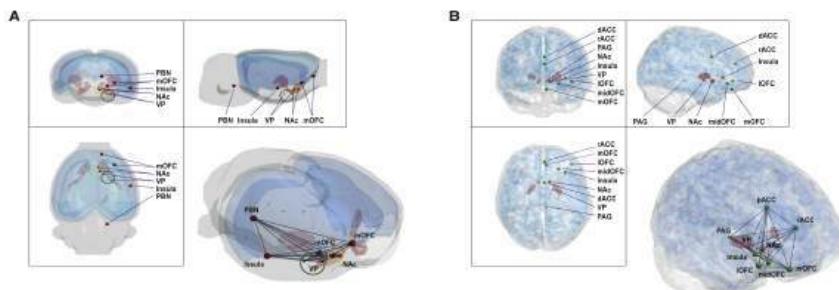


Figure 8

Therefore, it's understandable that an association with reward and the brain comes from an evolutionary standpoint. Most likely, millions of years ago, when most of the activities

required to be human were still taking place—eating, mating, sex, parenting, socializing—people found many of these activities enjoyable. Those who valued eating the most probably ate the most and the most often, procreating and surviving in the process. Therefore, with time, the reward system developed to assist mankind and the human population with continued survival (*direct fit to nature*).

This evolution explains how the brain may be vulnerable to addiction in the twenty-first century. The fact that the brain was wired in such a reward-sensitive manner at a time when it was improbable for people to overindulge or overmedicate suggests that when people began dieting or, inversely, using drugs, it was the brain's signal to take that moment to enjoy excess. The fact that reward-sensitized systems constructed for human enjoyment or drug use or enjoyment from food did not work in twenty-first century society, where people can have everything and anything whenever they want, all the time—and thus, excess is compounded by a multitude of psychiatric and physical disorders from obesity to opioid usage to binge eating disorders.

This is increasingly true with synthetic rewards. For instance, processed foods provide more sophisticated tastes and calories than ever found in any natural scenario where our ancestors inhabited. Thus, these hyper-palatable encounters overstimulate the brain's reward pathways outside of the natural realm, and people consume more than they need. The same is true with cocaine and meth, giving humans doses of dopamine which, as a human, you should never naturally have; the brain cannot handle it. It regulates by homeostasis, desensitizing itself to that much dopamine—which is why drug addicts require more and more to feel anything.

Much of social behavior is also regulated by the pleasure systems. Humans are social beings. Social interaction releases dopamine and oxytocin and learned social association. From the perspective of evolutionary psychology, this makes sense as a naturally occurring system to promote prosocial activities which would help or hurt our chances at survival. Ancestors had the need to rely on one another to group hunt and gather and fight off prey, thus the ability to bond prosocially was a clear advantage to evolution. Thus, it makes sense that people want to be around other people—even if it's via webcam and social media—and that the reward systems would respond in kind. Yet, like food and drugs, when it's too accessible (social media is all too easy with likes and comments), it breeds maladaptive behaviors such as social media addiction and inability to function in real-life interpersonal situations (*direct fit to nature*).

Conclusion

The brain is a wonderful thing. From the anatomy of it to its purpose and operation in the body, everything fits theoretically and practically. Each segment, from the somewhat arbitrary cerebrum (forebrain), which is responsible for executive control and decision making, to the limbic system (location undetermined in the readings), which is responsible for emotional/affective behaviors—makes sense for the brain to have a purpose for survival. That control of action generation was a learned behavior over time was a key takeaway, meaning that people came to understand what it meant. Furthermore, the idea that biological and AI neural

networks function similarly implies that relative progression across the board renders over-parameterization a possibility to apply generalizations from learned historical experiences to new situations/stimuli. Thus, through evolution, humankind supports that they intend to exist in particular situations and learn the best means of controlling their reward systems.

Yet, as societies progress, more and more artificial reward systems develop that learn from the natural reward systems that were rendered through evolution instead, taking advantage of such intricacies and resulting in great problems for the psychological and physical constitution of the modern man. Pleasure, motivation, and reward emerge from the pleasure centers of the brain and are connected via neural and neurochemical pathways. Thus, everything that can impact such systems needs to be well-learned and understood so they're not thrown easily out of balance.

From the appealing awareness that the brain has an ultimate purpose via evolutionary implications to the extent that it relearns (neuroplasticity) how to function throughout the years, far too many areas of awareness learned to dictate how the brain operates so largely in purpose, function, and cognition—making any modern-day society's abuse in the form of addiction and mental illness unwarranted. We glean from the anatomy of the brain and subsequent findings on evolutionary developments and hedonic pathways that the brain is complex and a masterpiece in progress. The more we learn about ourselves—and the more we still suffer from our distinct periods through today—the more we have yet to contribute to this masterpiece.

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**Google's Willow Quantum Processor Achieving Breakthroughs Beyond Supercomputer
Reach, By Sreenayan Palle**

Abstract

This review examines Google's Willow quantum processor, unveiled in December 2024, marking a significant milestone in quantum computing technology. The Willow processor addresses critical challenges in quantum error correction and computational speed, essential for developing scalable and practical quantum computers. Through an analysis of data from Google's technical reports, recent research publications, and the Willow Spec Sheet, this review evaluates Willow's architecture, focusing on qubit performance, error rates, and scalability. The Willow processor integrates 105 high-quality qubits which solved a computational problem in five minutes, a task estimated to require classical supercomputers approximately 10 septillion years to complete, achieving a fivefold improvement in qubit relaxation times compared to previous models and demonstrating exceptional performance in error correction and complex circuit simulations. Notably, Willow solved a computational problem in five minutes, a task estimated to require classical supercomputers approximately 10 septillion years to complete (Neven). These advancements highlight Willow's potential to revolutionize fields such as cryptography, materials science, and artificial intelligence. Additionally, Willow's design facilitates efficient expansion while maintaining low error rates, distinguishing it as a leading quantum processor. Although Willow remains largely experimental, its breakthroughs are pivotal for building large-scale, practical quantum computers. However, further advancements in cryogenic technology, which cools systems to ultra-low temperatures for enhanced performance, software development, and scaling methodologies are necessary to achieve full quantum advantage. Google's emphasis on enhancing qubit quality and employing advanced machine learning for error correction underscores its commitment to overcoming existing challenges and advancing the field of quantum computing.

Introduction

Quantum computing is poised to revolutionize various scientific and industrial fields by leveraging quantum mechanical phenomena to perform computations that are exponentially faster than classical counterparts for specific problems. Google's contributions to this domain have been substantial, with the unveiling of the Willow quantum processor in December 2024 marking a pivotal advancement. Building on the legacy of previous processors like Sycamore (Neven), Willow addresses enduring challenges in qubit coherence, error rates, and system scalability, as they are crucial factors for maintaining the integrity of quantum information, minimizing computational inaccuracies, and expanding the system's capacity to handle more complex and larger-scale problems. This review delves into the technological innovations of the Willow processor, evaluates its performance, and assesses its potential impact on both theoretical research and practical applications.

Methods

The analysis of Google's Willow processor was conducted through a comprehensive review of technical whitepapers, research publications, performance benchmarks provided by Google AI Quantum in 2024, and the Willow Spec Sheet available at Google AI Quantum Willow Spec Sheet (google). This section outlines the methodologies employed to assess Willow's architecture, performance metrics, and its standing within the current quantum computing landscape.

Data for Willow were sourced from:

- **Primary Sources:** Technical whitepapers, official announcements, research articles published by Google AI Quantum, and the Willow Spec Sheet.
- **Secondary Sources:** Peer-reviewed journals, conference proceedings, and reputable industry reports providing independent evaluations of quantum processor performances.
- **Supplementary Data:** Information from interviews with quantum computing experts and insights from ongoing collaborative projects within the quantum research community.

Performance benchmarking of Willow focused on several key metrics:

- **Qubit Coherence Times:** Measurement of T_1 (relaxation time) and T_2 (dephasing time) using standard pulse sequences and echo techniques (Kevin Satzinger).
- **Error Rates:** Evaluation of operational errors using quantum process tomography and error syndrome analysis facilitated by embedded classical processors.

The analytical framework employed includes:

- **Statistical Analysis:** Utilization of statistical tools to analyze coherence times, gate fidelities, and error rates, enabling the identification of significant performance trends and deviations.
- **Simulation Models:** Development of simulation models to predict the scalability potential of Willow's architecture, considering logical qubit encoding and fault-tolerance thresholds.

Results

The evaluation of Willow yielded significant insights into its performance and potential within the quantum computing landscape. The results are categorized into performance benchmarks, highlighting Willow's strengths and areas for improvement.

Willow demonstrated remarkable improvements in qubit coherence times. The average relaxation time (T_1) across all qubits was measured at 100 μ s, approaching a fivefold improvement over Google's previous generation of chips (Google AI Quantum 45). The average dephasing time (T_2) was recorded at 120 μ s. These values represent a substantial enhancement in qubit stability, essential for executing more complex quantum computations with reduced decoherence-induced errors (Kevin Satzinger)

Gate fidelity is a crucial metric for assessing the reliability of quantum operations. Willow achieved single-qubit gate fidelities exceeding 99.99% and two-qubit gate fidelities reaching 99.8% (Buntz). These high fidelities are essential for minimizing error accumulation in quantum circuits, thereby enabling deeper and more complex computations. The enhanced gate fidelities are attributed to improved microwave control techniques and reduced cross-talk between qubits.

Operating “below the threshold” has been a goal for error-corrected quantum computing since its inception in the 1990s. However, after almost 30 years of advancement in device fabrication, calibration, and qubit design, quantum computers still hadn’t passed this landmark (Neven).

Willow represents a significant leap forward in quantum hardware. It maintains the tunability of Google previous architecture, Sycamore, while improving the average qubit lifetimes (T_1) from about 20 μs to 68 $\mu\text{s} \pm 13 \mu\text{s}$. The qubits and operations in Google devices are optimized with quantum error correction in mind and run alongside Google error correction software, including state-of-the-art machine learning, reinforcement learning, and graph-based algorithms to identify and correct errors accurately (google Willow Spec Sheet, Kevin Satzinger).

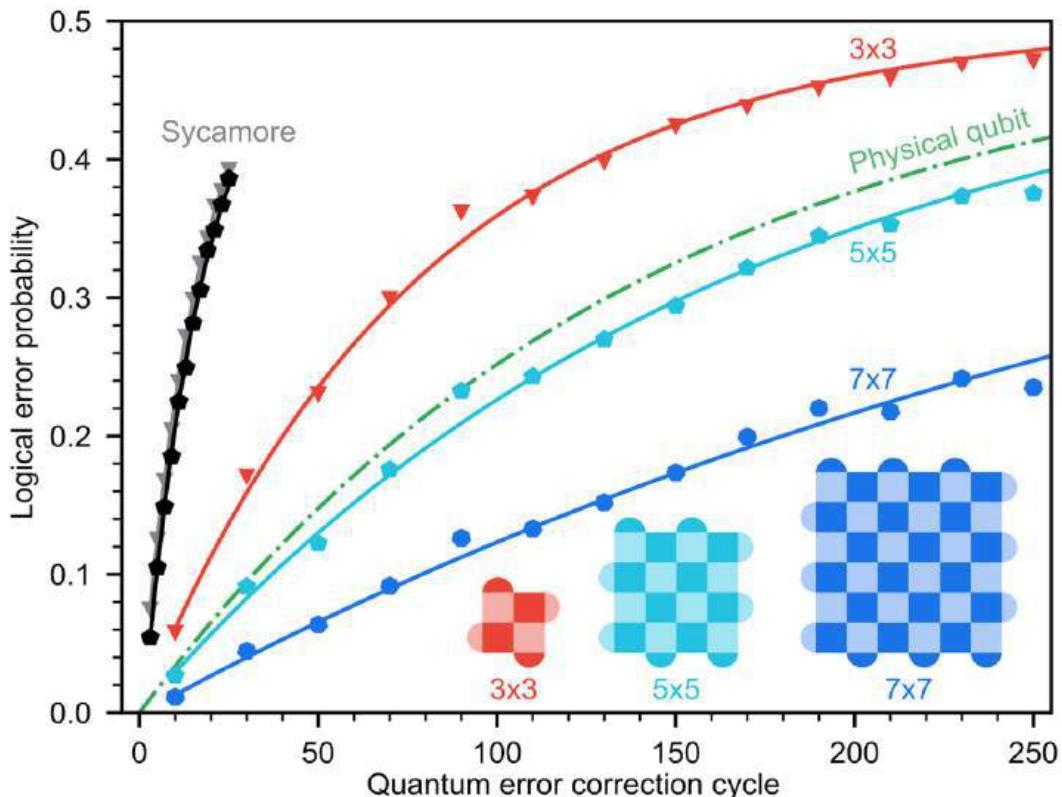


Figure 1 : Logical qubit performance scaling with surface code size. As we grow from 3x3 (red) to 5x5 (cyan) to 7x7 (blue), the logical error probability drops substantially. The 7x7 logical qubit on Willow lives twice as long as its best physical qubit (green) and twenty times longer than our previous surface code in Sycamore (gray, black).

Using Willow, Google reports the first-ever demonstration of exponential error suppression with increasing surface code size. Each time we increase Google lattice in size from 3×3 to 5×5 to 7×7 , the encoded error rate decreases by a factor of 2.14. This culminates in a logical qubit whose lifetime is more than twice that of its best constituent physical qubit, demonstrating the capacity of an error-corrected qubit to go beyond its physical components (Kevin Satzinger).

A logical qubit encodes information across multiple physical qubits using error correction for reliability. As the lattice size grows from 3×3 (red) to 5×5 (cyan) to 7×7 (blue), the logical error probability drops substantially. The 7×7 logical qubit on Willow has a lifetime twice as long as its best physical qubit (green) and twenty times longer than the previous surface code in Sycamore (gray, black) as shown in Figure 1.

Using Willow, Google reports the first-ever demonstration of exponential error suppression with increasing surface code size. Each time we increase our lattice in size from 3×3 to 5×5 to 7×7 (Figure 2), the encoded error rate decreases by a factor of 2.14. This culminates in a logical qubit whose lifetime is more than twice that of its best constituent physical qubit, demonstrating the capacity of an error-corrected qubit to go beyond its physical components.

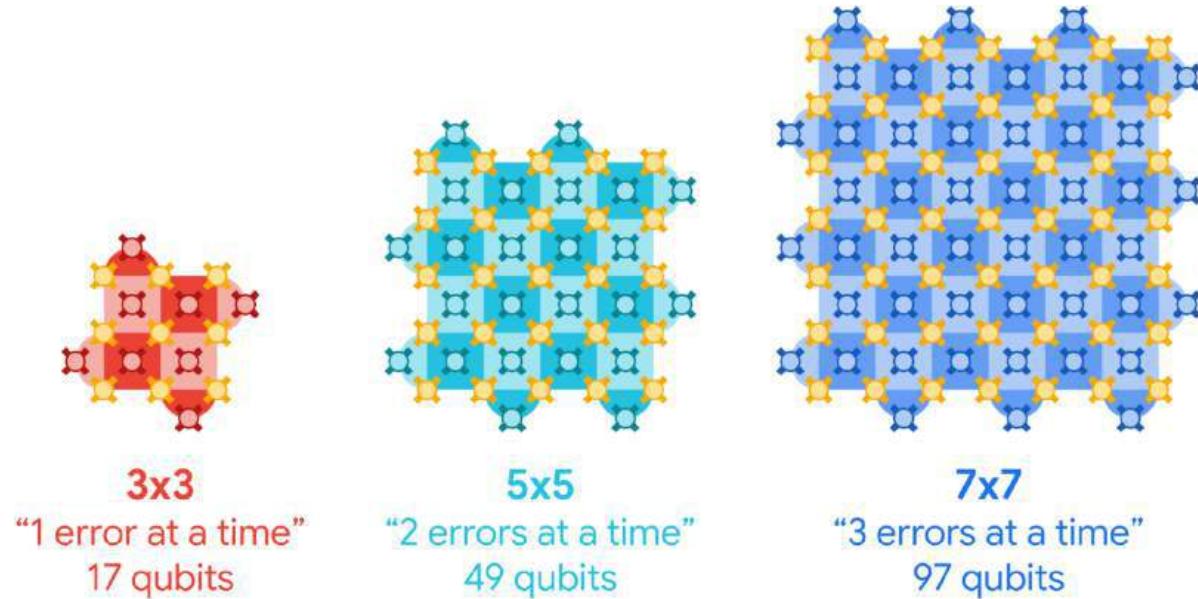


Figure 2: Surface code logical qubits of increasing sizes, each able to correct more errors than the last. The encoded quantum state is stored on the array of data qubits (gold). Measure qubits (red, cyan, blue) check for errors on the neighboring data qubits.

When running repetition codes on Willow, Google Reschers are able to realize nearly 10 billion cycles of error correction without seeing an error (Figure 3). Exhibiting that level of control over a quantum system, even when only protecting against bitflip errors, is quite exciting. However, when Google Rescher tries to push the encoded error rate lower by increasing the size of the code further, it won't budge. The reason for this behavior is currently under investigation, and Google Reschers are confident that they can find it and fix it, just as they fixed a similar problem with high-energy radiation on Sycamore (Kevin Satzinger).

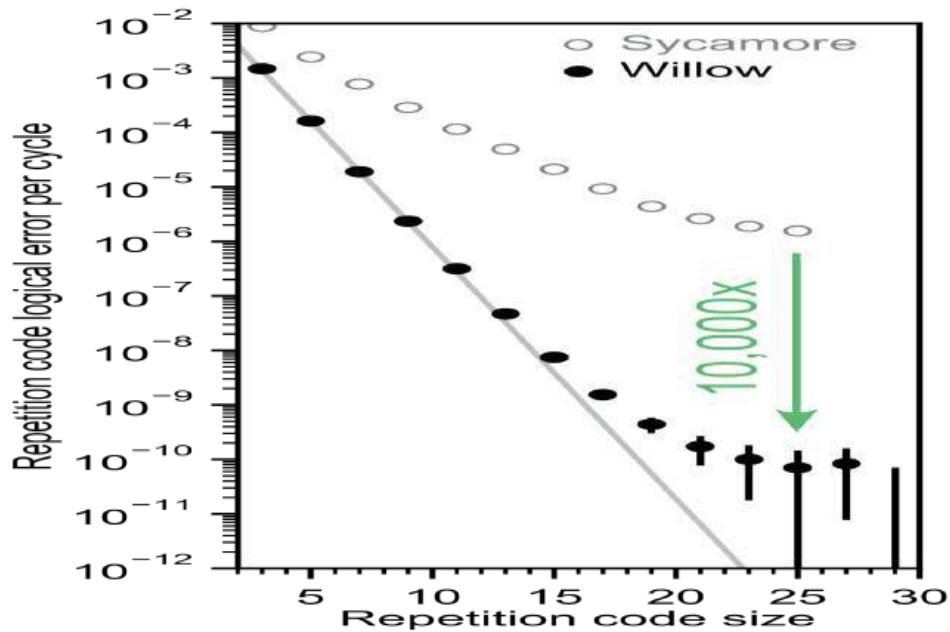


Figure3 : Repetition code performance scaling with repetition code size. Google achieves a 10,000x improvement compared to Sycamore, but observes an error floor around 10-10 logical errors per cycle.

Willow's performance on this RCS benchmark is astonishing, It performed a computation in under five minutes that would take one of today's fastest supercomputers 10 septillion (10^{25}) year, an unfathomable number that vastly exceeds the age of the Universe. This accomplishment not only demonstrates quantum supremacy but also validates the processor's ability to execute complex quantum algorithms that are beyond the reach of classical systems (google Willow Spec Sheet).

Discussion

Willow's exceptional coherence times and gate fidelities are crucial for advancing quantum computing toward practical and scalable applications. Its integrated error correction mechanisms significantly reduce operational errors, thereby enhancing the reliability of quantum computations. Furthermore, Willow's modular scalability strategy addresses one of the field's most pressing challenges, enabling the construction of larger quantum systems without performance degradation.

A key factor underpinning Willow's superior performance is its cryogenic technology. Superconducting qubits, the fundamental components of Willow, require ultra-low temperatures to operate effectively. Maintaining these temperatures presents significant challenges, as even slight thermal fluctuations can induce decoherence, thereby disrupting quantum computations.

Willow's ability to reduce errors exponentially as the number of qubits increases sets it apart from other quantum chips, which typically experience an increase in errors with more qubits. This breakthrough is crucial for developing fault-tolerant quantum computers capable of handling complex computations reliably. As detailed in Google's blog post (Kevin Satzinger) Willow achieved an exponential reduction in error rates by scaling up qubit arrays. By advancing from a 3x3 to a 5x5 and then to a 7 x7 grid of encoded qubits, each increment halved the error rate, demonstrating a historic accomplishment known as "below threshold." This milestone signifies the ability to drive errors down while scaling up the number of qubits, a challenge that has persisted since quantum error correction was introduced by Peter Shor in 1995.

Willow showcases real-time error correction on a superconducting quantum system, a capability not commonly seen in other chips (Kevin Satzinger). This feature is essential for practical quantum computing, preventing computation failures due to errors. These innovations enable Willow to maintain high fidelity in quantum operations, ensuring that quantum information remains coherent longer and computations proceed without interruption.

Google's approach focuses on enhancing qubit stability rather than merely increasing qubit count. With 105 qubits, Willow demonstrates best-in-class performance across quantum error correction and random circuit sampling benchmarks. This emphasis on quality ensures that each qubit contributes effectively to the overall system performance, making Willow the most convincing prototype for a scalable logical qubit built to date.

The successful implementation of the RCS benchmark further validates Willow's performance. By effectively executing RCS beyond classical capabilities, Willow not only achieves quantum supremacy but also establishes a robust framework for future quantum processors. This accomplishment underscores the importance of algorithmic benchmarks in assessing quantum hardware and sets a high standard for subsequent developments in the field (Kevin Satzinger).

However, despite these advancements, certain challenges persist. Maintaining ultra-low operational temperatures remains resource-intensive, and further improvements in cryogenic technology are necessary to enhance energy efficiency. Additionally, while Willow's software ecosystem has made strides, continued development of robust quantum algorithms and error correction software is essential to fully leverage the hardware capabilities.

Conclusion

Willow represents a significant advancement in quantum computing technology, achieving two major milestones, exponential error reduction and unprecedented computational speed. By incorporating 105 high-quality qubits with T_1 times approaching 100 microseconds, Willow demonstrates best-in-class performance in quantum error correction and random circuit sampling (Neven). The processor's ability to reduce errors exponentially as it scales up addresses a longstanding challenge in quantum error correction, while its computational speed, solving a specific problem in five minutes that would take classical supercomputers approximately 10 septillion years, underscores its transformative potential.

Willow incorporates 105 qubits and demonstrates best-in-class performance in quantum error correction and random circuit sampling. The processor's T₁ times, approaching 100 microseconds, represent a fivefold improvement over Google's previous generation of chips. While Willow is still largely experimental, it marks a significant step toward creating a useful, large-scale quantum computer .Potential applications include simulating systems where quantum effects play a crucial role, such as designing nuclear fusion reactors, understanding drug mechanisms.

Willow's error reduction strategy represents a significant breakthrough, characterized by:

- **Exponential Error Reduction:**

Ability to reduce errors exponentially as qubit numbers increase, operating "below threshold" (Kevin Satzinger) . This accomplishment cracks a key challenge in quantum error correction that the field has pursued for almost 30 years.

- **Scalability:**

As Willow scales up from a 3x3 to a 5x5 and then a 7x7 grid of encoded qubits, each increment halves the error rate (Kevin Satzinger).

- **Real-Time Error Correction:**

Demonstrates real-time error correction on a superconducting quantum system, preventing computation failures . This is crucial for any useful computation, as errors can ruin computations if not corrected promptly. (Kevin Satzinger)

- **Beyond Breakeven Performance:**

Qubit arrays exhibit longer lifetimes than individual physical qubits, indicating improved system performance through error correction. This "beyond breakeven" demonstration is a clear sign of Willow's superior error correction capabilities (Fritts).

By achieving these milestones, Willow represents the most convincing prototype for a scalable logical qubit built to date, bringing us closer to practical, large-scale quantum computers. Google's strategic roadmap, which includes research into topological qubits and advancements in fabrication techniques, underscores its commitment to overcoming current limitations and driving the quantum computing revolution forward.

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How/to What Extent does RBD(REM Sleep Behavior Disorder) Affect Functional Behaviors in the Elderly Population? By Sai Shreeya

Abstract

Background: REM sleep behavior disorder (RBD) is characterized by abnormal sleep movements due to the loss of muscle atonia. Research shows that about 70% of people with RBD go on to develop Parkinson's Disease (PD) within 12 years of their diagnosis (Kouli et al., 2018). This has prompted interest in RBD as a way to track prodromal features of PD, to widen the window of intervention opportunity, and to reduce the financial burden of this disease.

Sample: Participants ($N = 102$) were older adults ($M = 76.95$, $SD = 9.48$), primarily female (63.73%) and Asian (54.90%). In our study, "Asian" included people who originated in East, South, and Southeast Asia, but not from the Middle East or Central Asia. Twenty-three participants (22.55%) had a diagnosis of PD. Participants were recruited from nursing homes and a primary care/geriatric clinic in San Jose, California.

Method: We administered four clinical surveys. First, RBD was screened using the REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ). Second, the Center for Epidemiologic Studies Depression Scale (CES-D) was administered for depression symptoms. Third, the Hospital Anxiety and Depression Scale (HAD-S) was administered for anxiety symptoms. Fourth, the RAND SF-36 was administered for functional limitations.

Results: Findings showed that patients with PD had more severe anxiety and depression symptoms compared to people without, regardless of whether they met the threshold for RBD or not. In addition, people who did not have PD but met the threshold for RBD had more elevated symptoms compared to healthy controls.

Conclusion: Findings help characterize the clinical presentation of individuals with RBD, showing that they also display elevated symptoms in other domains of function (e.g., psychological, physical). Findings encourage the continued use of RBD screening to identify potential prodromal PD cases, given the high rate of disease conversion.

Introduction

The definition of PD

Aging is the main risk factor for many deleterious health outcomes, including neurodegenerative diseases (Hou et al., 2019). Biochemically, aging is caused by a series of molecular and cellular processes which can change and damage DNA, weakening one's physical and mental capacity over time and giving rise to diseases.

PD is an example of one such disease. The 3 main biochemical hallmarks of PD involve neuronal loss in the substantia nigra, aggregation of the protein α-Synuclein and mitochondrial dysfunction. In addition to neuronal loss in the substantia nigra, α-Synuclein aggregation can also contribute to neuronal loss when the protein misfolding occludes proper signal transmission between neurotransmitters and neurons (Surguchov & Surguchev, 2022). Due to these processes of neuronal loss, the brains of people with PD show a deficit of dopaminergic neurons which leads to clinical symptoms such as bradykinesia (slow or halting movements) and rigidity(Chen et al., 2022; Poewe et al., 2017). Lastly, mutations in the genes PINK1 and Parkin can alter regulation of mitochondrial functions, impacting the removal of defective mitochondria and disrupting the electron transport chain. Downstream, this also contributes to the dopamine loss and motor symptoms of PD (Morais et al., 2009).

PD is a fast-growing neurological disease with a prevalence of about 1.6 million people in the United States (Yang et al., 2020). Most people with PD start experiencing symptoms and get a diagnosis at an older age, typically between the ages of 65-69 years (Kouli et al., 2018). The disease continues to rise in prevalence with age. Due to the aging global population, researchers predict that PD will increase by more than 30% by 2030, greatly increasing the financial burden on society.

Clinical Description of PD

Currently, the clinical requirements for a PD diagnosis are resting tremor, bradykinesia, rigidity, and postural instability (DeMaagd & Philip, 2015).These symptoms become more severe as the disease progresses. PD is also linked to non-motor systems that occur many years before an individual shows the disease's hallmark symptoms. These 'prodromal' symptoms present an interesting area for study and potential intervention. The prodromal stage (i.e., before symptoms manifest) of PD begins 12-14 years before diagnosis and includes symptoms such as constipation, hyposmia, REM sleep behavior disorder (RBD), depression, anxiety, and cognitive impairment (Roos et al., 2022). The pathology of PD first starts in the autonomic nervous system and then spreads to the central nervous system, explaining the symptoms of rapid eye movement sleep disorders such as RBD and depression before motor symptoms start to appear. Prodromal PD symptoms can have a significant impact on a person's quality of life. Crucially, identifying these prodromal symptoms in patient populations deemed at risk of developing PD can widen the timeframe for prevention, which usually involves lifestyle modifications as individuals enter older age (Fan et al., 2020). There is a need for more research on prodromal symptoms of PD to better identify patients who are good targets for prevention.

RBD in the context of PD

REM sleep behavior disorder (RBD) is a promising candidate for study in the context of prodromal symptoms of PD. This is partially because RBD is highly prevalent in individuals who later convert to PD; RBD is reported in up to 50% of patients with Parkinson's disease (PD) (Poryazova et al., n.d.). However, only a few large-scale studies have addressed the

characteristics of people with RBD. And of those studies, they were conducted in countries with low immigration rates, resulting in less diversity and an inability to apply the results to individuals of other ethnicities.

Aims of the Study

The aim of this study is to investigate prodromal risk factors in PD with a focus on REM sleep behavior disorder (RBD). The question investigated was, "How/to what Extent does RBD(REM sleep behavior disorder) affect functional behaviors in the elderly population?" By using measures which probe sleep symptoms, mood disorder symptoms, and functional limitations of older adults, the present study aims to (1) quantify the prevalence of RBD in a sample of older adults and (2) assess how the presence of RBD can affect these adults' quality of life. The research question is: How/to what extent does RBD (REM Sleep Behavior Disorder) affect functional behaviors in the elderly population?

Literature Review

REM Sleep Behavior Disorder (RBD) in humans was first described in 1986. RBD is a REM-phase-associated disorder where the normal muscle atonia in REM sleep is lost, resulting in increased motor activity and abnormal behaviors such as dream enactment (Hu, 2020). Muscle atonia involves the brain sending signals to relax muscles in the limbs, but with abnormal muscle atonia, the movements of the patient become unpredictable. The prevalence of RBD in the general population is <1%, but in neurodegenerative disorders such as Parkinson's Disease (PD), a much higher frequency is found (Poryazova et al., n.d.).

In recent years, RBD has become an important marker of prodromal PD, being present in 25-58% of patients with PD (Hu, 2020). In a significant proportion of these patients, RBD occurs before motor symptoms. The onset of RBD is usually observed in individuals above 50 years of age. RBD is usually present in the late middle-aged population and is twice as prevalent among men in cohorts of this specific age group (Haba-Rubio et al., 2018).

Burgeoning research has uncovered some explanations for the link between RBD and neurodegenerative diseases. Studies have found that patients with idiopathic RBD, occurring with no relation to other neurological disease, are very prone to synuclein-mediated neurodegenerative diseases like PD and dementia with lewy bodies (Fulda, 2011). People with idiopathic RBD have a 40-65 percent risk of progressing to a synuclein-mediated neurodegenerative disease ten years prior to the onset of their symptoms. However, despite the high sensitivity (84%) and specificity (96%) of RBD screening tools (Poryazova et al., n.d.), idiopathic RBD patients are rarely evaluated at clinics. This can limit research on RBD as a marker for prodromal neurodegeneration.

The long prodromal window, where symptoms of RBD are present but symptoms of synucleinopathies like PD are not yet present, provides several advantages for clinical research. First, screening for RBD can be used to test other predictors of synucleinopathy such as olfactory loss, decreased color vision, and subtle motor problems. Second, studying patients with RBD

allows for the ability to observe the evolution of prodromal PD, which can shed insight on intervention points for neuroprotective therapy development.

Methods

Following researchers in the field(Högl & Stefani, 2017; Skorvanek et al., 2018; Stiasny-Kolster et al., 2007; Yao et al., 2019), data were collected through survey administration to older adults at nursing homes and a primary care geriatric clinic in San Jose, California, USA. The four surveys used were the REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ), Center for Epidemiologic Studies Depression Scale (CES-D), Hospital Anxiety and Depression Scale (HADS-A) and 36-Item Short Form Survey (SF-36). These surveys were used to track the prevalence of possible RBD, autonomic dysfunction, subtle motor problems, depression and anxiety(Postuma et al., 2013). These questionnaires were then analyzed to examine the prevalence of neurological diseases and associated health outcomes in older adults.

The four surveys used are described below.

1. The REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ) was created by(Stiasny-Kolster et al., 2007). for early assessment of prominent features of RBD. Items 1-4 ask about the frequency and content of dreams and their relationship to nocturnal movements and behavior. Item 5 asks about self-injuries and injuries of the bed partner. Item 6 consists of four sub-items assessing nocturnal motor behavior more specifically, e.g; questions about nocturnal vocalization, sudden limb movements, complex movements, or bedding items that fell down. Items 7 and 8 deal with nocturnal awakenings. Item 9 focuses on disturbed sleep in general. Lastly, Item 10 asks about the presence of any neurological disorder. The maximum total score on the RBDSQ is 13 points, and a cutoff score of 6 points is usually used to diagnose RBD.

2. The Center for Epidemiologic Studies Depression Scale (CES-D) was developed by Radloff, L. S. in 1977 and was intended to be a self-report depression scale for research in the general population. It contains 20 items with response options ranging from 0 to 3 for each item (0 = Rarely or None of the Time, 1 = Some or Little of the Time, 2 = Moderately or Much of the time, 3 = Most or Almost All the Time). Higher scores indicate greater depressive symptoms. The maximum score for this survey is 60.

3. The Hospital Anxiety and Depression Scale (HADS-A) was created by Zigmond and Snaith in 1983 and identifies anxiety and depression. The HADS has a total of 14 questions that measure anxiety and depression. Each question is scored between 0 (no impairment) and 3 (severe impairment), with a maximum score of 21 for anxiety or depression.

4. The 36-Item Short Form Survey (SF-36) was created by the RAND corporation and is used as a way to easily measure quality of life measures. This survey has eight categories: 1) limitations in physical activities because of health problems; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health (psychological distress and

well-being); 6) limitations in usual role activities because of emotional problems; 7) vitality (energy and fatigue); and 8) general health perceptions. The maximum score is 100 and higher scores indicate a better health status while a mean score of 50 indicates a normal value.

Ethical Clearance

A total of 102 participants were sampled from several nursing homes and a local clinic and were mostly above the age of 50. Data collection took place from August to December of 2023. Ethical clearance was obtained from a high school level Scientific Review Committee before conducting the study. Prior to administering surveys, verbal informed consent was obtained from all participants.

General Analysis Methods

Data collected from surveys were imported and statistically analyzed in the software R.

Results

There were 102 participants in total. All participants were above 50 years of age ($M = 76.95$, $SD = 9.48$). The sample was primarily female ($n = 65$, 63.73%) and Asian ($n = 56$, 54.90%). Twenty-three participants (22.55%) had a diagnosis of Parkinson's Disease (PD).

Table 1 shows participant demographic characteristics.

Table 1. Individual-level demographic characteristics for study sample (N=102)		
Variable	Frequency	Percent
Age		
50-60	6	5.88%
60-70	18	17.65%
70-80	45	44.12%
80-90	27	26.47%
90-100	6	5.88%
Sex		
Male	37	36.27%
Female	65	63.73%
Race		
White	11	10.78%

Table 1. Individual-level demographic characteristics for study sample (N=102)

Black	1	0.98%
Latino	34	33.33%
Asian	56	54.90%
Parkinson's Diagnosis		
Yes	23	22.55%
No	79	77.45%

First, we compared participants with and without PD on our measure of depression symptoms (CES-D), anxiety symptoms (HADS-A), and functional limitations (SF-36). A Welch's two-sample t-test showed that people with PD had more severe depression symptoms ($t(24) = -5.29, p < .001$) and anxiety symptoms ($t(25) = -5.85, p < .001$) compared to people without the diagnosis. There was no statistically significant difference between group means on the SF-36 ($t(38) = -0.11, p = .45$).

Second, we analyzed whether the presence of REM Sleep Behavior Disorder (RBD) impacted results.

We divided the participants into four groups:

1. PD diagnosis, positive RBD (score above 6 on the RBDSQ)(Roos, D. S et al., 2022)
2. No PD diagnosis, positive RBD
3. PD diagnosis, negative RBD
4. No PD diagnosis, negative RBD

Out of our 102 participants, 9 individuals met the threshold for having RBD (8.82%). Scores on the RBD were corroborated by informant reports from their bed partners. Informant reports were summarized qualitatively and contained endorsements of symptoms like sleep-talking and irregular movements while sleeping. For instance: "*He talks a lot while sleeping... about ½ hour on and off.*" Most participants who met the threshold for RBD had bed partners who said they talked in their sleep and sometimes even fell off the bed, then stopped talking afterwards.

We conducted analysis of variance tests on the differences between these four group means on depression symptoms (CES-D) and anxiety symptoms (HADS-A). We did not move forward with analyses about functional limitations (SF-36) given the non-significant results in the previous section. The four groups analyzed were Group 1 (PD diagnosis, positive RBD), Group 2 (no PD diagnosis, positive RBD), Group 3 (PD diagnosis, negative RBD), and Group 4 (no PD diagnosis, negative RBD).

Analysis of variance tests with Bonferroni corrections for multiple comparisons found significant differences between groups 1 and 3, groups 1 and 4, and groups 2 and 4 on CES-D

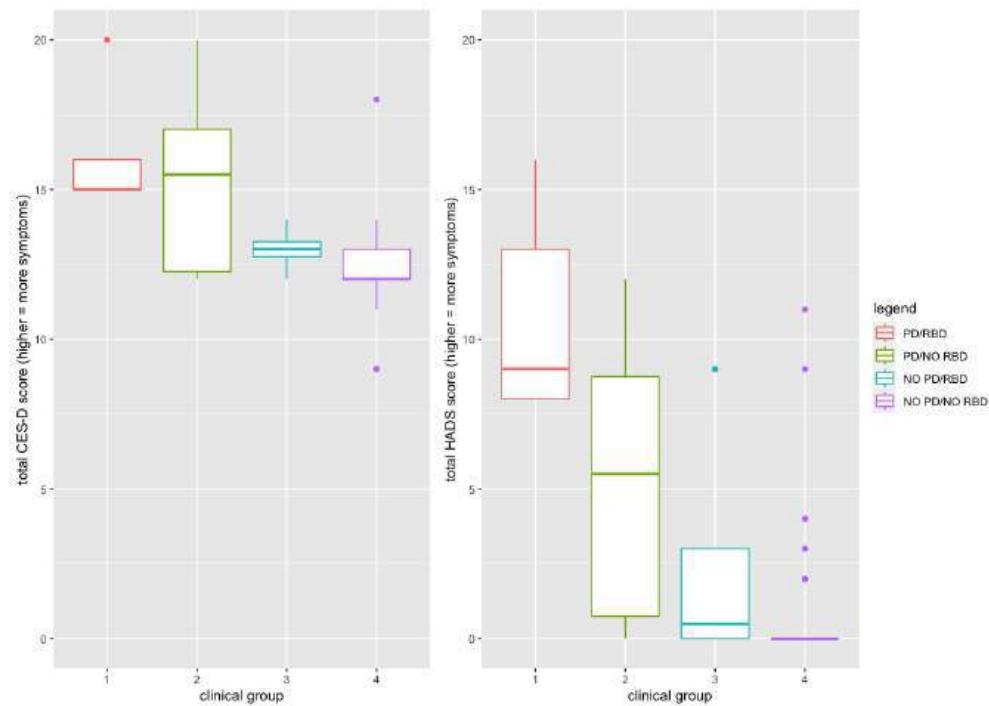
scores. Participants with PD diagnosis had more severe depression symptoms than those without, regardless of whether participants without PD had RBD or not. In addition, participants who did not have PD but met the threshold for RBD had more severe depression symptoms than participants who did not have PD or RBD.

PD diagnosis, positive RBD), Group 2 (No PD diagnosis, positive RBD), Group 3 (PD diagnosis, negative RBD), Group 4 (No PD diagnosis, negative RBD).

We also found significant differences between groups 1 (PD, positive RBD) and 2 (No PD, positive RBD), groups 1 (PD, positive RBD) and 3 (PD, negative RBD), groups 1 (PD, positive RBD) and 4 (No PD, negative RBD), and groups 2 (No PD, positive RBD) and 4 (No PD, negative RBD) on HADS-A scores. Participants with a PD diagnosis had more severe anxiety symptoms compared to participants with any other permutation of clinical impairment, including RBD. Participants who do not have PD but meet threshold for RBD had more severe depression symptoms than participants who did not have PD or RBD.

Figure 1 summarizes differences in CES-D and HADS-A scores between the four clinical groups. Please look at the relationship between prodromal factors such as sleep symptoms, mood disorder symptoms, and functional limitations of older adults and Parkinsons.

Figure 1. Participants with Parkinson's Disease, on average, had more severe depression and anxiety symptoms compared to participants without Parkinson's Disease.



Discussion

The present study contributes evidence to validate the existence of RBD as an ‘intermediary’ clinical stage for people who will likely progress to have Parkinson’s Disease. Although people with PD had higher depression symptoms regardless of whether they had RBD or not, participants with RBD but no reported PD diagnosis had elevated symptom scores compared to healthy controls. Additionally, people with PD had high anxiety symptoms according to the HADS survey.

During our analyses, we did not find significant results using the SF-36, a survey of functional limitations in our study sample. This null finding is most likely because our study sample was elderly, and as a result, the base rate of functional limitations was high, not allowing for appreciable variation that was detectable by this measure.

Our findings fulfilled the primary aim of this project, to assess the usefulness of RBD as a clinical category preceding PD. People with RBD had the same clinical symptoms at a slightly lower severity compared to people with PD. These findings are promising for researchers, as RBD patients have a high risk of disease conversion, and the prodromal stage is long enough for early intervention to be effective.

Many current studies about RBD and PD focused on less diverse populations, resulting in limited generalizability of results. To fill this gap in the research, the present study collected data on participants of various ethnicities with different medical histories. A strength of the present study is the higher generalizability as a result.

Limitations and Future Research

This study has limitations. The low rate of RBD in our sample (about 8%) led to a small group for comparison and lower-powered statistical tests. Additionally, our study did not involve a standardized sleep test like polysomnography, which can give a more comprehensive overview of the negative effects RBD has on sleep. For example, polysomnography provides information on sleep stages and can track physiological movements like eye movements, muscle activity, brainwave activity, and oxygen saturation levels that occur during sleep. Even though many screening questionnaires have been developed for RBD and can detect if RBD is probable, diagnosis can only be confirmed by polysomnographic data. Nevertheless, this data is very expensive, costing 3000 dollars on average without insurance, which is not universally available, which makes RBD screening questions and diagnosing RBD. Nonetheless, this study contributes more information about the clinical presentation of RBD, particularly in samples that are underrepresented in this line of research. In the future, screening for prodromal presentations of neurodegenerative disease like PD will decrease the financial burden on the elderly and increase the likelihood of the development of neuroprotective therapies.

Conclusion

Overall, it is important to acknowledge RBD as an indicator of prodromal PD and take action to conduct early intervention. RBD screening can be used to inform the patient that they have subtle progressive motor and cognitive features which are also present in neurological

diseases. This can be a highly important indicator which can change a person's life completely because of intervention options like regular aerobic exercises, taking supplements like Vitamin C and E and carotenoids, and eating a balanced diet (*Supplements for Parkinson's*, 2022). In more severe cases, specialized PD movement and speech therapies such as the Lee Silverman Voice Treatment (LSVT) BIG and LOUD programs have the potential to lessen symptoms and slow disease progression (*How LSVT LOUD and LSVT BIG Therapy Can Improve Speech and Movement in People With Parkinson's Disease*, 2024). LSVT LOUD, a method scientifically studied for 25 years, has been effective in training people with PD to use their voice at a normal loudness level at home, work, or their community (*Speech Therapy for Parkinson's Disease and Other Conditions | LSVT Global*, n.d.).) Additionally, LSVT BIG trains improved movements for any activity, such as small motor tasks like dressing oneself or bigger tasks such as getting up from a sofa. The treatment helps PD individuals modify their movements to match movements of others around them despite their condition. Since the LSVT BIG Treatment is customized to each person's needs, it can help regardless of one's stage in Parkinson's; however, more improvement can be seen in one's early or middle stages of his/her condition where functions can be improved and symptom progress can be slowed (*Physical Therapy for Parkinson's | LSVT BIG*, n.d.). Lastly, the LSVT LOUD has helped people in all stages of PD and is recommended to consult when one notices significant problems with his/her voice, speech, and communication, but it is never too late to start (*Speech Therapy for Parkinson's Disease and Other Conditions | LSVT Global*, n.d.)

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Using Machine Learning to Detect Malicious Certificates in CT Logs

By Rhea Anand¹

Abstract

The Man-in-the-Middle (MitM) attack is a major problem in the CT system in which attackers are enabled to intercept the communications between a website and its users. Certificate Transparency (CT) was a major contribution to the original Public Key Infrastructure (PKI) as it built trust for the system and efficiently by examining certificates more thoroughly for validity. In this literature review, we go over how Explainable Artificial Intelligence (XAI), Graphical Convolution Networks (GCN), and Deep Neural Networks (DNN) have a high accuracy in detecting malicious certificates and strengthen the reliability of the CT logs.

1 Introduction

The Man-in-the-Middle attack is a major issue in today's cybersecurity systems. This strike allows an attacker to interfere with the communication of a website and its users. Although measures have been taken to improve the PKI system, the attack remains a major problem. Certificate Transparency refined the PKI system's ability to detect malicious certificates efficiently, with more trust.

In this literature review, various machine learning techniques are brought up to discover which are beneficial to the safety of Certificate Transparency from phishing. The CT system contains numerous parts that collaborate to get rid of flaws. However, numerous attackers can create spiteful websites to access others' information. It is important to search through the CT logs in case of rogue certificates that justify the creation of malicious websites that can access private information. We can avoid these instances and mitigate phishing by applying AI to assess the validity of certificates in the logs efficiently.

2 Related Work

Previous research has been done on phishing and MitM attacks.

2.1 Public Key Infrastructure

Public Key Infrastructure (PKI) utilizes procedures and methods to ensure that public key certificates are secured and encrypted because there is a large amount of digital information on the web. The purpose of PKI is to confirm that every user has an authentic public key that can be accessed by another party while keeping a user's information and private key confidential. A Public Key Infrastructure (PKI) comprises several functional elements that enable secure digital communications and transactions.

2.2 Certificate Authority

The Certificate Authority is a major component of PKI. It acts as a digital notary and is responsible for issuing digital certificates that help verify the authenticity of entities' identities.

Its main functions are issuing and revoking certificates, publishing certificates in repositories for users to view, and archiving expired certificates. The CA is normally an organization that charges customers in return for a certificate. Companies install root CAs which are trusted and the template for intermediate CAs. The CA partakes in authentication, a major element in maintaining communication between parties. A CA issues a certificate to a user with a private key that aligns with the public key in the certificate. It inserts the company's name in every issued certificate and establishes a trust connection with the user. Verifying the signature with the public key ensures a certificate's validity. It is critical that the CA correctly protects its private key to access its users' public keys.

2.3 Browser

The CT-enabled browser assists in verifying certificates and SCTs by utilizing pre-installed public keys from the CA and log servers. It will reject the certificate if the certificate does not contain the valid amount of SCTs required. The browser periodically sends the SCTs to the auditor to ensure that it corresponds with a certificate in the public logs.

2.4 Website Owner

The website owner is also known as the domain owner, who requests to own a website. There are times where it needs to submit its own certificate to the logs for a SCT. A TLS handshake occurs where the SCT is sent with a certificate through the TLS extension

3 Limitation / Drawbacks in PKI

A major drawback of the PKI system is that every Certificate Authority is considered trustworthy, despite its many users. The PKI system does not differentiate between big and small CAs, which allows a compromised CA to issue certificates that provide the authenticity of fake public keys that an attacker can make. Additionally, it can be difficult to determine which user you're looking for when users have the same name, such as "Robert Allen." A website owner may switch CAs due to a lower cost; however, the browser does not warn users about this change. The new organization may be hazardous, revealing numerous users' data to attackers. PKI When a CA issues a CRL (Certificate Revocation List), it forms a blacklist of outdated certificates with issue date and when the next blacklist will be available. This application contains many roadblocks as it takes too much time and is expensive to review the large list of expired certificates.

4 MitM Attacks on PKI

A faulty PKI system and compromised CA can permit a man-in-the-middle (MitM) attack between a user and an inauthentic website. With a flawed Certificate Authority, rogue certificates can be authorized and applied to persuade victims to download software or updates that seem to be from a trusted third party. The malicious certificates have the appropriate credentials and identical domain names as the websites they disguise. This allows the attacker to

misdirect the user onto a site indistinguishable from the one they searched for and observe all the interactions between a client and the website; revealing private information.

5 Certificate Transparency

Certificate transparency is a web security measure used to verify that the data on digital certificates are reliable and cannot be altered; only added to. When an Internet user connects with a website, CT ensures that the website and its information are valid. This is made possible through a log that provides transparency, including text files that record security information about a system, including the IP address, number and times of logins, and usernames. Another major component of this system is monitors, which are publicly run servers that search for skeptical certificates and help inform website operators if there is an unauthorized certificate with unusual permissions and extensions in their domain. Additionally, user agents are applied in the software and assist users in interacting with web browsers and accessing web pages online. Some common user agents include Google Chrome, Microsoft Edge, and Apple Safari.

The process begins when the website owner requests a certificate from the Certificate Authority (CA) by sharing their public key to encrypt data or verify a digital signature. CA's are a third-party organization that monitors logs for any suspicious activity. CT and a special log are used to ensure transparency and security for information to only be added. Following this, the CA issues a pre certificate and checks if the domain owner, who requested for a registered web address, is authorized to make a request. If the owner is valid, the CA creates the pre-certificate which contains the same information as a certificate including the domain and public key. The operation sends the pre-certificate to the logs which gives a Signed Certificate Timestamp (SCT) in return. The SCT is a promise from the log to assign the certificate within a specific time frame known as the Maximum Merge Delay (MMD), which allows the log operators to fix issues and not delay the creation of certificates. During the MMD, the pre-certificates are added to the logs. The CT logs assist in keeping track of certificates by utilizing Merkle Trees which allow for public inspection with 3 methods. Logs are append-only where certificates can only be added; not altered or deleted. They are cryptographically assured which prevents tampering.

Furthermore, they are publicly auditable and any individual can check the log to ensure everything is reliable. These procedures make it difficult for rogue certificates to exist under the public eye. Monitors are publicly run servers that look for suspicious certificates to help website operators know if there is an unauthorized certificate (have unusual permissions/extensions) in their domain. To check a log's consistency, a monitor calculates a consistency proof to verify that a later version of the log includes everything from the earlier version. When the log returns the SCT, the CA attaches it to the certificate along with a X.509v3 extension that stays with the certificate for its life. The third-party signs the certificate and delivers it to the server operator who monitors and manages the server's security. At last, the CA sends the certificate to the domain owner where a TLS Handshake occurs. This is when two parties verify one another, their encryption methods, and keys through encrypted communication. Browsers and user agents are components of CT that help keep the web secure. Certificate Transparency is applied by websites

such as Google Chrome and Apple Safari.

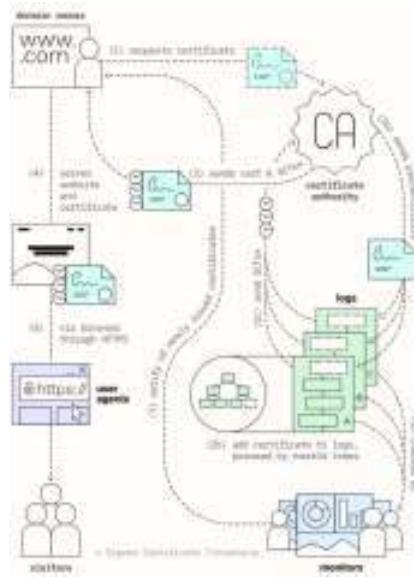


Fig. 1. CT System
Using Machine Learning to Detect Malicious Certificates in CT Logs 5

5.1 Monitors

Monitors are a major component of the Certificate Transparency framework and watch for suspicious activity in the public log servers. The monitor accesses certificates in the logs and decrypts them to check if they are fraudulent. If there is a problem in the monitor's functionality, attackers can exploit the exposure to prevent the detection of fraudulent certificates. These instances lead to man-in-the-middle (MitM) attacks and an unreliable CT system. Monitors are not as dependable when there are too many certificates as they are duplicated in the public logs to promote security and trust. The numerous certificates in the logs make it difficult for the monitors to assess all the certificates which takes up a lot of storage, bandwidth, and time. (Dong et al., 2016) Certificates are put into two types: Google-approved and Regular logs. The logs accepted by Google are more secure and trustworthy as they are trusted for their SCTs and have regular audits and pre-installed public keys. Whereas, the Regular logs are for general use with varied quality and have no guarantee for SCTs. As monitors were introduced by Google in 2018, various browsers have created third-party monitors that provide a running status of the public logs including the STH, uptime, and certificate scope. However, they are incomparable to Google monitors as they may deduplicate certificates. Of the various third-party monitors, many of them do not provide entirely trustworthy scans of a set of certificates for a domain. The monitors have trouble assessing all the certificates, while others can not cover all the certificates. This is caused by errors in monitor implementations where data was not recovered in time, in unsupported domains, or delayed in processing. Some countermeasures to these problems are to create a mechanism that detects the misbehavior of CT Monitors and evaluates their services. Another method to overcome this obstacle is to use an elastic resource allocation that ensures that the monitors have the necessary amount of resources to handle the large amount of

certificates in the logs.

6 Methods

This literature review explores the following research questions

- What machine learning techniques have been proposed for analyzing Certificate Transparency logs, and how effectively are they detecting phishing attempts?
- What performance metrics are used to evaluate phishing detection techniques using certificate transparency logs?
- What datasets have been used in the studies?

To find data on how AI can be incorporated into the CT system, the ACM method to find articles that resonated with the keywords: "certificate transparency," "machine learning," and "deep learning" on the Google Scholar application. Out of 52 articles that incorporated these keywords, 14 papers appear tained to the main topic of this paper. Some excluded research did not relate to 6 Rhea Anand how artificial intelligence could improve CT. From the 14 research papers, the most popular techniques used were XAI (Explainable Artificial Intelligence), DNN (Deep Neural Networks), and GCN (Graph Convolution Network).

7 RQ1

What machine learning techniques have been proposed for analyzing Certificate Transparency logs, and how effective are they in detecting phishing attempts? XAI strives to improve the transparency of machine learning through defensive and offensive tactics. It presents a better practice for model verification by ensuring AI models relay the correct predictions and mitigate possible attacks. XAI [?] is presented with user assistance, model verification, and explainable verification. ML models include white-box and black-box models. While white-box models are simpler, including data trees, black-box models are complex. They include neural networks and XAI can assist in providing explanations for data points that can affect the algorithm's predictions or how one point alters one prediction. Deep Neural Networks are a form of supervised machine learning that utilizes a pattern recognition method that can be convenient for detecting rogue certificates that the CA and Monitors did not recognize. DNN can help avoid these issues with its punctuality, accuracy, and compliance with the modern PKI system. Certificates are classified efficiently and allow for the investigation of rogue certificates. The correctness is achieved by utilizing this simulation trained to categorize certificates based on the root CA which is trusted by major operating systems and can cover all certificates that follow it. Lastly, as malicious certificates ensure that their behavior is protected and destabilizes the safety of networks, Graph Convolutional Networks (GCNs) can assist in applying useful features of prior knowledge on malicious certificates to graphing data to remember the manner and effectively detect the rogue certificates. This technique is beneficial for an algorithm that applies a dataset of digital certificates that are sorted by the PEM document format. GCN presented a

successful method for certificate classification with higher accuracy than past ML techniques.

8 RQ2

What performance metrics are used to evaluate phishing detection techniques using certificate transparency logs? Some metrics used to improve machine learning cybersecurity are precision, recall, and accuracy. Precision = True Positives / (True Positives + False Positives) Recall = True Positives / (True Positives + False Negatives) Precision takes the count of how many of the predictions by the model were correct, whereas recall measures if the algorithm correctly predicted the occurrence. Accuracy = (True Positives + True Negatives) / Total Population Accuracy provides the algorithm's results, determining if it was misleading or useful.

9 RQ3

What datasets have been used in the studies? The main dataset used was (Dong et al., 2016), contrasting the before-and-after decryption of benign and malicious certificates. Many of the research papers did not include datasets as they were unnecessary for their findings.

10 Conclusion

To conclude this literature survey, the AI techniques of: XAI, GCN, and DNN are featured as effective tools for detecting the highest amount of malicious certificates in the logs. We answered three questions on techniques and what metrics helped determine their accuracy. Among these methods, GCN held an advantage with the strongest trust links between the user and the system from certificate patterns. However, XAI illustrated the transparency in decision-making on whether the certificate was viable. DNN was efficient in detecting patterns but was flawed when it came to large datasets. Some limitations to consider in XAI are how it tends to oversimplify complicated models leading to misinterpreted results. GCN requires a distinct and clear graph structure to ensure optimal results, while DNN demands a significant amount of analytical resources, reducing its security and ability to explain. By integrating these techniques, the security of Certificate Transparency can be developed, and thus, the internet can be provided with secure websites that prevent the spread of one's private information. This literature review advocates for a different approach to detecting rogue certificates and upgrading the CT logs. This is another step to increasing the privacy and safety of user data by addressing ways to strengthen security.

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How Has a Lack of Political Stability Impacted Economic Growth in Pakistan?

By Hassan Khursheed

Introduction

Pakistan's economic development is necessary for over 240 million people in the country to thrive. In 2018, 21.1% of adults did not complete a primary school education and 28.8% of school-aged children were not enrolled in a school.¹ Economic growth and its benefits in ordinary life of Pakistanis in or out the country is not to be understated- going to school is rarer in Pakistan than it is in more developed nations, primarily due to poverty and unaffordable school fees. Without a basic education, a vicious cycle begins where those who can't afford an education get low-paying jobs and are then unable to afford education for their children. This cycle repeats for generations and is difficult to break out of. Food is becoming increasingly more expensive and nine out of ten Pakistanis are unable to eat out anymore,² food inflation has soared to 48.65% in May 2023.³ With low income and a high extreme poverty rate, Pakistan's quality of life is low. In recent times, Pakistan's economy has been going into a crisis, battling rising inflation and unemployment- meanwhile facing challenges of a struggling economy partly due to a decrease in industries such as agriculture and tourism. Pakistan's GDP growth estimates for the fiscal year 2022-2023 were drastically reduced from 2% to a mere 0.29%.⁴

It is evident that political instability has historically been a core problem in Pakistan. Martial law has been imposed numerous times and Pakistan has swung between civilian and military rule. Pakistan has seen three separate military coups, in 1958, 1977, and 1999. In 1958, the military commander-in-chief Muhammad Ayub Khan overthrew president Iskander Ali Mirza. In 1977, the coup was carried out by chief of army staff Muhammad Zia-ul-Haq who overthrew the government of prime minister Zulfikar Ali Bhutto. In 1999, a bloodless coup d'état was initiated, led by General Pervez Musharraf- prime minister Nawaz Sharif was overthrown. Pakistan's political history is clearly unstable, albeit not far from today's reality. Currently, Pakistan's biggest problems are socio-economic. Pakistan doesn't have strong political stability like other countries, even those similar to Pakistan like India. Pakistan's economy is also clearly failing, seemingly partly due to political unrest. Much of the political unrest appears to stem from religious extremism; terrorist attacks are common, deterring tourism, a huge source of economic growth. In 2019, the tourism industry contributed to 10.3% of the global GDP and provided 330 million jobs, the industry is only growing.⁵ Paul Collier mentions in his book 'The Bottom Billion' four curses that the bottom billion poorest people face. Pakistan has three: a conflict trap, a natural resources trap and a poor governance trap. The fourth is being landlocked by bad neighbours. Though Collier's book is not specifically about Pakistan, it is insightful in identifying weaknesses of the Pakistani economy. In this paper I will identify any links between

¹ 'Poverty and Equity Brief', *World Bank*, April 2023

² Sharma, Sandeep, 'Inflation bites Pakistan', *First Post*, April 2023

³ 'Pakistan Food Inflation', *Trading Economics*, August 2023

⁴ Asif Shahzad, 'Pakistan cuts growth forecast, foreign exchange reserves drop', *Reuters*, May 2023

⁵ Katie Birtles, 'Why is tourism so important to the economy', *Trafalgar Tours*, September 2020

Pakistan's economic growth and political instability; how exactly the two affect each other, and to what extent political instability might help Pakistan overcome its economic crisis.

Literature Review

Rani and Batool (2016) used an ARDL model estimate to check how political instability and foreign direct investment affects economic growth in Pakistan. It was concluded that in the short run, economic development is not affected significantly by political instability; in the long term the effects are negative and significant. Foreign direct investment has a positive correlation with economic development in the short and long term. For Pakistan to grow, there must be policies to help attract more foreign direct investment.

Mian (2019) discusses two major problems with Pakistan that has caused the Pakistani economy to fail: religious extremism and corruption amongst the elite. Animosity between religious groups has caused thousands of deaths and division in the people- this deters foreign investment as violence would bring instability. Corrupt elites use their power to partake in illegal business practices; tax evasion for instance, reducing potential tax revenue which could be used to invest back into the failing economy.

Masood (2015) applied regression analysis which investigated the relationship between inflation and FDI and found that though it was statistically insignificant, there was a negative impact of inflation on FDI. Pakistan's complex legal system makes it difficult for investors to find Pakistan appealing. Laws and regulations are complex and the tax and legal procedures required for foreign investors are many. By simplifying and making these laws and regulations more transparent, foreign investors would be more attracted to Pakistan.

Iqbal (2023) economist Atif Mian blames 'foolish policy choices' which have hindered the productivity of the economy, and large deficits and money printing causing rapid inflation. Looking at recent data, Mian explains that Pakistan's economy is going off the rails, citing several factors: a drop in exports possibly meaning a disruption in the supply-side of the economy- Mian referred to the inability to get into an IMF agreement and the government's 'extreme mismanagement' of this situation as reasons.

Methodology

In this paper, I follow a mixed methods research approach. Quantitative and qualitative approaches were both used to create a more comprehensive understanding of Pakistan's status-quo and to make both data types more understandable, more effectively assessing the impacts of political instability across different industries.

Quantitative approaches

For this paper, I have used measures of economic growth to recognize the past and current development in the country. For instance, I have sourced GDP, political stability and government effectiveness data in Pakistan from the World Bank since 1996. The World Bank measures political stability and absence of violence/terrorism as "perceptions of the likelihood of

political instability and/or politically-motivated violence, including terrorism".⁶ I compared the datasets of political stability and government effectiveness with GDP growth and carried out a regression analysis to try to establish any relationship between the two variables.

Qualitative approaches

In carrying out my research, in addition to collecting quantitative data, I also carried out qualitative research. This took two forms: desk-based research to review secondary sources on the subject matter; and interviews with people with lived experience of the topics investigated to add a primary research component to my study.

Desk-based research

My desk-based research included reading news and journal articles from a wide range of sources, including a variety of media outlets, journals and from different points in time. This helps reduce effects of bias and more effectively evaluate to what extent factors went to affecting economic growth across industries. I referred to a timeline graphic, included in the appendix, to scope out past regime changes. This helped in understanding what events were happening at different points.

Interviews

I also conducted interviews to see different perspectives from people with first-hand experiences in Pakistan and have seen the changes in regimes and political systems and its consequences on the economy; knowledgeable about the general people and their situations as well. All people interviewed have lived in Pakistan for several decades and therefore have comprehensive and helpful information and perspectives to share. I used open questions to give the respondents space to answer in as much detail as they wanted, I asked two measurable questions to better understand the intensity of their perspectives. The interviews corroborated my desk-based research: inflation is rising and worsening living standards.

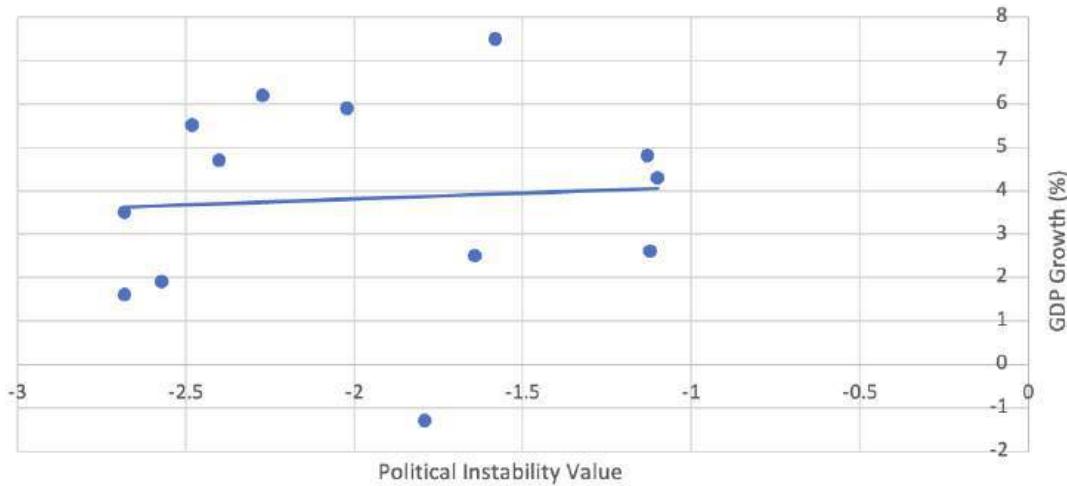
Investigating the relationship between political instability and growth

Discussion of Findings

Much of the qualitative data has shown Pakistan's lack of clear and transparent laws, and political instability as a deterrent for FDI which Pakistan depends on. However, the regression analysis shows that there is little correlation.

⁶ 'Metadata Glossary', *World Bank*

Relationship between Political Instability and Economic Growth in Pakistan



SUMMARY OUTPUT	
Regression Statistics	
Multiple R	0.0693382
R Square	0.0048078
Adjusted R Sq	-0.085664
Standard Err	2.4525208
Observations	13

Interviews

The first interviewee was born in 1967 in Lahore, Pakistan and is a Partner at a financial services firm. He rated Pakistan's future politically a 2/10 as the situation hasn't changed historically. He also rated Pakistan's future economically as a 4/10, stating that presently there has been decline in economic growth but there is potential for the status quo to improve. On a scale of 1-10, he said that a change in government would affect him a 1/10 as he works in the private sector- though for those working in the public sector, there would be a more significant shift due to a likely decrease in loans and government income. There would be a big impact nationally as Pakistan is dependent on loans for development and the government changing may reduce confidence in investors. If military rule took over civilian rule, there would be a decrease in investment from democratic countries as they tend to support other democratic countries. He stated that Pakistan's income is definitely below average; due to inflation, living standards worsened: people struggle to afford utilities, healthcare, housing and food. He also said that there was some consistency 10 years ago but now there are more frequent changes in political regimes. Economically, there is a lower output now than 10 years ago. He believes that the government has to spend more on education and widen the tax net. He estimates that only 15-20% of people

pay tax, the elites don't pay tax at all which is a major reason behind less government spending. There should be less dependence on imports. Corruption is common among the politically active elites.

The second interviewee was born in 1950 in Lahore, Pakistan and is a Chief Financial Officer. He rated Pakistan's future politically as a 1/10, emphasising the lack of stability. Economically, he rated Pakistan's future as a meagre 2/10. He said that a change in government wouldn't affect him personally but on a national scale it would be more drastic, especially in the long-term where economic growth could be hindered if the frequent government changes show a lack of political stability. This is because foreign investors look for stable countries, and a lack of it causes a reduction in foreign direct investment inflow. The interviewee said that foreign direct investment inflow is lower relative to other similar countries due to a lack of clear legislation and a poor justice system. To support his argument, he referenced the lack of adherence to the Constitution. According to Article 224(2), elections must be held within 90 days but elections have yet to be held.⁷ He believes it is easier to make the current economic and political situation worse than better and it's becoming increasingly more difficult to recover the economy. Rapid inflation was another cause of concern to him because the cost of living is increasing whilst many already struggle to make ends meet- he's affected personally, living expenses are increasing yet his income remains stagnant. Medical facilities, education, food quality and quantity are all poor. He said that crime is common and recalled an anecdote of when a person he knew claimed his pension and while walking out with his pension fund, he was robbed at gunpoint. A decade ago, he recalled a better economic and political situation. Unfair means of changing the government changed this situation, investment has reduced, unemployment is more common now than before. Confidence in the government has greatly reduced which has affected all industries.

Interviews' Summary

The interviewees shared similar perspectives which corroborated my desk-based research. They both agreed that the stability of the government impacted economic growth. Albeit, they said they personally didn't face substantial economic changes during regime changes other than inflation which is currently high and makes living expenses unaffordable to many. The interviewees highlighted corruption among the elites who often don't pay taxes. The second interviewee said that few people pay taxes and that the tax net should be widened for increased government spending. Upon further research, this broken tax net appears true and perhaps a reason for a declining rate of economic growth in Pakistan. 2.74 million people file income tax, just 4.1% of the labour force and 1.3% of the population. It should be noted that 35% of these individual filers fall below the taxable income threshold and therefore don't pay anything.⁸ Lower tax revenue means that there's less government spending and so a decline in the GDP.

⁷ Haseeb Bhatti, 'Single day's delay in holding polls beyond 90-day limit 'most grave' constitutional violation: Justice Minallah', *Dawn*, November 2023

⁸ 'Unlocking Pakistan's Income Tax Potential', *CDPR*

Conclusions

The paper analyses the effects of political instability on economic growth in Pakistan. I find that, statistically, there is no strong correlation between political instability and economic growth. However, this could be attributed to a time lag- the effects on economic growth take place later. The interviews show that changes in regimes do not have drastic effects on the interviewees' personal lives other than inflation but they did agree that political instability affects economic growth. There were only two interviews so this conclusion has limitations, more interviews would help increase the reliability of or differ from these findings. The data used is from a limited number of sources so inaccuracies from these sources will affect the regression analysis in the literature.

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Is There Such a Thing as Too Much Democracy? By Ashley Wei

Abstract

This essay will explore the concerns emerging in democratic countries, such as the majority's lack of expertise and flawed electoral systems, demonstrating that we are nowhere near having too much democracy. It will then show through an example of a positive application of democratic values that we can never have too much democracy if it is applied appropriately to its people without the interruption of self-serving representatives. While the idea of democracy was created to facilitate peaceful transitions of power rather than violent uprisings, it has become apparent that democracy has taken a different turn altogether.

What is Democracy?

According to the Cambridge Dictionary, democracy is “the belief in freedom and equality between people, or a system of government based on this belief, in which power is either held by elected representatives or directly by the people themselves.” After generations of adaptation, modern society takes for granted how democracy is meant to function. We have also forgotten what the original Greek thinkers and architects warned us about democratic processes.

“Those people without the skill...to vote could lead to the equivalent of societal shipwreck,” claims Socrates, a Greek philosopher who is widely recognized to be the “Father of Western Philosophy” (Britannica). In his cautionary quote, he is concerned about whether the voter has the appropriate level of expertise to make important, governing decisions. Socrates reflects the tensions that have been present throughout the history of democracy, a fear of this flaw disrupting the effectiveness of the system.

Democracy originates from the Greek word “demos,” representing “people,” and “kratos” signifying “power.” It is a form of government where the power is granted to the people; the version of democracy that underpinned the Athenian government was a direct democracy where the whole population rules directly. Eventually, other forms of democracy would develop - such as when rule is established through elected representatives. This is called a representative democracy, which is the type of democracy most applied in modern society. While Athenian democracy is imperfect, it laid the foundation for what would later influence the development of modern democracies.

Democracy in Today’s World

Today, more than 70 out of 167 countries surveyed in the Economist Intelligence Unit’s (EIU) 2023 Democracy Index, equivalent to 4.4 billion people, live under some form of democratic governmental system. As argued by the United Nations, democracy can play a significant role in maintaining peace and security, while at the same time allowing individuals the freedom of expression and association. In the disordered world that we live in today, the effectiveness of democracy is categorized by an index (a scale of up to 10) which considers the following factors: “electoral process and pluralism, functioning of government, political

participation, political culture, and civil liberties” (EIU). According to the EIU Index, only 7.8% of the world’s population has an index score of 8 or above on the scale. This small percentage of people live under what is referred to as “full democracies,” with fair elections, civil engagement, and individual rights. In contrast, 37.6% of the world’s population live in “flawed democracies,” which possess problems with the rule of law, political participation, and more.

Due to the increase of misinformation, political divides, and increases in bribery, citizens in many democratic countries have found it difficult to trust their governments, suggesting that democracy has been corrupted by modern humanity. Many countries have also displayed either a sudden or gradual decrease in their democracy index score, revealing a rise in social and political conflict together with a decline of democratic quality (EIU). When we understand the degradation of democratic values as seen in the last several decades, we can start to see that there can never be too much democracy if there is a balance between high-quality citizen involvement and the protection of individual rights. If decisions are ultimately made with care and not based on self interest, external influences, and bias, democracy would not descend into the world of chaos and corruption that seems to characterize it now.

A Lack of Expertise Leads to Manipulation

The majority’s lack of political knowledge has made manipulation and negative influence by corrupted, self-driven political candidates effortless and concerning. With widespread, targeted advertisement and misinformation on social media, citizens are more easily manipulated prior to elections and lean to public opinion rather than voicing their personal, well-informed judgments. Additionally, the increase of falsehood, conspiracy theories, and personal attacks can also lead to decision-making based on flawed information, skewing electoral outcomes. This disrupts the original fundamental principles of democracy. Instead of advocating for the freedom of expression and respect of human rights, which is democracy in its purest form, the manipulation seems like a different form of government claiming itself to be democracy through deception.

In 2024, for instance, the United States, one of the world’s leading political powers, is held up as a paragon of democracy. In the US, citizens depend on representatives to make political decisions rather than voting on laws directly themselves. Yet, its dysfunctional government and the nation’s divided beliefs and values no longer allow the country to showcase political harmony and peace. With its existing tensions, the country’s political candidates can quickly ignite further problems and create divides among unacquainted citizens who are vulnerable in believing misinformation. This, in fact, was what characterized Donald Trump’s political campaign in the 2016 election, which ultimately swung in his favor. On the other hand, US citizens do not always educate themselves in preparation for making political decisions. According to CNBC, polls have revealed how 34% of Republican and 32.5% of Democratic registered voters mentioned that “they did not know the names of their party’s congressional candidates in their districts” This shows the public’s deep disinterest and disengagement from democratic processes. According to the National Democratic Institute, if citizens do not have a

strong understanding of the political process and key policy issues, they are less equipped to make informed choices which benefit the country. The issues we face today were predicted by Socrates thousands of years ago - clearly where he questions whether crucial decisions might not be best handed to citizens without relevant knowledge or active engagement.

Besides the citizens, those running for office who lack wisdom have the possibility of using “their elected position for personal gain rather than for common good.” (Socrates). Again, as Socrates warned, the risk of electing an unsuitable leader becomes increasingly high when the citizens themselves are not politically literate. A recent situation in America comes to mind - George Santos, the former US representative for New York was expelled from congress not long after misleading the electorate. By embellishing his resumé and basing his entire candidacy on lies, Santos misled New Yorkers to vote him into the House of Representatives. This demonstrates how the perfect marriage of candidate corruption and voter illiteracy can lead to corrupted leadership. But again, none of this should be indicative of democracy, and absolutely not too much of it.

Flawed Electoral Systems Become Problematic

Electoral systems worldwide are becoming increasingly flawed, threatening the foundations of democracy. One of the most alarming trends is the rise in candidate bribery, a practice that brutally ignores the principle of free and fair elections. According to the Public Choice journal’s article “When is Buying Votes Wrong?”, bribery has become more sophisticated and widespread, with candidates offering monetary incentives, promises of jobs, contracts, or other forms of dishonest treatment in exchange for votes. Such practices distort the will of the electorate, allowing wealthy individuals to gain political power rather than earning it through the genuine support of citizens. Rather than those with the best leadership qualities who propose the more ethical ideas, voting comes down to who has the bigger wallet. While the initial democratic electoral system was designed for voters to have a chance to voice their opinion, humanity has slowly allowed elections to focus on the temptation of personal gains rather than benefits for the entire nation. The uneven “playing field” often leads to unstable, unrepresented governments and crushed democratic norms - not too much democracy at all but rather anti-democracy.

According to the official voting results posted by the New York Times, the United States’ 2016 presidential election showcased Hilary Clinton winning the popular vote, (combination of all voters in all states of America) but Donald Trump winning the electoral college (a group of presidential electors formed every four years who vote on the president and vice president) thus giving him the White House. If the fundamental and radical principles of democracy ensures the election to skew towards the “vote of the people,” why did the presidential position eventually go to Trump? This system was created by the original forefathers of America who were creating standards for a much smaller United States (the 13 original colonies). We find here the question of too much democracy shifting to now ask: is America’s system of democracy outdated?

Does an Effective Democracy Exist?

Democracy was created to govern a fair, free, and equal nation, yet its modern interpretation utilizes it for a different purpose. If democracy doesn't exist in its purest and intended form, there will never be such a thing as too much of it. This form of government, unadulterated by greed and self interest, is still needed for equality, freedom, and justice in the modern world (United Nations). In its purest form, democracy remains essential for protecting human rights and ensuring economic prosperity. According to MIT Economics, economists have revealed that democratization causes a 20-25 percent increase in GDP per capita. Moreover, during an International Social Survey Program (ISSP) survey, it was also found that more exposure to democracy results in healthier emotional well-being as individuals find more opportunities to participate politically. In the survey, a sample of citizens of different countries were asked to rate their mental state on a scale "very happy" to "not at all happy". Ireland, which was ranked 7th on the Democracy Index is now ranked 1st out of all the countries surveyed with 44% of its citizens claiming that they were "very happy" while Russia, ranked 144 on the Democracy index had less than 5% saying they were "very happy". Clearly, democracy can and does work in some parts of the world - and is not being applied too much in these areas. But nations like America should learn from them because their democracy is not working.

Conclusion

Ultimately, there is no such thing as too much democracy, especially when it enables civic participation without flaws and corruption by human nature that violate basic integrity and human rights. While it is rare for a country to have a "perfect" democracy, its core principles should attempt to preserve the notion of the will of the people. In its purest form, it depicts a direct democracy where the power is exercised directly by the people. In today's world, Switzerland is the only country which governs through a direct democracy. All residents in the country over the age of 18 are able to vote in an election to determine how the country is run (World Economic Forum). Citizens can also launch their own popular initiative when demanding a change in the constitution, but this requires the prior agreement of 100,000 individuals with their valid signatures. This places Switzerland on the 2023 Democracy Index with an overall score of 9.14 out 10, also categorizing it as a full democracy. If all democracies came in their purest form, there might never be too much of it. Citizens can voice their opinion in the nation's politics and have the freedom and right to vote independently, without the interruption of misleading representatives who abuse their power. Though democracy will always have flaws by virtue of being human run, enhancing transparency and access to information will make it harder for flawed information to exist, ultimately feeding the public with valid and accurate knowledge. Educating and awareness-raising through public campaigns is also crucial to cultivate a culture that rejects corruption and fraud. With these available solutions to access, democratic institutions can be strengthened and empowered, allowing democracy to deliver its promise of equal rights, opportunities, and representation at last.

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A Review of Plant-Based Diets in The Adult and Neonate in Terms of Cognitive, Neurological, and Psychiatric Function By Sadie Heiger

Abstract

In recent years, vegetarianism has become more common worldwide. Because of this, more studies have been conducted analyzing the effects of restrictive diets. As we look closer into the effects of diet on the body, connections have been made regarding the differences between an omnivorous and vegetarian diet, specifically regarding brain development. The differences in micronutrients (vitamins and minerals) and macronutrients (lipids, proteins, and carbohydrates) in vegetarian and vegan diets have been shown in some studies to impact neurological function. Plant-based and omnivorous diets have many different levels of nutrients that impact the brain's cognitive, neurological, and psychiatric functions. Through recent advancements in neuroimaging technology, we can assess the brain's growth and development in terms of structure and function. These technologies have improved how we can analyze how different dietary compositions affect the function and structure of the human brain. Our study will highlight the changes and patterns in brain development caused by a plant-based diet and how it affects cognition and behavior.

Introduction

Energy is required to fuel development and growth in the body (Hall et al.). This energy comes from the food that we eat every day. In terms of neurological development, this energy is crucial to ensuring the healthy brain function of any given individual (Clemente-Suárez et al.). Different dietary compositions have shown varying intakes of critical vitamins and nutrients regarding neurological development. Specifically, when analyzing restrictive diets we can see wide-ranging variability in terms of measurable brain development at the neurological, psychiatric, and cognitive deficits (Berkins et al.; Byrne et al.; Zhang et al.). The analysis of this paper will focus on how vegetarianism and vegan diets affect neurologic, cognitive, and psychiatric development as well as how a plant-based diet can impact the function of an individual's brain. These results will be compared to individuals following an omnivorous diet. Vegetarianism is a diet in which an individual does not eat meat. Veganism, however, is a diet that excludes meat and all animal products (Petti et al.). Pescetarianism, which is a diet that includes fish and all animal products but no poultry or red meat, will be discussed as well. Vegetarianism and veganism are commonly referred to as plant-based diets and this term will be used to reference them together. This paper will examine the differences between plant-based and omnivorous diets and the effects that both have on the developing brain.

Vegetarianism has a rich history, stemming back to Greece in the sixth century (Harden). In more recent years, vegetarianism has become more common worldwide for a multitude of reasons, including more year-round accessibility, growing health concerns, and increased animal welfare activism (Mb). This has resulted in a significant increase in research on the effects of

plant-based diets on health. According to a wide range of nutritionists and food experts, plant-based diets have been known to be linked to lower rates of cardiac disease, stroke prevention, obesity, and cancer (Tuso et al.). This can be attributed to lower levels of sodium, cholesterol, and saturated fats in plant-based diets (Tuso et al.). The disadvantages of this diet can include an increased likelihood of developing vitamin deficiencies that can lead to conditions such as anemia (Chouraqui). Anemia is the condition of having low iron levels in the blood, which can be caused by improper protein intake (Pawlak et al.). In regards to human brain development, these small vitamins and minerals can have a tremendous effect on our behavior, attitude, and overall psychological development (Berkins et al.).

Many critical vitamins and minerals aid in the development of neurological, psychiatric, and cognitive functions (Kennedy and Haskell). One example is Vitamin A, which is responsible for immune system support and growth and development (De Azevedo Paiva et al.). Vitamin B6, is responsible for energy levels and brain function (Tardy et al.). Vitamin B12 is responsible for helping with DNA growth and development, while Vitamin B9, also known as folate, is responsible for healthy cellular development (Tardy et al.). Finally, omega 3-6 is responsible for healthy brain development and energy function (Innis). Additional factors associated with prolonged vitamin deficiencies include muscle weakness and impaired eyesight (Jen and Yan). Long-term deficits in nutrient intake specifically in vitamin D and calcium have been shown to lead to osteoporosis (Heaney). Vitamin D deficiency has also been linked to a 300% increased risk of cardiovascular disease (Wang et al.). Deficiency in folate and folic acid are associated with severe neural tube defects as well as congenital heart defects. Supplementation or dietary intervention has been shown to reduce the rates of these vitamin deficiency-related diseases (Czeizel et al.).

Medical technology has rapidly evolved, including new tools such as MRIs and CTs for analyzing neurological activity. These technologies facilitate analysis of neurological development and change than ever seen before. The analysis of brain development and change is crucial because of how critically it affects the future of every individual (Stiles and Jernigan). Research has indicated that a plant-based diet can impact the brain's development due to deficiencies in vitamins and nutrients including Vitamin B6, B12, folate, and omega-3 fatty acids. (Kapoor et al.; Firth et al.; Cheatham). Analysis of cognition, behavior, memory, and physical development of subcortical brain volumes can provide insight into the effects of vitamin deficiency. Due to the small sample size of studies in this field, clear conclusions cannot be drawn from the results of many of these studies. It has also been shown that in many cases the effect size for relationships between a plant-based diet and neurological development is small (Medawar et al.).

When analyzing the molecular composition of omnivorous and plant-based diets, a variety of differences have been observed most commonly surrounding protein intake and micronutrient composition (MacArthur et al.; Gibbs and Cappuccio). These differences were analyzed in a study reviewing plant-based diets from around the world, composed of

observational and intervention studies that excluded diets that had been prescribed or an “overly restrictive” diet such as a raw food diet from 2000 to January 2020 (Neufingerl and Eilander). Out of the 141 studies analyzed, it showcased that, across the board, vegetarians and vegans had lower amounts of protein, but the majority did fall within the normal range. Additionally, fiber intake was also measured, and the highest fiber intake was found in vegans. Whereas in the meat eater population, the majority was under the recommended consumption. Vitamin consumption was analyzed in some of these studies and showed that individuals who ate plant-based diets were generally low in vitamin B12. This was concluded from observing 48 studies.

A protein is composed of an assortment of amino acids that are then formed into polypeptide chains and then folded to create the protein structure (Sun et al.). There are 20 essential amino acids, and our body can produce about 11 of them naturally. Dietary supplementation is the way we get the other nine essential amino acids (“Amino Acid”). Lack of protein has been shown to affect neurological health and decrease in neurotransmission and memorization (Sato et al.). This deficiency also causes muscle weakness and loss of muscle mass, known as sarcopenia (Beasley et al.). These effects can be attributed to how important amino acids are in cellular function in all areas of the body, including the brain. How a vegetarian compared to an omnivore consumes protein has shown to be very different. For omnivores, poultry and red meat are two of the most common sources of protein (Services) A study on protein intake showed that vegetarian and vegan-based diets were the lowest in protein intake. Additionally, the protein that plant-based individuals were ingesting was suggested to be more beneficial than the meat-based protein (Papier et al.). These proteins were considered more beneficial because they showed an overall lower risk of contributing to ailments such as obesity, heart disease, and stroke over time.

Research suggests that following a plant-based diet may have positive health-related impacts such as lower blood pressure and cholesterol along with a decrease in diabetes and significantly lower rates of heart disease (Kahleova et al.). However, it has been noted that following a plant-based diet may result in a higher likelihood of an individual developing nutritional deficiencies over time, leading to deleterious neurological impacts (Tuso et al.; Berkins et al.). Additionally, many scientists have attributed both positive and negative developmental factors related to plant-based diets and the brain development of adults, children, and unborn babies (Chaudron et al.; Cofnas).

Neonatal Development

Research has shown that the development of an individual's brain can be hindered by vitamin and mineral deficiencies caused by a vegetarian and vegan diet (Sanders). However, there is very little research to support the theory that vegan and vegetarian diets are negatively impact a developing child's brain (Crozier et al.). When looking at the vegetarian diet as it affects pregnancy, research has not demonstrated that vegetarianism affects cognitive development or that it is linked to an unequal sex ratio of newborns (Cofnas). It was shown that vegetarian

mothers give birth to much higher numbers of girls instead of boys due to the “selective spontaneous abortion” of male fetuses. Spontaneous abortion can be defined as the loss of pregnancy without additional intervention before the 20th week of pregnancy (Griebel et al.). This additional stress could be linked to a deficiency in vitamin B6 or B12 or a deficiency in omega-3-6 because they play an important role in behavioral function as well as neurological development (Cofnas). Lastly, it is now known that vegetarian mothers have lower amounts of specific omega-3-6 fatty acids, also known as arachidonic acid and docosahexaenoic acid, compared to their omnivorous counterparts during gestation (Cheatham). This difference may lead to more noticeable behavioral issues in young children.

Cognitive Development of the Neonate

It has been noted that in infants, docosahexaenoic acid is a critical nutrient in terms of cognitive brain function (Brenna and Carlson). Arachidonic acid and docosahexaenoic acid (DHA) are nutrients responsible for aiding in the neurodevelopment process. Docosahexaenoic and arachidonic acids are omega-3 fatty acids commonly found in fish oils. They specifically assist in the functional and structural development of the brain (Niemoller and Bazan). Scarcity of this nutrient during the gestational period and in the child’s infancy has been shown to result in cognitive and neurologic structural impairment. (Derbyshire). There is evidence of decreased cognitive development in infants and toddlers due to the absence of these nutrients (Brenna and Carlson).

The most notable time that a fetus is gaining this nutrient is the 2nd half of the gestational period and through the first two years of life. Mothers gain these nutrients through diet and additional supplementation when indicated. Infants gain a majority of these nutrients from their mothers after birth through breast milk (Brenna and Carlson). It has been shown that with additional supplementation of these nutrients, more progressive neurological development has occurred and accelerated progression in beginning milestones such as cognition and memorization activities have been demonstrated. It should also be noted that breast milk from omnivorous mothers had a higher concentration of DHA compared to vegetarian mothers' breast milk and formula feeding (Brenna and Carlson). These levels are measured in infants and adults through omega-3 panels which are blood tests that measure the acid content in red blood cells (Bernardi et al.).

In addition to being sourced from nutritional supplements, arachidonic acid, and DHA can be found in dairy fat. Dairy fat is a substance that not only provides essential fatty acids for cognitive function but also protein and minerals, such as calcium, phosphorous, and iron, necessary for human development (Erick; Brenna and Carlson). One critical component of breast milk and bovine milk is the milk fat globular membrane (Hernell et al.). This membrane is what surrounds the fat in mammalian milk. It has been shown that these membranes are associated with health benefits, including immune support and higher cognitive performance. Comparatively, infants fed formula without this membrane were shown to have lower cognitive

function, increased rates of diabetes, and as a group, were found to have higher incidences of immunocompromise. For this reason, technology is continuing to work on adding bovine MFGM into formula to better support the infant population and the formula industry as a whole (Hernell et al.).

Neurological Development of the Neonate

During the gestational period, vitamin B12 deficiencies can be passed onto the fetus due to the decreased level of this nutrient in the mother. In one notable case, it was found that a vegan mother's infant had suffered an extensive decrease in neurological functioning between the ages of 3 months to 9 months. Specifically, these researchers noted a lack of fine motor skills and abnormal lethargic behavior (Wighton et al.). It was shown that the severity of the deficiency was caused by the deficiency in the mother's diet which had then passed onto the infant through the vitamin deficient breast milk. The infant slipped into a comatose state and was later diagnosed with megaloblastic anemia. The treatment in this circumstance was to provide extensive supplementation to the infant and mother with vitamin B12. This case demonstrated that the vitamin deficiency of the mother is what caused the deterioration of the infant at such an alarming rate. With the assistance of medical staff, additional parts of his brain became functional but he will likely suffer from lifelong neurological deficits. The current recommendation that all pregnant people adhering to plant-based diets supplement their food intake with vitamin B12 is to prevent these potential neurological deficits from occurring in the future (Wighton et al.).

Normal brain development requires specific micronutrients and macronutrients, such as folate and docosahexaenoic acid (Cheatham; Irvine et al.). In recent years, lack of folate has been shown to impact neurological development quite significantly. In a developing fetus's brain, folate is used to help form the neural tube, which is responsible for neurotransmission (Irvine et al.). At this time, research has only demonstrated improvement in neurological development with folate supplementation in animal studies. At this point, human studies conducted have been inconsistent due to the different methods used and the sample size of the population included (Irvine et al.).

Additionally, the absence of docosahexaenoic acid (DHA); also known as omega-3 fatty acids, has also been a nutrient linked to increased neurological development in fetuses and infants (Cheatham). DHA is passed from the mother to the fetus in the gestational period. Most of this transfer takes place during the last trimester of pregnancy. Normal levels of this nutrient help increase fetal cognitive skills in the early years of education and help reduce the risk of developing a neurological disorder (Cheatham).

Effects of Deficiency in Adults

It is important to look at the impacts and effects of nutritional deficiencies through all different stages of life; in adulthood the brain shifts and reacts constantly to changes in an

individual's environment (Johnson et al., 2015). As reviewed thus far, some of the most notable deficiencies associated with a plant-based diet that demonstrate a negative correlation regarding neurological impact are vitamin B12 and omegas 3-6. In addition to the neurologic impacts on development; these deficiencies can contribute negatively to an adult's overall health status in a multitude of ways. Deficiency in vitamin B12 has been found to be linked to megaloblastic anemia as well as chronic inflammation of the digestive tract (Langan and Goodbred). This can lead to bowel disease and negatively impact the digestive system long term. Additionally, supplementation with omegas 3-6 has been found to improve symptoms of ADHD, specifically regarding behavior regulation and increased task completion as well as improvement in overall cognitive function, specifically relating to memory (Gow and Hibbeln; Bauer et al.).

Cognitive Effects of Deficiency in Adults

Cognition is the process of acquiring knowledge and understanding by using one's brain as well as senses (Bayne et al.). Cognitive function in adults can be measured in a multitude of ways. One of the best ways to measure cognition is through cognitive assessments (Snyder et al.).

The purpose of this study was to analyze the impacts of a plant-based and omnivorous diet on cognition. We reviewed a case that used a comprehensive neuropsychological battery with 132 test subjects (Gatto et al.). A neuropsychological battery is a type of assessment that helps assess neurological and cognitive functioning using an array of data analysis (Neuropsychological Test Battery - an Overview | ScienceDirect Topics). Prior to the initiation of the study, it was shown that 19.7% of the individuals had previous memory impairment. This was taken into consideration when analyzing the results. As this study was being completed, researchers analyzed various dietary groups. Some included vegans, vegetarians, pescetarians, and individuals who ate meat, dairy, and vegetables (Gatto et al.). The results show no substantial differences in cognitive ability between vegetarians and meat eaters. It was however noted that among all individuals adhering to diets that were stable and consistent, greater memory and language skills were present (Gatto et al.). In terms of differences in processing speed or reaction time among the various groups, the experiment was inconclusive, and no major differences were identified.

Neurological Effects of Deficiency in Adults

In terms of neurological development, by the time an individual reaches approximately 25 years of age, development is complete. A diet after this point will no longer threaten an individual's health or well-being from a developmental standpoint (Arain et al.). With this information, we can ascertain that in the early years, it is critical to supplement omega-3 fatty acids as well as vitamins B6 and B12 in order to promote optimal neurological function of the developing brain (Rathod et al.). These nutrients play a critical role in the neurological development of children and continue to increase healthy brain function in the adult years

surrounding impulse control, cognitive function, and mental health. Deficiencies in these nutrients have been shown to cause adverse mental health effects and can lead to long-term problems if not addressed in the early years (Rathod et al.). The research currently available on this topic has so far been measured in small data samples, so consideration for all additional variables is essential. Although some cases showed no substantial negative effects, other individuals in various studies encountered unpleasant effects due to deficiencies in several of the nutrients examined in this study (Rathod et al.).

Psychiatric Effects of Deficiency in Adults

Vitamins B12 and B6 have been observed to have adverse effects that are most commonly associated with depression and anxiety (Berkins et al.). Studies have also shown that these deficiencies are more common in women and that supplementation did show positive development in brain matter over time (Berkins et al.).

Additionally, brain imaging showed that deficiencies in these vitamins can lead to loss of brain matter over time (Berkins et al.). Loss of this critical matter has been linked to schizophrenia and depression. Additionally, individuals who were observed to have heightened levels of B12, B6, and folate were shown to have larger amounts of gray matter and overall were at less risk for developing a mental illness later in life (Erickson et al.).

Future Direction

Since research investigating the connection between a plant-based diet and neurological development is a relatively new field of study, there are many ways that current research can continue moving forward. In a more recent study conducted, the physical structure of subcortical brain matter and function was observed and showed a positive relationship associated with vitamin B6 and 12 (Berkins et al.). However, more studies are needed to clarify the effects of plant-based diets on the brain and the overall health status of individuals. Additionally, studies utilizing cutting-edge techniques and longitudinal design are necessary to advance our understanding in this field. Past studies have demonstrated mixed results up to this point; for example, a study on B12 and folate deficiency highlighted no significant changes in terms of subcortical volumes or function. However, in a recent study, the opposite result was highlighted. In this study, the dangerous neurological effects that the lack of vitamin B12, and folate can have were showcased and supported by current research (Kapoor et al.). Because of the additional steps that vegetarians must take to ensure adequate nutritional value, they are more likely to have vitamin deficiencies that can negatively contribute to neurological developmental health at all ages to some degree.

Limitations and inconsistencies were seen throughout all areas of the research in this field. Two main areas of these inconsistencies were sample size and inconsistent results (Kapoor et al.) (Medawar et al.). It has been shown that a larger unbiased sample improves the generalizability of the results. In many studies, the standard deviation was much lower in many

cases with larger sample sizes. Results with a lower standard deviation show greater precision of the results analyzed. In many of these studies, participants selected through online forum searches may lead to selection bias throughout these results. This bias compromises the validity of these results. More research in this field will lead to more accurate and consistent results for future studies regarding the neurological development and function of those adhering to plant-based diets.

Conclusion

As a whole, vegetarianism can provide many benefits to many individuals around the world. However, it is important to note that there are instances in which our bodies can be negatively affected by long-term restrictive diets (Benzie and Wachtel-Galor). Individuals who maintain vegetarian diets for a long duration may be deficient in essential nutrients that most meat eaters regularly ingest. Without consistent sources or supplements of nutrients found primarily in meat, vegetarians may subject themselves to poorer neurological development of the brain while increasing their propensity to develop future mental health issues (Wighton et al.; Berkins et al.). The development of the brain is something that will take place on a different timeline for everyone, but with adequate knowledge of the effects that vegetarianism can have, it sets more people up for greater success in the long term by providing the information to make dietary changes, including proper supplementation, part of their daily routine (Yaseen et al.).

As we reviewed the data, it has shown that many of the processes occur at various rates depending on factors including age and pre-existing health status. The data we have analyzed has shown that an individual's diet does not just affect one part of the human body. As stated previously, the food we eat produces the energy to fuel the development and growth of the whole body. In adults, we saw most commonly that there was a direct link between depression and anxiety related to the absence of B12 and B6 in a vegetarian diet (Berkins et al.). However, in the focus on neonatal cases, it was shown that the lack of arachidonic acid and docosahexaenoic acids were passed down in lower amounts to the developing fetus and could overall contribute to abnormal behavioral function in the first few months of life (Cheatham). These findings show that although research is limited at this time, continued study on this topic is essential to better understand how vitamin deficiency related to neurological function and ultimately to improve outcomes.

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The Cashless Payment Effect On Economic Growth By Sofi Memelbekova, Gleb Shubin, Yerassyl Alpysbay, Zhanadil Kerimbek.

Summary

This research investigates the impact of cashless payment systems on economic growth, reflecting the global transition toward digital financial practices. It examines their influence on consumer behavior, business operations, financial inclusion, and economic stability, hypothesizing that the benefits of cashless transactions—such as enhanced efficiency, reduced crime, and increased consumer spending—outweigh potential drawbacks like overspending and technical vulnerabilities.

A survey targeting younger participants reveals that 70.4% frequently use cashless payment methods, citing convenience, security, and transaction speed as primary advantages. However, 44.4% noted an increase in spending, while 37.7% expressed uncertainty about the broader economic effects. Respondents highlighted the potential for cashless systems to support small businesses but pointed to barriers such as technological limitations and low public trust.

The findings indicate that cashless payments can drive economic growth and inclusivity by streamlining transactions and broadening financial access. However, challenges like infrastructure gaps and limited financial literacy pose significant obstacles. Addressing these issues is crucial to minimizing risks such as unequal access and technical vulnerabilities while maximizing benefits.

The study underscores the need for a balanced strategy to enable a sustainable and inclusive transition to a cashless economy. This approach can unlock the full potential of digital payments while mitigating unintended consequences, fostering economic resilience, and enhancing financial participation.

As cashless systems reshape the global financial landscape, they present both opportunities and challenges. Understanding their impacts on consumer behavior, business efficiency, financial inclusion, and crime reduction is vital for leveraging their role in economic growth.

Introduction

The shift from cash to cashless payments is transforming the global financial landscape, offering both opportunities and challenges for economic growth. The growing use of digital payment systems, such as mobile wallets, contactless cards, and blockchain technology, demands a comprehensive examination of their impact. These systems influence key economic factors, including consumer behavior, business efficiency, financial inclusion, crime reduction, and technological progress, all of which have important implications for the wider economy.

Understanding the effects of cashless payments is essential, as they are starting to replace traditional cash in numerous countries. Research has shown that cashless payments can lead to increased consumer spending due to the reduced psychological impact of paying with cash, known as the "pain of paying" (Feinberg, 1986; Prelec & Loewenstein, 1998). From the business

fostering perspective, cashless transactions improve efficiency by reducing transaction times, cutting costs related to cash handling, and reducing the risk of theft (Ong & Chong, 2022). Additionally, there is evidence that cashless payments may enhance financial inclusion by providing access to financial services for unbanked populations, which can stimulate economic development (World Economic Forum, 2021).

However, despite the many benefits, the shift to cashless payments have certain risks. These include potential vulnerabilities during crises when technological infrastructure may fail, as well as the psychological and behavioral effects on consumer spending, leading to higher levels of debt and financial instability (Pacillo, 2024). This research work aims to examine the multifaceted impacts of cashless payments on economic growth, focusing on both their benefits and drawbacks. Specifically, the research will investigate key areas, such as consumer spending, business efficiency, crime reduction, financial inclusion, and technological advancements.

The primary purpose of this paper is to evaluate the effects of cashless payments on economic growth while identifying the challenges and risks associated with transition to cashless payment. The hypothesis explored is that while cashless payments can stimulate economic activity, they also create the risk of increased financial instability and potential exclusion during times of crisis. The results indicate that cashless payments contribute to economic growth but also require careful consideration of the risks associated with their widespread adoption.

Key Takeaway Points

- Cashless payments can enhance consumer spending and business efficiency, fostering economic growth.
- Technological innovations such as blockchain and biometric authentication can further drive economic advantages.
- Challenges, such as economic vulnerabilities during crises and the risk of overspending, must be addressed to ensure the long-term sustainability of a cashless economy.

Results

The quantitative data collected through the Google Form survey will be analyzed to identify trends, preferences, and perceptions of respondents regarding cashless payments. Next, statistics will be used to summarize the frequency of non-cash payment usage, perceived advantages over cash, and opinions on the economic effects of increased cashless transactions. In turn, responses regarding barriers to adoption, impacts on small businesses, changes in personal expenses, and perspectives on a future shift to fully cashless transactions will provide insights into societal attitudes and potential economic implications of transitioning toward a cashless economy.

The first question measured the frequency of cashless payment usage, with a majority of 70.4% reporting frequent use, while 25.9% used them occasionally (Figure 1, Question 1). This suggests a clear preference for digital transactions over cash.

The second question explored the benefits of cashless payments, with convenience being the most cited advantage (85.2%), followed by security (44.4%), transaction speed, and expense tracking (66.7% each) (Figure 2, Question 2), underscoring the positive perception of digital payment systems.

In the third question, 50% of respondents agreed that cashless payments have a positive economic impact, while 37.7% were uncertain, and 13% disagreed (Figure 3, Question 3), reflecting general optimism about their economic effects.

The fourth question identified barriers to adopting cashless payments. While 64% saw no obstacles, 14.8% cited a lack of trust, and 9.3% pointed to limited understanding of the technology (Figure 4, Question 4), highlighting some concerns around widespread adoption.

The fifth question examined the impact of cashless payments on small businesses. A majority of 66.7% believed it benefits them, while 20.4% disagreed (Figure 5, Question 5).

The sixth question focused on spending behavior, with 44.4% reporting increased spending, 38.9% noticing no change, and 16.7% spending less (Figure 6, Question 6), indicating varied effects on consumer habits.

The final question gauged opinions on the future of cashless transactions, with 40.7% considering it inevitable, 44.4% seeing it as possible but not imminent, and 14.8% believing cash will never fully disappear (Figure 7, Question 7).

Discussion

In our survey, we set out to gather insights from society on various questions that pique our interest. To reach respondents, we employed a method of distributing the questionnaire among friends and acquaintances. The average age of the participants is under 30, which means we are capturing the perspectives of a young, modern generation.

The survey results reveal a strong preference for cashless payments among young people, with 70.4% using them frequently, reflecting the global shift towards digital financial practices. This trend is strengthened by respondents' focus on the benefits of cashless transactions, particularly convenience (85.2%), security, and expense tracking. These factors highlight the practical advantages of cashless payments, which likely contribute to their growing adoption.

The perception that cashless payments are beneficial to the economy, with 50% of participants agreeing, indicates optimism among the younger generation regarding the positive economic impact of digital transactions. This suggests that digital payments are not seen as disruptive, potentially encouraging policymakers and businesses to further support their adoption.

While most respondents (64%) saw no barriers to cashless payment adoption, 14.8% expressed concerns about trust, and 9.3% cited a lack of understanding of the technology. These issues could slow the broader acceptance of cashless systems, especially among older or less familiar with technology populations. Addressing these concerns will be important to ensure that the transition to digital payments is inclusive.

Regarding small businesses, 66.7% of participants believed that cashless payments would have a positive impact, suggesting that digital transactions could improve efficiency and customer experience. This insight may be valuable for policymakers aiming to support small business growth that will have crucial impact on the overall economy of the country.

However, spending habits varied among respondents. While 44.4% reported increased spending, 16.7% spent less, and 38.9% observed no change, indicating that the impact of cashless payments on individual behavior can be different.

Opinions on the future of cashless payments were various, with 40.7% believing a fully cashless society is inevitable, while 44.4% thought it possible but not soon. This indicates optimism tempered by concerns about the speed of adoption.

Limitations and Future Research

A limitation of this study is its reliance on self-reported data, which may be biased by participants' willingness to accurately describe their payment behaviors. Future research could include a more diverse sample, considering generational and regional differences in cashless payment adoption. Additionally, exploring the effects on various socioeconomic groups would offer a deeper understanding of the barriers and benefits associated with cashless systems.

Conclusion

In conclusion, cashless payments are widely valued for their convenience and security, with increasing recognition of their positive economic potential. While concerns about trust and understanding remain, the overall trend points to a growing shift toward digital financial practices, with significant implications for both individual behavior and the broader economy. Further research is needed to assess the long-term effects of this transition and to address the challenges that could hinder full adoption.

Material and method

Quantitative research was used because it makes data collection more effective, which is important for our research topic.

The sampling process for this research will involve a combination of stratified random sampling. Stratified random sampling will be used to ensure representation from various socio-economic backgrounds.

For the quantitative aspect of the study, a Google Form survey was chosen to define society's view. It will be identified by asking various questions designed to capture respondents' frequency of use, perceptions, and attitudes towards cashless payments, as well as the potential economic implications and challenges associated with this shift. The survey responses were then analyzed to draw conclusions about public opinion and identify trends related to the adoption of cashless payment methods.

Figures and questions

1. How often do you use non-cash payments (bank cards, mobile payments, etc.)
2. From your perspective, what advantages do non-cash payments have over cash?(multiple options)
3. Do you think that the increased use of cashless payments has a positive effect on the country's economy?
4. What do you think are the main barriers to using cashless transactions in your country?
5. What impact can cashless payments have on small businesses?
6. Have you noticed changes in your expenses after switching to cashless payments?
7. Do you think your country will move towards completely cashless transactions in the future?

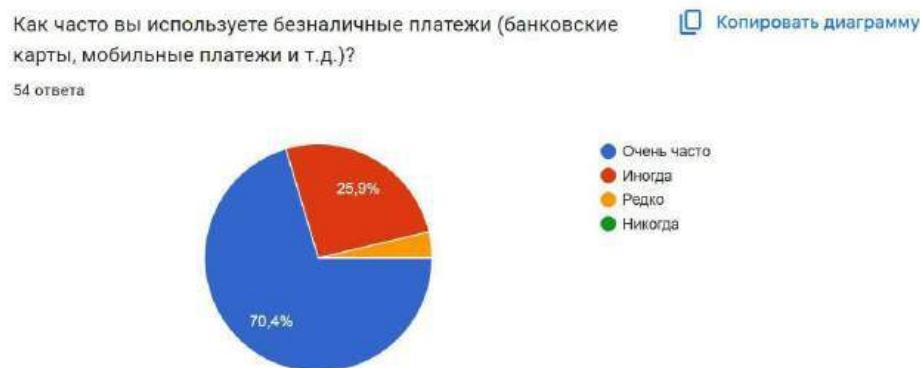


Fig. 1: How often do you use non-cash payments (bank cards, mobile payments, etc.)

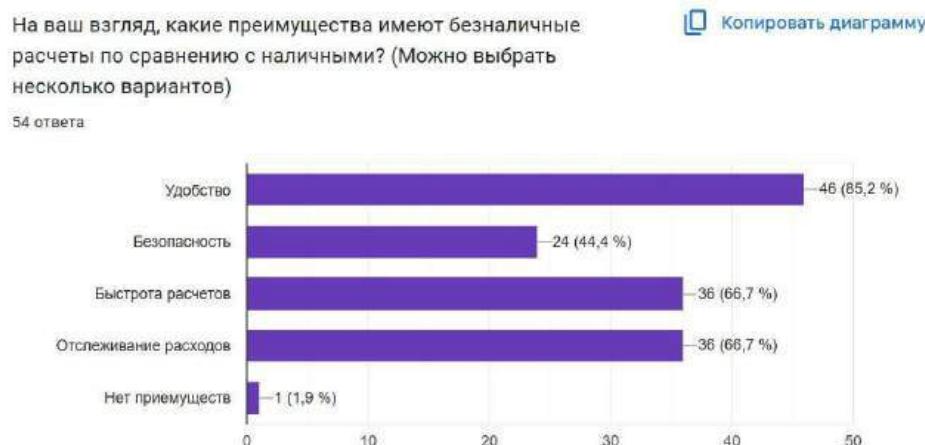


Fig. 2: From your perspective, what advantages do non-cash payments have over cash? (multiple options)

Считаете ли вы, что увеличение использования безналичных расчетов положительно влияет на экономику страны?

Копировать диаграмму

53 ответа

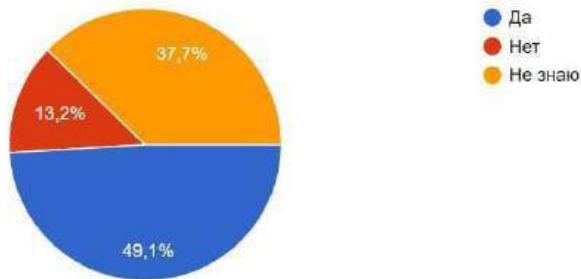


Fig. 3: Do you think that the increased use of cashless payments has a positive effect on the country's economy?

Как вы думаете, что является основным препятствием для использования безналичных расчетов в вашей стране?

Копировать диаграмму

54 ответа

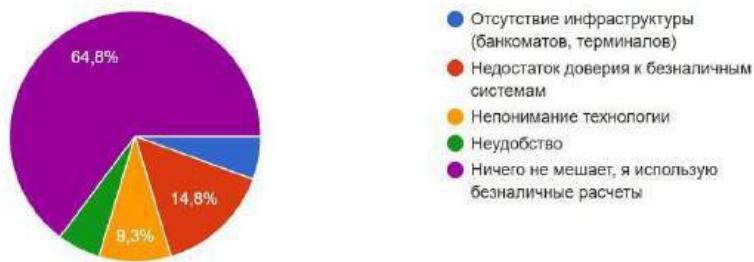


Fig. 4: What do you think are the main barriers to using cashless transactions in your country?

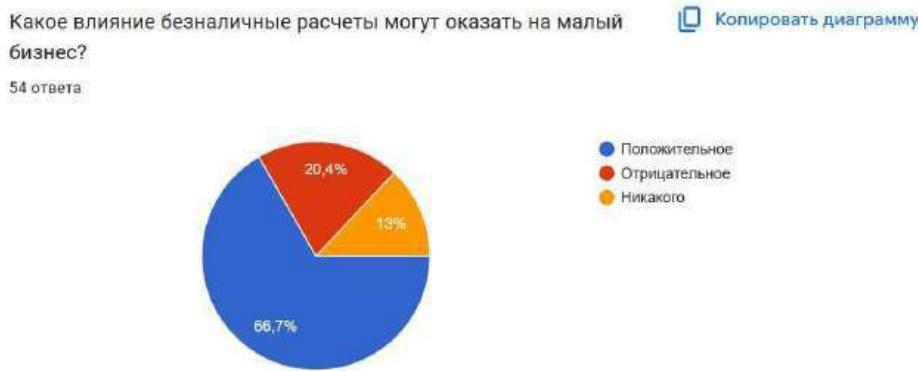


Fig. 5: What impact can cashless payments have on small businesses?

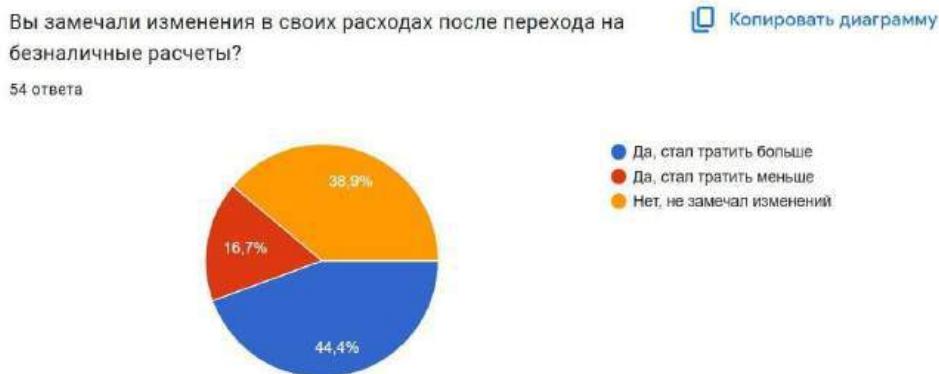


Fig. 6: Have you noticed changes in your expenses after switching to cashless payments?

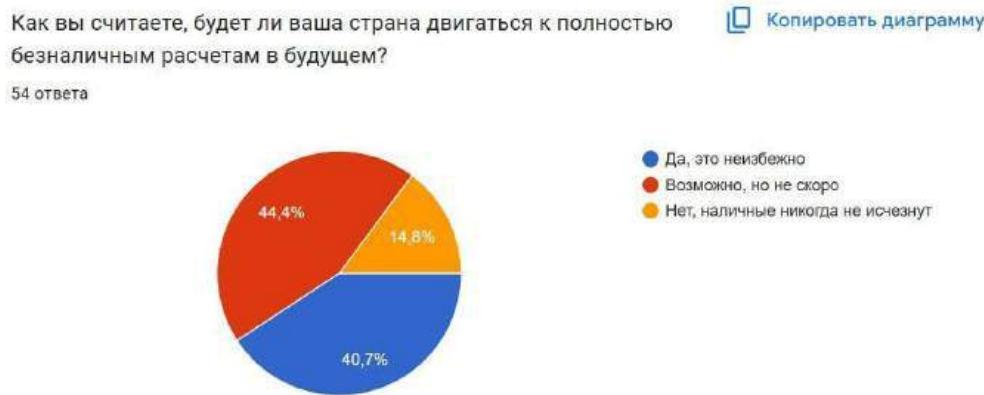


Fig. 7: Do you think your country will move towards completely cashless transactions in the future?

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The Conquest of Obstetrics: How Physicians took over Midwifery By Joelle Kardos

Childbirth is an integral part of the human experience, and many cultures approach it differently. Throughout each of these cultures, however, there was often the role of a midwife. So why is the midwife no longer such an important part of the birth experience in our culture—Western civilization?

In Northern Europe, the undue and ill-realized transition of primary obstetric caregivers from midwives to physicians was harmful to mothers and infants, as well as the midwives' profession. A synthesis of these two professions was present in Holland during the 17th-18th centuries and allowed for trust and security for all parties involved. Our modern view of obstetrics, and the proper places of the midwife and physician, are very different from those of our ancestors.

For mothers in early Modern Europe, the midwife was the primary healthcare professional they had access to before, during, and after their pregnancies. These midwives were typically women from the village, who the mother felt comfortable with attending the birth. A midwife would typically be trained through apprenticeship to the village's prior midwife, and they would only be entrusted with births after they had proved their readiness.⁹

The role of the midwife was considered a communal duty, and often they would not receive monetary compensation for their work. A mother would repay the midwife by providing them food and lodging during the time their services were required and by providing acts of service to the midwife after her work was completed.¹⁰

Despite the poor pay, a midwife was an honored individual in the community. She was entrusted by civic authorities to provide courts testimonies in cases of rape and infanticide. The church also gave her authority to perform religious rituals on infants if necessary, such as providing a baptism to a premature baby in the absence of a priest.¹¹

The general philosophy of midwifery was to care for both the woman and child and empower the family as they adjusted to a new member and life.¹² This would often manifest itself in ways beyond strictly providing physical care and extend into the social sphere as well. As such, many midwives did not view their occupation as a way to provide a living, but a way to minister to their community.¹³ Such a philosophy was in striking contrast to the perspectives of many other healthcare professions, such as a surgeon or physician, who depended upon their occupation for survival. This is seen in the almost mercenary struggle physicians engaged in as

⁹Jacques Gélis, *History of Childbirth*, trans. Polity Press (Polity Press, 1991). pp. 103-106.

¹⁰Gélis, *History of Childbirth*, 1991. pp. 103-106.

¹¹Maria Kontoyannis and Christos Katsetos, "Midwives in Early Modern Europe (1400-1800)," *HEALTH SCIENCE JOURNAL*, vol. 5, 2011, <https://www.itmedicalteam.pl/articles/midwives-in-early-modern-europe-14001800.pdf>. p. 33.

¹²Della Sherratt, "A history of midwifery" (The State of the World's Midwifery, June 2011), <http://www.bnemid.byethost14.com/HISTORY%20OF%20MIDWIFERY%201.pdf?i=2>. p. 3.

¹³Gélis, *History of Childbirth*, 1991. pp. 103-106.

they attempted to establish themselves and their practice.¹⁴ This struggle lays at the heart of causes behind the conquest of obstetrics that took place during this time.

Midwives would also call in help from surgeons or physicians if necessary. This, however, would often only occur when medical intervention was needed, as when a fetus was dead and had to be removed by forceps. These professions had slightly different focusses, though, and most births were attended only by a midwife.

In the 1750's, surgeons attending birth rose in popularity from previous stigma, because of new innovations with the use of forceps during birth.¹⁵ Surgeons were licensed to use the surgical instruments, something forbidden for midwives. No longer limited to fatal births, surgeons became more desirable in the eyes of the public. This presaged the overtaking of obstetrics by the male medical profession.

There were three primary types of medical professionals in Early Modern Europe: the surgeon, the physician, and the pharmacist. Out of these three, only the physicians were university trained; the other two trained by apprenticeship.¹⁶ For our purposes, we will focus on surgeons and physicians. Many physicians and surgeons struggled to establish successful practices. It was difficult to earn the trust of the public, wary from past experiences from other doctors. Many physicians lacked the ability to practically apply their training from university, and their communities would not trust them until their skill had been tested.¹⁷

The only distinction setting them apart from other professionals (university training), stripped of its importance by the inability of villages to trust them without seeing their abilities, only suffered more as surgeons and pharmacists gained increasing access to the resources used to train the physicians in university. Not only were physicians losing their distinction, they would also often be passed over in favor of medical aid from a surgeon or pharmacist, whose services were cheaper and more available.¹⁸

Thus, it is not beyond belief to say physicians began to attend births more as their need for a niche and money increased. Jonathan Barry says in his article *Educating Physicians in Seventeenth-Century England*, "But in early modern times, in England at least, there was no standard procedure... nor funding except from family resources, a very uncertain process of certification, and a mixed level of regulation to ensure any kind of protection for those then offering their medical services in competition with others without such qualifications to ensure that they reaped a suitable reward for their educational investment."¹⁹ This view is strengthened by the fact physicians tried to institute a birth tax dependent on the sex of the infant.²⁰

¹⁴Jonathan Barry, "Educating Physicians in Seventeenth-century England," *Science in Context* 32, no. 2 (June 1, 2019): 137–54, <https://doi.org/10.1017/s0269889719000188>. p. 141.

¹⁵Kontoyannis and Katsetos, "Midwives in Early Modern Europe (1400-1800)." pp. 33, 35.

¹⁶Barry, "Educating Physicians in Seventeenth-Century England," June 1, 2019. pp. 137-138.

¹⁷Barry, "Educating Physicians in Seventeenth-Century England," June 1, 2019. pp. 137-138.

¹⁸Barry, "Educating Physicians in Seventeenth-Century England," June 1, 2019. pp. 138-139.

¹⁹Barry, "Educating Physicians in Seventeenth-Century England," June 1, 2019. p. 137.

²⁰Gélis, *History of Childbirth*, 1991. p. 90.

With the Enlightenment popularizing science and medicine as a science, birth came to be viewed as a science in of itself— a natural procedure requiring medical intervention.²¹ Physicians popularized this belief in many ways. Many began to slander midwives, insulting their care. As Liane McTavish relates in her book *Reproduction and Regulation in Early Modern Europe*, “Some men-midwives²² even discussed the pregnancies and labours experienced by their close female relatives, including wives and sisters, to bolster their claims to bodily authority. Many male authors of French obstetrical treatises referred to the physical labour they undertook while assisting at difficult births, describing themselves as becoming more exhausted than the newly-delivered woman.”²³ Male-midwives published books degrading their female counterparts. *Chitchat of the New Mother* is one of these such books, though published anonymously. Its contents speak against the “immeasurable degree of agitation and garrulousness” the author sees in women and midwives.²⁴

With physicians collaborating with the Church to promulgate the image of midwives as witches,²⁵ and the efforts of civic authorities to keep the balance of proper society—that is, to reduce the midwife to a place proper to a women and reduce their hand in tasks unbefitting to their sex, such as their courtly roles—, the position of midwives in Early Modern Europe was significantly undermined.²⁶

Not all was lost, however. There was not an immediate and sweeping shift in public favor from midwives to physicians. Indeed, many nations tried to institute licensing for female midwives to provide legitimacy to their practices and keep public safety. In France, the state had a moral code all midwives had to adhere to during their practice, and all midwives had to pass an exam administered by the state before being allowed to practice. Apprenticeship was another popular method of making sure midwives were receiving proper training. In Holland, midwives had to attend four years of training under an experienced midwife and anatomy lessons from medical authorities before they were awarded a practicing license. As were most of Holland’s occupations, midwifery was governmentally organized and supervised.

Despite the many benefits licenses provided midwives, many were unable to afford licenses.²⁷ Depending on the location of the midwife and what sort of patients she ministered to, a license was not necessary. Due to the communal role of the midwife and the fact her services often only extended as far as her village, the trust she had earned from her village nullified the need for a license. As seen with some physicians and surgeons, a license did not assure quality care, nor did a lack of one guarantee malpractice.

²¹Lianne McTavish, “Reproduction and Regulation in Early Modern Europe,” in *The Routledge History of Sex and the Body in the West, 1500 to the Present*, ed. Sarah Toulalan and Kate Fisher (Routledge, 2014), 351–71, https://www.academia.edu/9922040/Reproduction_and_Regulation_in_Early_Modern_Europe. p. 360.

²²‘Men-midwives,’ ‘male-midwives,’ and ‘obstetricians’ were all terms used synonymously to refer to any male medical professional attending a birth. ‘Physician’ and ‘surgeon’ are also used almost interchangeably in this context.

²³McTavish, “Reproduction and Regulation in Early Modern Europe.” p. 360.

²⁴Gélis, *History of Childbirth*, 1991. p. 100.

²⁵Kontoyannis and Katsetos, “Midwives in Early Modern Europe (1400-1800).” p. 32.

²⁶Kontoyannis and Katsetos, “Midwives in Early Modern Europe (1400-1800).” p. 32.

²⁷Kontoyannis and Katsetos, “Midwives in Early Modern Europe (1400-1800).” 32-33.

The physicians succeeded in their efforts, and by the beginning of the 18th century, most European nations had seen a large decrease in midwifery. Contrary to popular trend, though, Holland retained their government supervised midwifery. Holland viewed midwives as an unique role in medical and social care, one that a physician should not and could not absorb fully. To the present day, Holland, now part of the Netherlands, boasts a robust system of obstetric care handled primarily by midwives, with physicians to intervene and provide more intensive services if necessary.²⁸

This system is beneficial to the country, and the presence of midwives helps relieve strain on overworked physicians. Furthermore, their roles fill a relational and social need from women that conventional medicine often overlooks. Midwives help transition the mother to her new life, provide support and friendship, and nourish the needs of families beyond the simple delivery of the baby.

Just as midwives are recognized for their unique role, so are physicians, and when a mother needs help, a physician will be called. The symbiosis presented by this model has earned the Netherlands a spot in the top 15% of countries worldwide with the lowest infant mortality rate (IMR), beating the United States, who sits in the top 24%.²⁹

Findings from scientific research supports primary care from midwives. Holly Powell Kennedy, the Helen Varney Professor of Midwifery, and Joan Combellick, assistant professor of nursing, have found that first time mothers with care from midwives are 74% less likely to have induced labor, 75% less likely to receive oxytocin augmentation, and 12% less likely to undergo a c-section. Lower mortality and morbidity rates, interventions, premature births, and less low birth weights are also associated with midwifery.³⁰

Midwifery is designed to give a personal birth experience, something that women have expressed desire for. This personal care has been found to be influential in a mother's safe birth and lack of need for postpartum care. Midwifery also lowers the cost of healthcare for countries and individuals.³¹

The transition of primary obstetric care from midwives to physicians was undue and ill-realized. As seen in Holland from the 17th-18th centuries, a partnership between physicians and midwives affords care and trust to all parties involved. This partnership can be brought into our own age as well.

That transition has turned into the predominant belief in Western civilization that obstetrics and postpartum care should fully be the responsibilities of the physician. However,

²⁸Kontoyannis and Katsetos, "Midwives in Early Modern Europe (1400-1800)." 35.

²⁹"Infant mortality rate Comparison - The World Factbook," 2024, accessed November 8, 2024, <https://www.cia.gov/the-world-factbook/field/infant-mortality-rate/country-comparison/>.

³⁰Robert Forman, "Midwifery Review: Adding Care by Midwives Improves Birth Outcomes," Yale School of Medicine, August 15, 2023,

<https://medicine.yale.edu/news-article/the-value-of-midwives-during-prenatal-care-and-birth/>.

³¹Laura Andriassi et al., "The Influence of Doctor-Patient and Midwife-Patient Relationship in Quality Care Perception of Italian Pregnant Women: An Exploratory Study," *PLoS ONE* 10, no. 4 (April 23, 2015): e0124353, <https://doi.org/10.1371/journal.pone.0124353>.

after looking at the way in which physicians came to dominate this field, this idea is challenged. Both the role of the midwife and physician are valuable and have different areas of focus.

As exhibited by Holland from the early modern period to the present day, a model of care for the mother and child primarily dependent on first hand care by a midwife is more advantageous for all parties involved. Though each family is unique, I would encourage them to consider midwifery as part of their birth plan.

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Study of Time-dependent Degradation in Fiber Bundle Models as a Model for Social Breakdown By Aditya Arora and Nishchal Dwivedi

Abstract

The fiber bundle model is one of the most prominent models used for assessing breakdown phenomena quantitatively. Several corollaries have emerged historically: the global load sharing model was introduced, and the mathematics delineated, followed by the introduction of the time-dependent load threshold model. Different types of time-dependent load thresholds were outlined, including exponential, linear, constant, logarithmic and polynomial decay. An analysis of finite fiber bundles was conducted, with an exponential decay model, varying the probability distribution functions (namely, poisson and normal distributions) for the initial thresholds, and the results were analysed by comparing a ‘point of no return’ and the failure time of bundles. Other potential extensions, like rupture latency, were ideated, but a further analysis remains to be pursued. The results highlighted how ‘weak links’ can cause the whole system to fail at earlier times.

Introduction

Imagine a derelict elevator suspended precariously from a thick bundle of metal wires, the wires slowly elongating, weakening, and subsequently rupturing until the bundle of wires eventually collapses. Now, imagine a queue for limited edition shoes; each individual ushers on due to a desire to possess the coveted shoes and consequently contemplates breaking the line to ensure their victory. Following the violation of one miscreant, other potential buyers of the shoes cut the line as well, and eventually, the queue, like the bundle of wires, collapses. Surprisingly enough, both scenarios are an example of the same *breakdown phenomena*.^[1] More specifically, a large number of elements (wires/people) are subjected to a driving force (weight of elevator/desire to possess the shoes), with each element being in *one* of several possible states (it’s impossible to both have and not have the shoes simultaneously) and interacting (the longer the line, the stronger the temptation).

An analytical tool that can be used to quantitatively describe such breakdown phenomena is the fiber bundle model. In its essence, the analogy is almost identical to the situation of the derelict elevator, except the ‘wires’ are referred to as *fibers*, and the elevator is replaced by a nameless *load*. As the load gradually weakens and causes individual fibers to *rupture*, the load borne by the previously intact fibers is now redistributed amongst the currently intact fibers, which triggers a new set of ruptures: this causes a cyclical process.

This paper will lay out the mathematical basis for the fiber bundle model, with global load sharing throughout, and will evaluate the impact of degradation model type--- exponential, linear, constant, logarithmic and polynomial --- for time-dependent load thresholds. It will also conduct an analysis of poisson and normal probability distribution functions for a time-dependent load threshold model. It will then conclude with an evaluation and conclusion.

Section 1: The Democratic Fiber Bundle Model

The fiber bundle model, first introduced in 1927 [2], consists of $N_0 (\rightarrow \infty)$ fibers that are being equally pulled due to a democratically shared load, which this paper will refer to as λ . Each individual fiber has a threshold of force that it can withstand — drawn from a probability distribution function —, and if the individual force applied on that particular fiber exceeds the threshold, the fiber *ruptures*. After each subsequent rupture, the load borne by the recently-ruptured fibers is distributed amongst the intact fibers; as the load per fiber increases, the next set of ruptures is triggered, eventually leading to either the complete breakdown of the whole bundle or the bundle's stabilization after a certain set of ruptures.

Before developing a mathematical representation, the assumptions of the fiber bundle model need to be discussed. Firstly, the fiber bundle is a set of discrete, parallel fibers that support only longitudinal deformation. This allows for analysis of the bundle parallel to the fibers only. Secondly, each individual fiber ruptures only once, and, for the sake of the initial model, that the fibers break instantaneously, and the load borne by a ruptured fiber instantly goes to 0. Furthermore, it is also assumed that the load threshold of each fiber remains same, with no decay/strengthening, until the fiber ruptures completely; once a fiber breaks, it remains broken, unable to withstand any load whatsoever. In other words, no *healing* phenomena are taken into account.

Additionally, load sharing constraints must too be discussed. The most straightforward of the fiber bundle models in literature involve a global load sharing (GLS) redistribution model [3]. More specifically, after a rupture, the load is redistributed equally to all fibers throughout the bundle instantaneously, with no considerations of proximity or time dependency. While other models exist, like the local load sharing model [4][5], the GLS model will be considered throughout this paper.

The conditions outlined thus far are applicable only for this specific version of the fiber bundle model. The model allows for different levels of load-sharing, from partial load sharing [6], where load is redistributed to neighbouring fibers, to cluster based and hierarchical [7] approaches, where load is redistributed to the next cluster of neighbouring fibers, with cluster size being a specified parameter.

With the assumptions having been discussed in adequate detail, a mathematical representation of the situation can now be developed. The failure thresholds of each fiber are determined by an independently distributed random variable through a probability distribution function $p(x)$, and the cumulative distribution function:

$$P(x) = \int_0^x p(x')dx' \quad (1)$$

Now, let the total number of fibers in the bundle be N_0 , and, as stated above, the total democratically shared load be λ . Therefore, it follows that the load withstood by each individual fiber before the first rupture is N_0/λ . At this point, a certain number of fibers will have their load threshold exceeded, and will rupture. Let N_i denote the number of fibers intact after the i^{th} rupture. This results in the following:

$$N_1 = N_0 - N_0 \int_0^{\lambda/N_0} p(x)dx \quad (2)$$

Without loss of generality, (2) can be re-written to express the number of intact fibers after the $(i+1)^{th}$ rupture, given the probability distribution function and the number of intact fibers after the i^{th} rupture:

$$N_{i+1} = N_i - N_0 \int_{\lambda/N_{i-1}}^{\lambda/N_i} p(x)dx \quad (3)$$

Now that a recursive function has been established, the breakdown phenomena can be analysed for various probability distribution functions for the load thresholds. The distributions influence significantly the final state of the bundle. For example, three scenarios have been identified by [1]:

- 1) There are always an appreciable number of robust fibers, and some fibers in the bundle are strong enough to withstand the load indefinitely.
- 2) The number of fibers decreases continuously, the number of intact fibers gradually decreasing until there are no fibers left.
- 3) The bundle remains intact until a critical point, after which all fibers discontinuously fail and fall.

Graphical analyses of these scenarios are supremely informative. In any case, the scenario that the bundle will exhibit is dependent on the chosen probability distribution function, representing different orders and forms of randomness due to the material of the fiber.

Section 2: Time-dependent failure

Consider a singular fiber with a failure threshold F_f . Now, consider a load F_s suspended from this singular fiber such that :

$$F_s + h = F_1 \quad (4)$$

According to the initial model discussed, this fiber would remain intact until $F_s > F_1$, even though the difference between the two is negligible. Therefore, it follows that there are certain limitations to the initial model. Intuitively, we can infer that the fiber eventually ruptures due to the load F_s gradually weakening.

This introduces a new corollary of the original model, more specifically, time-dependent load thresholds. Introduced by [8], a time-dependent formulation of the model can be discussed. Assume that the load threshold of each individual fiber is a monotonically decreasing function dependent on both the time for which and the magnitude of the load suspended from the individual fiber. To illustrate this, let's revert back to the example posited at the beginning of this situation. For the sake of simplicity, we will assume that the threshold decay rate is linearly related to both load per fiber and time, with proportionality constant 1.

$$F_{f_1} = F_1 - F_s t \quad (5)$$

F_{f_1} = instantaneous load threshold of the fiber

F_f = initial load threshold of the fiber

F_s = load suspended from fiber

t = time

For this particular example, the fiber will rupture --- and the bundle consequently fail --- when the following is true:

$$F_{f_1} < F_s$$

$$F_s + h - F_s t < F_s$$

Therefore, the time at which the individual fiber ruptures is $t=h/F_s$, where the *degradation rate*, the rate at which the instantaneous load threshold of an individual fiber decreases, is given by the product of the load and the time for which the load is suspended.

Now, let us consider a fiber bundle with N_0 fibers at $t=0$ and r ruptured fibers at any given time t , from which a load λ is suspended. Therefore, the degradation rate is given by a function of time, as written below:

$$D(t) = \frac{\lambda t}{N_0 - r} \quad (6)$$

The degradation rate is the same for all fibers in a bundle, given global-load sharing. Additionally, let the fibers be arranged in ascending order, according to their initial load thresholds. It is important to note that, since the degradation rate is the same, all intact fibers' instantaneous threshold will also be arranged in ascending order. To write this, we can say that the fibers are arranged such that:

$$f_{i+1} \geq f_i$$

f_i = the initial load threshold of the i^{th} fiber

f_{f_i} = the instantaneous load threshold of the i^{th} fiber

Therefore, on each individual fiber, the instantaneous load threshold when all fibers are intact is given by the following:

$$f_{f_i} = f_i - D(t) \quad (7)$$

Following the first rupture, the value of $D(t)$ changes, as it does after every subsequent rupture as well. Therefore, the instantaneous load threshold for each fiber is, given that t_i is the time at which the i^{th} fiber ruptures, given by:

$$f_{f_i} = f_i - \frac{\lambda}{N_0 - i} (t - t_{i-1}) - \sum_{k=0}^{i-2} \frac{\lambda}{N_0 - k} (t_{k+1} - t_k), \quad t_{i-1} < t \leq t_i \quad (8)$$

This can be used to find the time at which each individual fiber ruptures in a bundle. It is important to note that, while the *prima facie* impression may be that this formula requires only one rupture to occur at a time, and the rupture of no two fibers coinciding, this is not true, as if two ruptures do indeed rupture at the same time, t_{i-1} will be the same as t_i , and the part of the summation during which t_i is the weakest fiber (and hence will be the next fiber to rupture) will simply be 0, as $t_i - t_{i-1} = 0$.

As mentioned above, the rupture phenomena are driven by 2 processes: the redistribution of fibers following ruptures as well as the degradation rate. Therefore, each rupture can also be divided into two classes.

- 1) When there are no fibers with load threshold between λ/N_i and λ/N_{i+1} , where N_i is the number of fibers intact after the i^{th} rupture. Conventionally, in a fiber bundle model without a degradation rate, this is where a fiber bundle would stabilise.
- 2) When there are fibers with load thresholds between λ/N_i and λ/N_{i+1} , where N_i is the number of fibers intact after the i^{th} rupture. Conventionally, in a fiber bundle model without a degradation rate, this would also indicate continued breakdown.

With the phenomena laid out, we can move onto running simulations using different probability distributions and degradation rates.

Other time dependent variations of the model include healing [9][5] and fibers that can rupture multiple times [10][5].

Section 3: Varying Degradation Rates

First, it is worth noticing that in models with linear degradation rates, irrespective of the probability distribution, the fiber model does eventually fail. That being said, a linear degradation rate is not the only kind, and other models of the same can be constructed: namely, a uniform degradation rate, a logarithmic degradation rate, a polynomial degradation rate and an exponential degradation rate. For example:

$$D(t) = e^{0.3\lambda t}$$

A graphical representation of these varying degradation rates is present below. This includes all the aforementioned models of degradation rates. Due to system limitations, however, only 1000 fibers were simulated at a time. Therefore, while the representation may not be an accurate, quantitative representation of the conventional scenario (N_0 tends to infinity), the first rupture and the ‘point of no return’ in these finite-fiber bundle models is indicative.

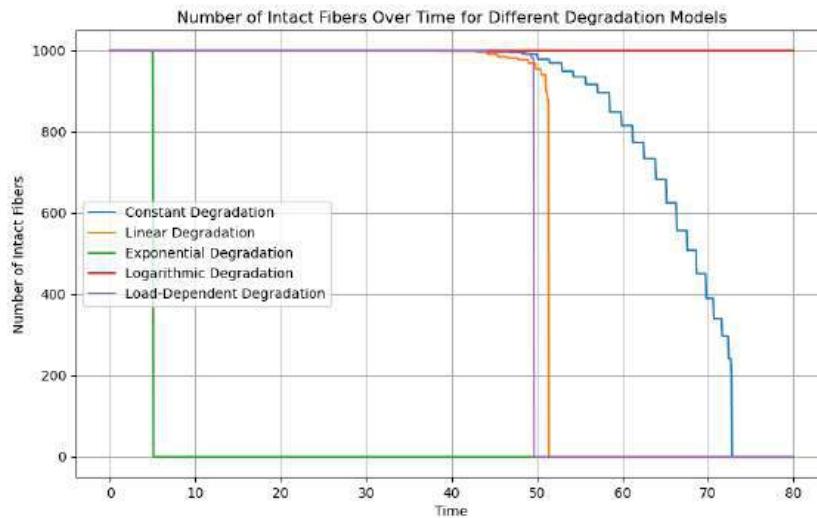


Figure 1: Visual representation of the breakdown of different fiber bundles with varying degradation rates; the time is graphed on the x axis and the number of remaining fibers is graphed on the y axis.

The coefficient of λt in each of the degradation models was kept constant at 0.7, as well as a constant poisson distribution with $\lambda=1000$ and 1000 fibers. As can be deducted from the graph, as intuition would suggest, the exponential degradation model results in the bundle approaching failure significantly before the other models.

Additionally, while interpreting this graph, it is important to note that the ‘steps’ are not due to the discretisation of the fibers, but rather, because the ruptures where there is a plateau before a sudden drop are due to them being of ruptures of class 1. This is because the number of intact fibers is plotted against, not the i^{th} rupture, but against time.

Section 4: Varying Probability Distribution Functions

The other important factor to consider while modelling breakdown phenomena is the probability distribution of the initial thresholds. In non-time-dependent fiber bundle models, the nature of the probability distribution functions determines whether or not the bundle fails. For time-dependent models, we can determine how long a bundle stays intact for, given similar means. To analyse different probability distributions and the nature of the breakdown, two tools will be used:

- 1) ‘point of no return’ – the time after which the number of fibers per time step increases monotonically (on average).
- 2) Failure time - the time at which the whole bundle fails completely.

Comparing two popular probability distribution functions, namely, the normal distribution and the poisson distribution, we can see a stark difference in both the failure time and ‘point of no return’. Given below are the histograms for the ‘point of no return’ for 1000 iterations of the same simulation.

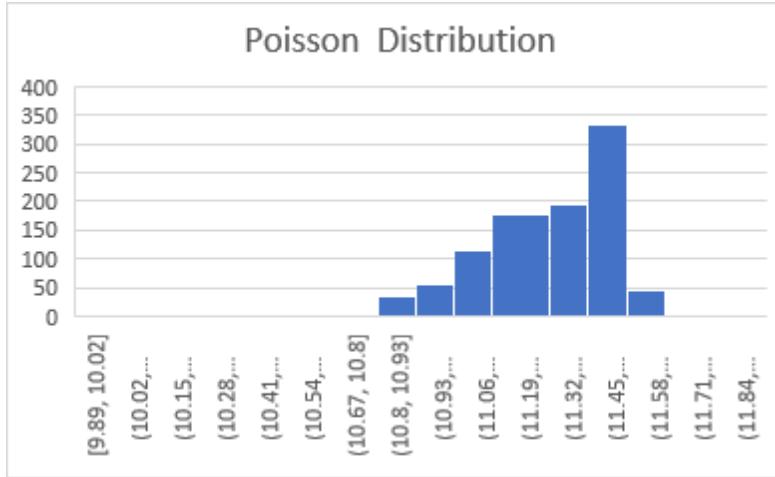


Figure 2. The rupture intervals for a poisson distribution with $\mu=50$: the time intervals for ruptures plotted against the frequency of ruptures in each interval.

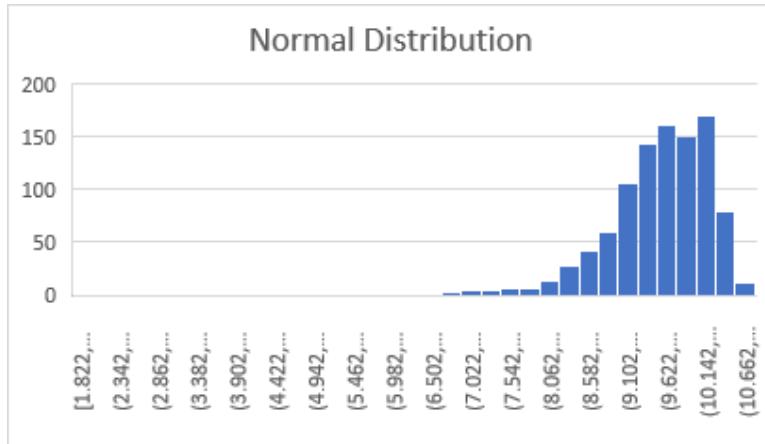


Figure 3. The rupture intervals for a normal distribution with $\mu=50$: the time intervals for ruptures plotted against the frequency of ruptures in each interval.

As is visible through the graphs, even though the normal distribution and the poisson distribution have the same mean, the ‘point of no returns’ occurs, on average, $\sim 17.97\%$ earlier. Additionally, the failure time too occurs earlier for the normal distribution (standard deviation =10), by approximately 4.7%. Therefore, this shows that, even though the average strength of the fibers might be the same, the order in which the strengths are distributed impacts the strength of the bundle as a whole greatly.

A similar result arises when we take normally distributed thresholds with different standard deviations. Below is a graph of the average failure time, plotted against standard deviation of the normal threshold used.

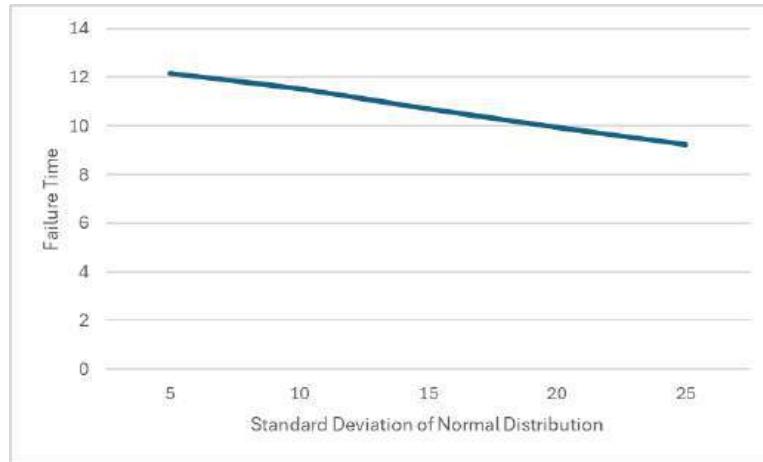


Figure 4. The rupture time of different normal distributions of fiber bundles is plotted here, with the failure time of bundles on the y axis and the standard deviation of the normal on the x axis. Calculated by taking curve of best fit for values $\mu=5, 10, 15, 20$ and 25 .

As the standard deviation increases, and therefore, the number of fibers that have lower thresholds, the failure time of the bundle too decreases. Intuitively, this is because the weaker fibers rupture earlier, leading to a larger proportion of λ being borne by the intact fibers. More rigorous quantitative analysis methods, however, need to be developed.

Other researches conducted in the area have also included an analysis of Weibull distributions [11] and Extreme Value distributions [12] [13]. The Gaussian and Poisson distributions were chosen for ease of comparison. The extreme value distribution was not used, as the model itself presupposes that the weakest link will determine the rupture of the model [12].

Section 5: Conclusion and Evaluation

In summary, we can see that, despite the average strength of fibers across different bundles being the same for normal and poisson distributions (this was set by taking the same mean), the bundles fail much quicker due to weak links. This is indicative of social scenarios as well, where the weakest and most vulnerable links will be the first miscreants, first ones to break the lines, but also, the first ones to fail.

A corollary of the model that was not explored, but will be explored in future investigations, is latency in failure: consider fibers whose rupture threshold has been exceeded, and yet, haven't ruptured yet. After all, ruptures may not be instantaneous. Different variations of this *latent-rupture* model can be explored as well, with latency being constant or dependent on other factors like load. Moreover, the arrangement of the fibers in more intricate lattices, for example, in a 1 dimensional or 3 dimensional lattice [5], also remains to be explored.

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Shifts in the Roman Diet Over Time By Lukas Odenius

Food plays an integral part in every human's life. From providing basic sustenance for people to bringing communities together over shared meals, it is clear that food has had an immeasurable impact on human history. Food has also changed over time, from when archaic humans consumed it during the Agricultural Revolution all the way to the modern day. This fact is especially apparent when studying one of the greatest and most impactful empires to ever exist, the Roman Empire. Roman food and drink evolved over time as Rome went from a small Republic to its peak territorial extent and then during the late Empire, as evidenced by archeological findings of plant, animal, human, and ceramic remains. These archeological findings make it clear what types of food and drink were consumed during the different stages of Rome's existence and provide insight into the inevitable changes in diet as Rome expanded and then declined throughout a millennium.

In the early years of the Roman Republic, meat was a scarce commodity as proven via limited findings of faunal remains, revealing that due to the small size of the early Republic, it lacked the ability to provide meat to all of its citizens. According to faunal remains in Rome dating from 500 BCE that underwent zooarcheological analysis, sheep and goats were the most common domesticated animals during the Early Republic, followed by cattle and then pigs (Moses 263). The incredibly limited amount of faunal remains from this overall time period suggests that the total number of domesticated animals was quite small. Butchery damage was only present in about 21% of the specimens in Rome, while burning damage was even rarer, with only 10.5% of the specimens showing evidence of having been burned (Moses 264). The limited number of specimens that showed signs of butchery or burning damage indicates that very few of the domesticated animals in the Roman Republic were eaten, and this fact coupled with the already limited number of domesticated animals in the Republic makes it apparent that meat was a scarce commodity that was not commonly eaten due to its rarity.

During the Roman Republic, plants such as grains and olives played a crucial role in the sustenance that was available to many people, as evidenced by lipid analysis and microbotanical remains. As a result of lipid analysis performed on a large amount of ceramic remains dating to the period of the Roman Republic, it is apparent that olive oil was quite common due to its status as a bulk good which meant that it was frequently traded in large quantities across the Republic, making olives a staple of the Roman diet (Candy 62). Similarly, grain was also an incredibly important food source during the Roman Republic, once again due to its status as a bulk good and its cheap nature, with evidence of its widespread availability coming as a result of the sheer amount of ceramics that have been discovered to contain grain microbotanical remains (Candy 62). It is clear that due to the simplicity of obtaining grains and olives in the Roman Republic, they had become staples of the Roman diet.

During the Roman Republic, wine was frequently consumed as evidenced by ceramic remains, revealing the importance of the drink to Roman society and the vast impact that it had on Roman trade. The prevalence of wine can be seen from the 400 shipwrecks in the Western

Mediterranean between Italy and Gaul dating to the latter stages of the Republic, showing increased trade in that area (Candy 56). After archeological analysis was conducted on 1,975 amphorae deposits throughout Gaul, it was determined that the amphorae were frequently used to transport wine, with an estimated number of six million liters of Italian wine being exported to Gaul annually (Candy 56). This staggering amount of trade suggests that wine consumption was frequent in regions beyond Italy, but also shows that there was enough Italian wine during this period to be exported in the first place while still leaving enough for consumption within Italy, suggesting that a large amount of wine was being produced in Italy and consumed throughout the Roman Republic.

During the Roman Republic, trade for the sake of food was mostly limited to trading already common goods such as wine and olive oil internally with other parts of the Republic, as based on archeological evidence from shipwrecks, showing the relatively mild impact that trade had on the food variety of the Roman Republic. From the late Republic period, roughly 500 shipwrecks have been found, with their main purpose being to transport the aforementioned bulk goods of grain, olive oil, and wine to and from different parts of the Republic (Candy 56). This implies that the majority of the trade during this period was not focused on obtaining very valuable or exotic food materials from distant lands, but rather was fixed on monetary gain and the domestic trade of already established staples of the Roman diet. This fact reveals that while Rome's influence was steadily growing, during this time the Republic was not large or important enough to trade with wealthy empires that held exotic foodstuffs,

At the peak territorial extent of the Roman Empire, the types of meat that were common were shifting, turning meat into an accessible commodity that more people throughout the Empire could access, revealing how the vast size of Rome allowed it to provide its people with greater access to meat. Zooarcheological analysis of 273 faunal remains near a Roman necropolis in Barcelona that was in use during the first half of the second century AD concluded that cattle made up 41.8% of the specimens and pigs made up a further 26.7% of the specimens (Salazar-García et al. 1). These specimen's proximity to the necropolis implies that they were used as sacrifices during funerary rituals, with the large number of faunal remains showing that domesticated animals such as cattle and pigs were becoming commonplace in many parts of the Empire (Salazar-García et al. 1). On top of this, one can further conclude that if these animals were being used as a part of funerary practices then everyday Romans were certainly not lacking meat as a part of their diet, something which is backed up by analysis of the human remains in the necropolis which showed that they had meat as a part of their diet (Salazar-García et al. 1). This abundance of meat implies that due to the newfound size and wealth of the Empire, more people had access to meat as a food source than ever before.

At the peak territorial extent of the Roman Empire, plant staples of the Roman diet such as grain and olive oil only grew in importance due to the vast amount of people the Empire had to feed, revealing how as Rome grew so did its dependence on cheap and easily accessible plants. According to isotopic data collected from human remains at a necropolis in Barcelona that was in use in the first half of the second century AD, the diet of the people living there was

based on terrestrial resources with plants being a main staple (Salazar-García et al. 1). While the specific types of plants that these people ate were not specified, archaeobotanical methods in other areas of the Empire have determined that two parts of the “Mediterranean Triad,” notably grain and olive oil, were still staples of the Roman diet (Erdkamp and Holleran 2). On top of this, the researchers also discovered that other cereals and beans were present in the diet of the time (Erdkamp and Holleran 2). The archeological evidence makes it clear that not only were grains and olive oil still common in the Roman diet, but other plants such as beans were also becoming important, showing that as the Empire expanded so did its diet due to the large amount of people it now had to feed.

At Rome’s peak territorial extent, wine-making practices were being used throughout the Empire which increased the amount of wine in circulation, revealing how as the Empire expanded so did the amount of wine present. Throughout the Roman region of Gaul, archeologists have found evidence of winemaking in the form of buildings responsible for the production of wine, as well as vineyards and wine presses, revealing a bustling viticultural scene that flourished throughout the years of the Empire (Bernigaud et al. 1). This evidence shows a stark contrast to the years of the Empire when wine was simply being exported from Italy to Gaul, showing that the once-exclusive process of winemaking was now being taken up in regions of the Empire beyond Italy. This increase in production hints at higher demands for wine in the Empire due to the expanded population, showing that as the Empire grew so did the need for wine.

At Rome’s peak territorial extent, exotic foods from India were being imported for the first time, drastically changing the way food was prepared in Rome and showing how as the Empire expanded so did the Roman palate. During this time, Rome was particularly keen on importing black peppercorns, rice, and coconuts from India, as evidenced by archeological excavations at the sites of Myos Hormos and Berenike, both of which were major ports in Egypt that played a crucial role in the Indian trade (Cobb 1). These findings clearly indicate an uptick in trade with powers outside the Mediterranean, trade that according to written sources was often not in Rome’s favor due to the large amounts of gold and silver they were required to export (Cobb 1). This unfavorable trade imbalance shows just how keen Rome was to have access to these exotic resources, and the fact that trade continued unfavorably for quite some time proves that Romans did not wish to live without them.

As Rome began to decline in the latter phase of the Empire, meat production and consumption began to follow suit and high-quality meat became a luxury, showing that as Rome declined in power and wealth its ability to produce meat also declined. Archeological analysis of animal bones at the Settefinestre villa in Italy shows that higher-status parts of the villa had higher percentages of pig remains and thus consumption than the lower-status parts of the villa, such as the slave quarters (King 2). This discrepancy shows that meat, especially pig, was becoming a much more exclusive part of the Roman diet. In wealthier cities such as Rome and Ostia where they were able to raise animals in a “fairly intensive manner,” the rates of pig consumption as based on animal bone percentages from assemblages are relatively high (King

3). This evidence indicates that in the late period of the Empire, as it was under much duress, meat consumption was becoming an increasingly high-status activity, thus leading to a decrease in overall meat consumption.

Despite Rome's decline in the late Empire, the importance of plants to the Roman diet continued to hold importance, in particular with the expansion of olive cultivation in parts of the Empire that previously had no importance to Roman agriculture. New archeological findings of oil mills and presses in the coastal regions of the Roman province of Dalmatia make it clear that in the late Empire, olive cultivation specifically for the purpose of making olive oil expanded into this region (Glicksman 44). The coastal regions of Dalmatia had previously never had any experience with the cultivation of olives despite the perfect Mediterranean conditions that the area experiences, showing that olive oil was in high demand in the Empire and new regions were being utilized for their agricultural potential. This high demand for olive oil even in the late Empire reveals that despite the overall decline, olives were still a staple of the Roman diet.

Despite Rome's decline in the late Empire, the importance of wine to the Roman diet continued, in particular with the expansion of grape cultivation in parts of the Empire that previously had no importance to Roman viticulture. The archeological discoveries of wine presses at sites in the coastal regions of the Roman province of Dalmatia dating to the late Empire show that winemaking was coming to the area for the first time (Glicksman 44). At the Kumenat site in Dalmatia, there are many pits spaced about one meter apart from each other which is too close for the site to have been an orchard, indicating that it was used as a vineyard (Glicksman 46). The site would have needed a lot of investment from the owner due to the work that would have been necessary to turn the infertile soil in the area into something usable, implying confidence from the owner that he would have turned a profit (Glicksman 46). This fact hints at the demand for wine being very high at the time, making it clear that despite the decline of the Empire during its later stages, wine was still a precious commodity of much importance.

Despite Rome's decline in the late Empire, the importance of exotic imports such as spices to the Roman diet continued to grow, particularly with the trade from India which grew over time. Archeological findings of large amounts of imported pottery and vessels from India imply that the trade with India during the late Empire was "large scale, long-lived, and extensive" (Selander 1). This statement makes it clear that despite Rome's general decline, the Empire still maintained its trade with India and even expanded its imports to include spices (Selander 1). This expensive trade with India despite the dire economic conditions that Rome found itself in during this time makes it clear that Indian imports had become an integral part of Roman cuisine and diet, showing that over time Roman trade changed the way food was prepared and experienced.

It is evident that over the course of Rome's existence, some of its food sources and diet changed drastically while many of its staples were preserved. Meat went from being a rare food source during the Republic to being relatively accessible during the peak Empire and then reverting to a commodity during the late Empire. Plant staples such as olive oil and grain were major food sources for the entirety of Rome's existence and were consumed by people from all

walks of life. Wine was a valuable drink for all of Rome's existence, but it can be inferred that more people had access to it as time went on due to the increase in production. Finally, trade was mostly internal during the days of the Republic, but during the peak and late Empire, trade with India made it possible for Rome to access valuable foodstuffs such as peppercorns and spices. A major question resulting from this research revolves around what impact the Roman diet has had on the modern-day Western diet, especially in the Mediterranean areas that Rome controlled.

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Effects Of Artificial Intelligence On Mental Illness And Employee Well-Being: An In-Depth Analysis Of Literature By Anusha Nigam

Abstract

The complex effects of artificial intelligence (AI) on workers' mental health and wellbeing in the modern workplace are examined in this review. In addition to addressing possible issues including financial instability, quick adaption, and technostress, the research emphasizes the benefits of using AI to optimize time-consuming jobs. It becomes clear that a key tactic for reducing AI-related worries is continuous learning. The evaluation emphasizes the value of a comprehensive strategy and stresses that variables like job stability and flexibility affect how AI affects workers' well-being. It ends by arguing in favor of empirical research, statistical evaluations, and organizational recommendations to traverse the rapidly changing field of AI and mental health and promote a fair and positive influence on workers in the contemporary workplace.

Keywords

Robotics and Intelligent Machines; Workplace Challenges; Artificial Intelligence; Employee Well-being; Adaptation Strategies.

Introduction

A revolutionary age in the workplace is being ushered in by artificial intelligence (AI), a fast-developing discipline of computer science that enables machines to mimic intelligence similar to that of humans. AI systems are significantly altering the nature of work, changing skill needs, and posing possibilities and difficulties for employees across a range of industries as they are incorporated more and more into workplaces and businesses. Understanding the complex effects of AI on the workforce is now a serious social issue rather than a topic for academic inquiry. This high-level review aims to investigate the underlying ideas behind AI, consider how it will really affect employees, and emphasize why it is crucial to be concerned about these advancements.

This paper aims to delve into a crucial dimension of the AI revolution in the workplace—the impact on workers' mental health. The mental well-being of employees is a vital aspect of their overall quality of life, job satisfaction, and long-term productivity. As AI disrupts traditional work structures and expectations, understanding how it influences workers' mental health becomes critical. We will present the findings of a comprehensive literature review and survey examining the ways in which AI in the workplace affects mental health.

In this survey literature review, we seek to delve deeper into the intricate relationship between AI-induced changes in the workforce and the consequent mental health challenges faced by workers. Specifically, we will focus on the pronounced financial instability resulting from job displacement and the rapid adaptation required in an evolving labor market heavily influenced by AI technologies. Additionally, emphasis will be placed on the significance of continuous learning

and adaptation as proactive strategies to mitigate AI-induced worker concerns. Furthermore, we will investigate the phenomenon of "technostress" stemming from the digitization of office work, exploring its effects on reduced job satisfaction, diminished commitment to employment, and decreased productivity, thereby enriching the understanding of the broader implications of AI in the contemporary workforce. In conclusion, this comprehensive examination of AI's impact on workers' mental health, spanning areas such as financial stability, adaptive strategies, and technostress, underscores the urgency of understanding and addressing the multifaceted challenges posed by AI in the contemporary workforce.

Discussion

While the impact of AI on worker well-being is multifaceted, with both positive and negative aspects, it is evident that financial stability plays a pivotal role in determining the mental health of employees affected by AI, as highlighted by Nazareno and Schiff as well as Muro and Whiton, et al.'s studies (Nazareno & Schiff, 2021; Muro et. al., 2019). Work by Nazareno and Schiff highlights the different ways AI can impact worker wellbeing in the workplace, including through job security (Nazareno & Schiff, 2021). Since job security is directly linked to worker's financial liquidity, the case can be made that AI's impact on worker well-being is often interlaced with financial stability concerns. Workers affected most by AI may be perceived as replaceable, and thus higher levels of stress due to unstable financial conditions erode the mental health of these individuals. In a similar vein, work by Muro and Whiton et al. also mentions the impact AI will have on job insecurity is connected with worker health, clearly indicating a bridge between stability in long-term employability and a deterioration of worker's health conditions due to mental health challenges (Muro et. al., 2019). On the other hand, Maria, Guerreiro et al. also mention the positive impacts AI can have on increasing productivity which can eventually contribute to higher company revenues which could lead to better job security for employees (Maria & Guerreiro, 2021). These findings underscore the intricate relationship between AI, financial stability, and worker well-being, paving the way for an exploration of how workers are compelled to adapt swiftly to a fast-changing labor market and system of work due to AI's pervasive influence.

The impact of artificial intelligence (AI) and automation on the labor market is undeniable, leading to a rapidly changing landscape that necessitates workers to adapt swiftly. As highlighted by Nabila, Santoso et al., the introduction of robotics and AI technologies creates a dynamic environment where the boundaries between humans and machines become blurred (Nabila et. al., 2021). This shift inherently demands that workers acquire new skills and adapt to evolving job roles. Frank, Autor, et al. emphasize the transformative potential of AI and automation, shedding light on the efficiency gains and job creation in non-competitive sectors (Frank et. al., 2019). However, this implies that workers must be agile in acquiring these new skills and embracing evolving work dynamics. Furthermore, Kamran, Iqbal, et al. underscore the diverse impact of automation across geographic regions (Dar et. al., 2023). It reveals that AI technologies tend to be more prevalent in large cities, influencing high-wage cognitive

employment, while physical low-wage tasks are more common in smaller cities and rural areas. This geographical variation implies that workers in different regions face distinct challenges adapting to the changing labor market. Thus, the combined insights from these papers underscore the compelling argument that workers are indeed compelled to adapt rapidly to a fast-changing labor market and system of work due to the pervasive influence of AI. Nevertheless, amidst the demands for rapid adaptation driven by AI's influence on the labor market, it's imperative to explore how the optimization of tedious tasks in the workplace can offer a counterbalance by fostering better work habits, flexibility, and ultimately, a positive impact on workers' mental health.

Optimization of tedious tasks in the workplace, as illuminated by Ramachandran and Shibani, et al. and Wan-qing, offers a compelling avenue for enhancing worker well-being and mental health (Ramchandran et. al., 2022; Wan-qing & Li, 2022). Wan-Qing underscores the role of artificial intelligence (AI) and machine learning (ML) in automating repetitive tasks, liberating employees from monotonous activities and thereby boosting their productivity and job satisfaction (Wan-qing & Li, 2022). By streamlining these tasks, employees can cultivate better work habits and experience increased flexibility in their work schedules. This flexibility matters because it empowers workers with greater control over their work-life balance, allowing them to allocate time for personal well-being and reduce the stress associated with rigid work hours.

Furthermore, Wan-Qing delves into the adoption of AI in the manufacturing industry, revealing a positive impact on the mental health of workers (Wan-qing & Li, 2022). While not directly linked to the reduction of tedious tasks, the enhanced work environment facilitated by AI contributes to improved worker well-being. This matters because a positive work environment can alleviate stress, reduce workplace-related mental health issues, and create a more fulfilling work experience for employees.

Collectively, these insights suggest that optimizing tedious tasks through AI not only enhances worker productivity and job satisfaction but also empowers individuals with more flexible work arrangements, fostering better mental health outcomes. This is of paramount importance in modern workplaces, as it can contribute to a more motivated, engaged, and healthier workforce, ultimately benefiting both employees and employers. However, while optimizing tedious tasks through AI offers promising avenues for worker well-being and flexibility, it is crucial to recognize the parallel challenges posed by the digitization of office work, which introduces "technostress" and its potential consequences for job satisfaction, commitment, and productivity.

The digitization of office work, as highlighted by Malik and Tripathi, et al. as well as Huo and Keng, has given rise to a phenomenon known as "technostress," which significantly impacts employees' job satisfaction, commitment to their work, and overall productivity (Malik et. al., 2023; Huo & Siau, 2023). Malik and Tripathi, et al., who conducted a global survey on the impact of artificial intelligence (AI) and computer systems, revealed that the adoption of digital workspaces, while promising increased productivity and flexibility, has also introduced the concept of technostress (Malik et. al., 2023). Excessive use of information and communication

technologies (ICTs) in personal time and space can lead to stress and social isolation among employees, resulting in reduced job satisfaction and lower commitment to their jobs. Similarly, Huo and Keng discussed how the integration of AI and automation technologies, such as ChatGPT, into educational settings has raised concerns about technostress among teachers, impacting their job satisfaction and well-being (Huo & Siau, 2023). The implications of technostress are significant, as it can lead to decreased employee productivity and commitment, ultimately affecting organizational success. Thus, addressing the issue of technostress is crucial for creating a more satisfied and motivated workforce, which directly contributes to the overall success and effectiveness of organizations. In light of the challenges posed by technostress in the digitized workplace, it becomes evident that continuous learning and adaptability play a pivotal role in mitigating the broader concerns and impacts of AI on workers, a topic we will delve into next.

Continuous learning and adaptability emerge as essential strategies to mitigate AI-induced worker concerns, as illuminated by research by Nazareno and Schiff, Muro and Whiton et al, Lane and Saint-Martin, and Wang and Siau (Nazareno & Schiff, 2021; Muro et. al., 2019; Lane & Saint-Martin, 2021; Want & Siau, 2023). These papers collectively emphasize the imperative of ongoing skill development and flexibility in the face of AI advancements. As exemplified in “The Impact of Automation and Artificial Intelligence on Worker Well-Being” by Nazareno and Schliff, AI's influence on worker well-being extends to job security (Nazareno & Schiff, 2021). Workers exposed to higher automation risk may grapple with heightened job insecurity, posing challenges to their mental health. This underscores the importance of adapting skill sets and acquiring new competencies to maintain long-term employability in an AI-driven world. Similarly, Muro and Whiton et al. emphasized the intricate relationship between AI, job insecurity, and worker well-being (Muro et. al., 2019). It highlights the need for workers to continuously learn and upskill to remain competitive in the evolving job market, thereby mitigating potential mental health challenges linked to job insecurity. Moreover, Lane and Saint-Martin delved into the dual impact of AI on the labor market, emphasizing the importance of workers developing new skills to navigate the changing landscape (Lane & Saint-Martin, 2021). AI's potential to complement human capabilities and improve job quality underscores the significance of continuous learning and adaptability for enhanced worker well-being. Lastly, Wang and Siau delve into the widening wealth gap resulting from AI-driven job displacement and calls for strategies like the development of creative and social intelligence skills to facilitate workers' transition into new roles (Want & Siau, 2023). These insights collectively support the argument that continuous learning and adaptability are essential tools to mitigate AI-induced worker concerns, ensuring their mental well-being and long-term employability in a rapidly changing work environment. Overall, continuous learning and adaptability stand as vital strategies to address the multifaceted challenges posed by AI in the workplace, promoting worker well-being and long-term employability.

Conclusion

The literature review delves into the intricate relationship between artificial intelligence (AI) and worker well-being, revealing a multifaceted landscape. It highlights the critical role of financial stability and job security, which can either enhance or deteriorate worker mental health in the AI-driven workplace.

Rapid adaptation to evolving job dynamics, the optimization of tedious tasks through AI, and addressing technostress in digitized workplaces are identified as crucial factors influencing worker well-being.

Continuous learning and adaptability emerge as essential strategies to mitigate AI-induced concerns, emphasizing the importance of holistic approaches in fostering a balanced impact of AI on worker mental health. The relationship and impact of AI on the mental health of workers can be quite complex and reflected through several points of contact between the idea of labor and mental health itself. For example, the way work by human workers is respected, treated, compensated for, and secured has a direct influence on the mental health and stability of workers. As such, phenomena like labor dynamics are directly intertwined with both AI and its impacts on mental health.

One notable conclusion is that the effects of AI on worker well-being are not inherently positive or negative; rather, they depend on various factors such as the level of job security, adaptability of workers, and the nature of the tasks being automated. It is evident that addressing these challenges and harnessing the benefits of AI for mental well-being requires a holistic approach that considers the broader context of work and technology. To effectively discuss and address the toll that AI is taking on mental health in the workforce, it is essential to encourage open and transparent communication within organizations. Employers should foster an environment where employees feel comfortable discussing their concerns related to AI and mental health. Training programs and support systems can be implemented to help workers cope with the changes and challenges brought about by AI.

Future work should include empirical studies on the effects of AI on the mental health of workers, including robust statistical analyses and sociological critical analysis. These studies should explore the relationship between AI-induced changes in the workplace and the mental well-being of employees.

Additionally, research should focus on developing guidelines and best practices for organizations to ensure that the introduction of AI is accompanied by strategies to mitigate potential negative impacts on mental health. In conclusion, as AI continues to reshape the modern workplace, it is crucial to recognize its implications for the mental health of workers. By addressing the challenges and harnessing the opportunities presented by AI, organizations can create a work environment that promotes both the well-being and productivity of their employees. This multidimensional issue warrants ongoing research, discussion, and action to ensure a balanced and positive impact of AI on worker mental health.

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Childhood Abuse and its Effects on Mental Health By Riya Goel

Introduction

Child maltreatment is an important issue. Although the number of abused children has varied slightly throughout the years in the US, too many children experience abuse. For instance, in 2015 alone, 683,000 cases were reported, excluding how many cases were unreported (D. Finkelhor et al., n.d. as cited in McLeigh et al., 2018, p. 154; "Child Maltreatment 2015," 2017, as cited in McLeigh et al., 2018, p. 154).

In this paper, I argue that childhood physical and emotional abuse is overlooked and psychologically harmful due to the consequences abuse has a high correlation with. There are various issues associated with childhood maltreatment. It often diminishes children's mental health. There is also a strong correlation between abuse and the development of several mental health issues, such as depression, anxiety, and suicide. I will discuss this topic throughout this paper.

Here are some key terms that I will use and their definitions. First, physical abuse is when a person injures another person intentionally, such as slapping, kicking, choking, and more (*Types and Signs of Abuse | DSHS*, n.d.). The second type of abuse I will discuss is emotional abuse, which is when a person induces trauma in a non-physical way, such as yelling or manipulation (*What Is Emotional Abuse*, n.d.). Depression (also referred to as major depressive disorder) is a mental disorder that causes a person to feel, think, and act negatively. People with depression often feel hopeless and alone (*What Is Depression?*, n.d.). The next one is anxiety. Anxiety is an emotion where a person constantly feels tension and is in a constant state of worry. It differs from fear because it tends to be long-lasting, whereas fear is felt briefly (*Anxiety*, n.d.). Lastly, suicide is the actions of a person taking their own life of their own free will (*Suicide Definition & Meaning - Merriam-Webster*, n.d.).

Numerous children experience abuse throughout their lifetime. It is a huge problem that needs to be addressed because of the various consequences it can lead to. The number of children who are abused is exceptionally high. In the US alone, 4.276 million child maltreatment cases were reported in 2022 (which fails to account for the children who never get reported). The 4.276 million cases involved a total of 7.5 million children (*Child Maltreatment & Neglect Statistics*, n.d.). This is a problem that is often overlooked. Out of the 7.5 million maltreated children in 2022, only 3.096 million of those children received care and treatment through social workers or law enforcement (*Child Maltreatment & Neglect Statistics*, n.d.). This statistic shows how overlooked this issue is due to the drastic number of cases the government fails to follow through on. Physical and emotional abuse during childhood is highly overlooked and psychologically detrimental because there is a strong correlation between childhood abuse and mental health issues later in life, including depression, anxiety, and suicidal ideation.

In this paper, I will first introduce the topic of abuse, focusing on two types of abuse: physical and emotional. Then, I will talk about three types of mental health issues that correlate

strongly with childhood abuse: depression, anxiety, and suicide. Finally, I will state my analysis and thoughts based on the information in the paper.

Abuse

In this section, I will discuss the two most prominent types of abuse that children face during childhood. The first one is physical abuse, and the other is emotional abuse. Then, I will talk about an essential factor many people fail to account for: the cultural aspect of how we understand and define abuse.

Many causes may lead to abuse throughout childhood, including underdeveloped neighborhoods, parents who are heavily addicted to alcohol and drugs, and more. McLeigh et al. (2018) researched the rates of childhood abuse in underdeveloped communities. The authors of this article sought to lower childhood abuse rates and focused on the underlying issues to help accomplish this goal. They collected data from randomly selected caregivers with children under ten years of age, and they found that there was a direct correlation between neighborhood poverty and abuse rates. The findings furthermore suggested that if the poverty rates in a neighborhood were to be reduced, the likelihood of childhood abuse would most likely decrease. This article suggested that abuse is a prominent factor in many households, especially those in diminished neighborhoods, which are common throughout today's world (McLeigh et al., 2018). This could be because parents who experience poverty have financial issues and are often under a considerable amount of stress. Most parents in poverty feel overwhelmed by the lack of money they need to survive, and since they have children, their responsibilities may seem even more extensive. Because of this, they tend to use their children as an outlet for their stress, which, unfortunately, results in them abusing their children.

Parents who are heavily addicted to drugs and alcohol also are more likely to both physically and emotionally abuse their children. One study collected data from a survey across numerous cities and found that the higher rate of drug addiction was related to more frequent physical abuse. This research suggests that reducing the use and supply of illegal drugs will most likely also minimize child abuse (Freisthler et al., 2017). This article does not offer much analysis of how they reached this conclusion. I believe it is because when people are addicted to drugs, their emotions and behavior are usually negatively affected, and they lose control of their actions, which are typically arbitrary. This means that they could experience increased anger or stress, which they may use to abuse their children. After their drugs wear off, they tend to feel in a low place and disappointed with themselves, and some may act out in several ways, such as abusing their children. So, if drug rates were to lower, theoretically, abuse would reduce as well.

The aforementioned research shows that a prominent underlying factor of child maltreatment could be due to a parent's addiction to drugs and alcohol. Another study that further demonstrated the correlation between abuse and addiction reported the rates of children experiencing abuse if their parents abused alcohol or drugs. The authors concluded that compared to children who have non-addicted parents, a child who has one or two addicted parents to either drugs or alcohol is 2 to 13 times more likely to undergo adverse childhood

experiences (Dube et al., 2001). These rates show that addicted parents often have a greater chance of abusing their children, possibly because, as I mentioned before, they have unpredictable emotions and actions and tend to blame their children for numerous scenarios in which the child may not be involved. After examining a few of the possible causes of childhood abuse, I will now delve deeper into the details of both physical and emotional abuse and culture.

Physical Abuse

Physical abuse is widespread, and the rates of physical abuse solely in the US are considerably high. There are approximately 95,026 children (around 17%) who are abused in a year in the United States. In 2022, 1,990 children died as a result of abuse. Furthermore, of the children who died, 42.1% underwent either solely physical abuse or physical abuse combined with another type of maltreatment, such as emotional abuse or neglect. 44.7% of children who died from abuse were under a year old. The number of cases reported in 2022 of childhood maltreatment was the highest for children under one-year-old (82,329) and gradually decreased for older children (e.g., 26,255 for children who were nine years old). This failed to include the number of cases that went unreported. Finally, child abuse is prominent across all socioeconomic levels (although it is more of an issue in poverty). It is also prominent throughout every educational level, religion, ethnic, and cultural group. It is not isolated to a specific type of family, which shows how it is spread throughout the world (*Child Maltreatment & Neglect Statistics*, n.d.). These statistics display the importance of this issue since it affects numerous children.

One article showed that physically abused children often experience long-term consequences of the abuse. Specifically, abused children tend to experience seven types of negative consequences: they tend to engage in criminal behavior, lean towards drug abuse, have more violent actions, suicidal ideations, emotional issues, problems with relationships, and academic difficulties. These are only a few of the issues that children will have a more likely chance of encountering if they are physically abused when growing up. The relationship between abuse and the consequences that I mention are affected by various outside factors, individual and environmental, that may suggest these consequences are not related to abuse. The evidence I previously mentioned reveals a strong correlation between the two despite outside factors (Malinosky-Rummell & Hansen, 1993). This shows the severity of the consequences a physically abused child can experience, further highlighting the fact that this is a severe issue.

Emotional Abuse

Emotional abuse is another prominent type of abuse. There are around 38,030 children annually (around 6.8%) who are psychologically maltreated (*Child Maltreatment & Neglect Statistics*, n.d.). Emotionally abused children are often belittled, intimidated, or humiliated. Because of this, children increasingly start to fear their parents. Parents in these situations tend to gain a sense of control and power over their children. Emotional abuse often damages a child's self-esteem and their self-worth. Emotionally abused children feel worthless and hopeless,

causing them to blame themselves, be self-destructive, and have a lack of motivation, among other effects. Infants and young children can fail to thrive, while older children may shut down in school and not try anymore. When they are adults, they tend to disconnect from others and often suffer from various mental health disorders. One article suggests that a child's brain development depends on the emotional care provided throughout childhood and how healthy the relationship between parents and children is. Emotional abuse is, therefore, one of the most serious threats to the physical, emotional, social, and behavioral development of children (Norman et al., 2012). Emotional abuse is a severe issue and is extremely detrimental to a child's mental health.

Emotional abuse can also be highly damaging to a child's relationship with their parents. Emotionally abused children often have an increase in anxiety about whether their parents can care for them and themselves. The anxiety increases when parents are addicted to substances such as alcohol or drugs, are violent, or have mental disorders. As soon as children enter this world, the first people that they depend on are their parents. However, when their parents are addicted to substances, their first and only safe haven at the time is often taken away from them either emotionally or physically. However, it has severe consequences either way (Halvorsen et al., 2013).

One article conducted a systematic review concluding that childhood psychological abuse is strongly linked with various issues that children experience when they grow up. Emotionally abused children are three times more likely to develop depression than children who are not abused by their parents. Furthermore, children who undergo psychological maltreatment can develop mental health disorders, including anxiety, drug abuse, and suicidal ideations (Norman et al., 2012), further showing the consequences an emotionally abused child can experience.

Finally, the damage done by emotional abuse is exacerbated by the fact that, often, it is neglected and overlooked. This could be because an adult failed to recognize the abuse and also the children's fault for voicing their situation out loud to others. Many adults purposely avoid acknowledging the abuse that children undergo and, instead, ignore it. Perhaps they downplay the risk the child is facing. Some adults will see a child experiencing abuse and will find reasons to explain the abuse and rationalize it. Adults also tend to distance themselves from the child's suffering and loneliness, choosing to look the other way. Finally, adults are easily able to shift the reasoning of the abuse onto the child's behavior, claiming that this is a result of the way the child acts and it is by no fault of the parent's misconduct (Halvorsen et al., 2013). Since emotional abuse is usually overlooked by other adults in a child's life, the issue cannot be resolved. Therefore, the children experience this abuse for years, further depleting their health and causing severe consequences.

Many emotionally abused children in school may seem independent, but this is often because they refuse to ask for help because they do not want to draw attention to themselves. Emotional abuse is also difficult to detect or prove, and when someone first looks at a child's household, the situation may not seem as bad as it truly is. Since emotionally abused children are not physically harmed, it makes it more difficult for other adults to understand how bad a child's living situation may be, which causes the trauma to go on. Finally, many children who are

psychologically maltreated often look as if they have a healthy family life since, usually, their basic needs, such as shelter and food, are met or even exceeded, causing numerous adults to overlook their issues and the signs they struggle until it is too late (Hensel, 2021).

Cultural Considerations of Abuse

When examining abuse, there is an important consideration that is overlooked but plays a significant role in this topic, which is culture. In various cultures, abuse is defined by different actions. Some cultures see specific actions as non-abusive, whereas others see those actions as highly abusive.

Cruise et al. (1994) delved deeply into this issue of cultural abuse. In the article, they discussed how every group studying childhood abuse fails to account for the fact that the children they examine may all report what is happening to them differently because they all have different perspectives of abuse in the first place. Because of the various environments children grow up in, their definitions and perceptions of physical abuse change since numerous children are taught through their culture that the abuse they undergo is “normal” for all children to experience, even though it is not the right thing for a child to undergo. Suppose the parents who physically abused their children were also physically abused as a child because of how normalized it is in various cultures. In that case, they will most likely think this is normal and also pass this way of thinking to their children, therefore resulting in the children physically abusing the next generation as a result. The researchers in the article collected data asking various children how serious different abusive acts are to understand and research the factors, such as gender and age, that alter children’s perspectives on abuse. The data showed that the children’s perspectives were strongly dependent on their age and the type of abuse. Overall, younger children ranked abuse as less serious than older children. The younger children ranked abuse by a significant amount for a few different types (Cruise et al., 1994). There could be a factor of age because as children get older, they start interacting with people from various backgrounds outside of their own culture and community. Older children are also exposed to social media more than younger children. Both of these changes in their environment can cause them to realize that not everyone’s parents treat them the same way as their parents do, showing that the way their parents treat them is not “normal” and is, in fact, abuse.

The ratings of these children were then compared to ratings by earlier studies of different children, community members, and mental health professionals. They found that the present children, the first set of ratings, rated the abusive acts as less serious than the previous children and community members did in the past, the second set of ratings (Cruise et al., 1994). The present children may have rated their abuse as less severe because they are accustomed to abuse and think that it is not an unusual or unethical act. Furthermore, they may have ranked this as less serious than community members because community members are adults and often know when an act is abusive because they have more exposure, similar to the older kids I mentioned before. Although there were many limitations to this investigation, and this was surface-level research, they hypothesized that various mental health professionals may also be rating physical

abuse and other forms of childhood maltreatment as less serious than they are, which is concerning since they are professionals. They believe this because they found that the children and mental health professionals both marked the abusive acts as less serious, showing that mental health professionals often overlook certain unethical acts and think they are not as severe of an issue as the acts may be (Cruise et al., 1994).

Various African tribes implement certain rites of passage onto their children. During these rites, children often have beatings, facial scarification, and more. These rites seem extremely bizarre to Western people and are often labeled as abusive. However, in some African cultures, this is normal and not abusive. On the other hand, some Western ideas seem strange to others. For example, practices such as letting children cry until they cannot anymore seem like a suitable method for them to stop crying in the viewpoint of Western culture; however, other cultures would see this as strange and damaging to a child, labeling it as abuse (Korbin, 1980).

Furthermore, Korbin (1980) discusses how physical trauma differs in various cultures. For instance, Vietnamese practice a *cao gio* (coin rubbing) tradition. Heated metal coins are seared onto the child's skin, and numerous bruises would form as a result of this. Vietnamese people believe this would reduce a child's fever and chills. In these scenarios, it is challenging to differentiate between child abuse and culture since they go hand-in-hand. This is why culture needs to be a factor in child abuse since every culture has a different definition of what they believe abuse is based on their family's practices (Korbin, 1980).

Another example of how Western ideas and culture are incredibly different from other cultures is potty training. In Western culture, when children are toddlers, they are taught to sit on the toilet and use it so that they may solely use the toilet and no other areas to do their business. This process is seen as a step where children can mature. However, other cultures would view this as parents "training" their children as they would a dog, showing the drastic difference in how a simple idea for Westerners can seem abusive to others.

Culture is another reason why abused children are often overlooked. If a child's home situation was reported to law enforcement and social workers showed up, parents could easily argue that this practice is what their culture believes in and, by their definition, it is not abuse. Furthermore, because of generational trauma, parents could say that this is how they were raised, and this is how they choose to raise their children. So, since everyone has a different definition of abuse, there is no correct answer. In that case, the social workers cannot arrest any parents or take the children into foster homes where they can be treated better (Korbin, 1980).

Because of this critical factor of culture, there is no one definition of child abuse, which means that children often are abused in various cultures, whether Western, African, etc. Since some dictate certain practices are not abusive, and others dictate they are, the lack of definition manages to decrease the amount of help children receive, and, as a result, the children suffer.

Mental Health Consequences

In this section, I will discuss how there are numerous mental health consequences associated with childhood maltreatment. I will be focusing on the three main ones that are often

present with abuse: depression, anxiety, and suicidal ideations. Specifically, I plan to discuss how there is a strong correlation between child maltreatment and these mental health consequences. For all three types of mental health consequences, I will discuss the various statistics found, how overlooked this issue tends to be, and the fact that it affects not only themselves but also the people surrounding them as well, such as their closest friends and family.

It is essential to note that gender is also an important aspect. One study focuses on women. They split their sample, grouping the forty-nine women into four categories: women who had never experienced childhood abuse or mental health conditions (presented as the control group), women with a diagnosis of depression who also have a history of child abuse, women who do not have depression and were abused as a child, and finally, women with minor depression and no childhood abuse. All four groups completed a stress test, in which they were examined under various stressful conditions. One of their findings was that abused women had an increase in cortisol levels in response to the stress test. Cortisol is a stress hormone, so the more stress an individual experiences, the more cortisol is secreted (Penza et al., 2003). Therefore, to support my thesis, since childhood abused women experience more stress, it declines their mental health, which can make them more susceptible to mental health issues. This study solely focuses on women. So, it would be interesting to apply the same methods to men so the research is more gender diverse.

Depression

The first significant mental health consequence of childhood maltreatment that I will discuss is depression. There is a strong correlation between childhood maltreatment leading to depression.

Depression can affect anyone and everyone regardless of age, race, gender, etc. Additionally, those whose depression is undiagnosed or untreated are at greater risk for their symptoms getting worse because if an individual does not know that they have depression, they lack the resources to treat it. If they are unable to treat it, they will continue to have poor mental health. Depression is extremely taxing on a person's physical well-being since some symptoms include fatigue, lack of energy, difficulty concentrating, difficulty sleeping/oversleeping, physical aches or pains, and many more (*Depression - National Institute of Mental Health (NIMH)*, n.d.). This shows how severe of an issue depression is and how damaging it can be on an adult's mind and even more so on a child's.

Research has shown that the causes of depression are best represented using the biopsychosocial model. Various biological, environmental, and psychological factors impact depression. Some examples of biological factors are hormone levels and genetics. For environmental factors, a child could grow up in poverty or have a history of childhood abuse. And finally, psychological factors, such as stress and personality, can impact a person's risk of depression (*Depression - National Institute of Mental Health (NIMH)*, n.d.). Overall, the biopsychosocial model demonstrates how factors that a child might experience, such as abuse, can increase their risk for depression.

There are various types of depression. In this paper, I will focus on one primary type: dysthymia. There are some limitations to the knowledge regarding dysthymia; researchers have not yet found a definitive source that causes it. Some have found that dysthymia can occur due to genetics. However, most of the research done so far has found that people who experience dysthymia have often undergone trauma, such as abuse, therefore making it the most relevant to this paper.

Dysthymia is a longer-lasting version of depression. Another name for it is persistent depressive disorder, and people who fall under this category tend to experience major depression for an extended period. Furthermore, some psychologists believe that dysthymia is a gene passed down between families. However, other professionals think that other factors could lead to persistent depressive disorders, such as environmental and psychological issues and chronic stress and trauma (*Dysthymia*, 2023). Since dysthymia can be affected by stress, trauma, etc, I believe we should correlate dysthymia to maltreated children since abused children often undergo the same factors that cause dysthymia, such as environmental and psychological issues.

For instance, one study was conducted where psychologists researched the effects of child abuse and how those children experienced depression as adults. They selected 776 children randomly, all of whom were around five years old, and tracked them and their families into adulthood (around 17 years). They concluded that adolescents who were mistreated as a child were three times more likely to become depressed than a child who was not. Even though they concluded other adverse factors could have interfered with this finding, such as the characteristics of the parents and children and their overall family environment, those factors usually impact a person's risk for depression when they are a child and not when they are an adult. For instance, a factor could be a person's poor home environment, which will affect a child as they live there but will not affect an adult who has moved out already. So, these factors are less important when the child is older (Brown et al., 1999). This causes depression to have the largest effect on them as adults.

Unfortunately, depression is highly overlooked in families. A group of psychologists conducted research where they tested 64 patients who ranged from ages 6 to 12 for depression. They asked the children's parents to complete a form evaluating if the parents were depressed, and they were asked about their child's behavioral issues. The results concluded that 50% of the children were depressed, and out of the parent's answers, the results showed that 39% of the parents were mildly depressed. The 50% of children who were depressed usually had a parent who fell under the category of the 39% who were mildly depressed, showing that depression usually tends to cluster inside families. Also, every parent who was ranked as severely depressed had children who were ranked as depressed, further showing the strong correlation of depression appearing in clusters. Additionally, the parents who were mildly depressed who had depressed children believed that their children had behavioral issues, showing that even though their children were also depressed, the parents often mistook this for behavior problems (Davis et al., 1987). This research exhibits how parents frequently overlook their child's depression. So, if an

abused child has depression, their parents have a high chance of overlooking it, causing their mental health to be undiagnosed, untreated, and decline further.

Finally, Felitti et al. (1998) showed the strong connection between abuse and the greater risk of adversity that it leads to. The researchers asked a group of adults to list the adversities they faced as a child and the problems they now face. Around 10,000 respondents filled out the form. Judging by the data, they concluded that the people who faced an increased amount of abuse (specifically around four types of abuse - e.g., physical, emotional, sexual, and household dysfunction) were 4 to 12 times more likely to have depression and/or than those who never experienced childhood maltreatment (Felitti et al., 1998). This conclusion shows that the children who experience more abuse have a higher rate of experiencing depression, strongly correlating the two situations.

Anxiety

Another major mental health consequence that abused children face as adults is anxiety. Many major anxiety disorders in adults usually begin with anxiety as children (*Depression - National Institute of Mental Health (NIMH)*, n.d.). Many abused children often associate abuse with shame and guilt. This connection is because even though the abuse is not the child's fault, they often feel as if they could have prevented it either if they were better children, stopped it, or fought back (EndCAN, 2021). The constant state of shame and guilt leads to an increased amount of worry and panic since it causes a lot of mental distress, and their emotions become unpredictable, increasing many children's anxiety. Anxiety takes a toll on the children's minds and their bodies. Anxiety is a correlated consequence that can commonly stay with them for years. Furthermore, to hide their abuse from others, children tend to draw away from their classmates and friends, which makes it hard for them to fit in, only increasing their worry.

Child maltreatment also affects surrounding family or community members as well. When an outside member notices the abuse, they are often shocked and confused and start to be in a constant state of anxiety for the victims of the abuse. So, not only can the victims develop anxiety, but also their closest family and friends, who may have been unaware of the situation at first ("Understanding Child Abuse and Its Effects on Mental Health," 2023). Since the mental health of not only the abused children is declining but also the mental health of the adults surrounding them, this increases the significance of this issue.

Three types of anxiety are most relevant to this context. The first one is social anxiety disorder (SAD), where a person may experience anxiety in front of others because they may fear judgment (*Social Anxiety Disorder*, n.d.). The next is post-traumatic stress disorder (PTSD), where a person develops anxiety or stress from an event that occurred that may have been highly traumatic (*Post-Traumatic Stress Disorder - National Institute of Mental Health (NIMH)*, n.d.). Finally, generalized anxiety disorder (GAD) is when an individual is in a constant state of anxiety, stress, and fear due to everyday life issues such as work, money, family, etc (*Generalized Anxiety Disorder*, n.d.).

However, the main issue is that anxiety disorders are often underdiagnosed, misdiagnosed, and incorrectly treated. One reason that causes this is that some types of anxiety are less visible than others. For instance, social anxiety tends to be more discreet than generalized anxiety. Since anxiety is under-diagnosed, it is also under-treated. Fewer than one in five people with anxiety receive the appropriate medicine to help. Undiagnosed or untreated anxiety often has negative consequences correlated with it, such as loss of productivity, disabilities, and a high risk of suicide, all of which limit a person's quality of life (Kasper, 2006). Since anxiety is often underdiagnosed and undertreated, abused children who have anxiety often face this issue as well, causing their mental health to decline.

Another main consequence of anxiety in children is that it severely affects their schoolwork. There is an increase in social phobia, which leads to children emotionally withdrawing from school, affecting their work and grades in the process. One article conducted a study and researched around 200 students, comparing their mental health disorders to their schoolwork. Approximately 49% of the students (98 precisely) reported that they left school earlier than usual, and 24% of those students (23 students specifically) admitted that anxiety was the main reason for this decision. Those who leave school prematurely are also more likely to have social phobia and a past of alcohol addiction, among other effects, than the students who completed their education. The researchers concluded that for these children to reach their full potential, they may have to undergo treatment, whether through medication or other methods (Van Ameringen et al., 2003).

Suicide

Suicide is another significant consequence of child maltreatment. Psychologists at the University of Manchester and the University of South Wales examined 68 studies of 262,000 adults eighteen or older from various countries. They concluded from their experiments that adults who were abused as children, whether physically or emotionally, were two to three times more likely to have suicidal ideations and commit suicide. Furthermore, they found that older adults had an increased risk of suicide (Angelakis et al., 2019). So, this study shows that adults who were abused as children are more likely to commit suicide, especially the further they age. One way to prevent this is possibly by conducting an intervention when the adults are younger because they have a lower chance of suicide, and professionals may be able to help them before their chances increase. Another site reported statistics based on studies and found that the rate of suicide attempts was two and a half times more likely for people who experienced either emotional or physical abuse as a child than for people who did not. Furthermore, children who experience multiple types of abuse, such as physical and emotional, are five times more likely to attempt suicide. Suicide attempts are seen in adults more than children because as maltreated children age, the risk of suicide attempts increases since, without treatment, their poor mental health consistently keeps them in their mental health in a depleted state (*Child Abuse Linked to Risk of Suicide in Later Life*, n.d.). This shows that abused children have an increased risk of

suicidal ideations, which increase as they age, further worsening the issue because their mental health gets worse, and they are more likely to commit suicide.

Finally, as I mentioned before in the anxiety section, mental health scenarios like these are often underdiagnosed or misdiagnosed and, as a result, undertreated or mistreated. Therefore, children who fail to receive proper mental health treatment are placed at the highest risk for suicide. This increases the severity of the issue that abused children experience and shows that their mental health can have risks.

Another article researched the children who had adverse childhoods and connected this to rates of suicide since, in Hong Kong, the location of the study, the incidents of child abuse have been rising over the past decade or so. The authors conducted this research by looking at patients under eighteen spanning from January 1995 to July 2016 and studying who was abused and who was medically treated for suicide attempts. They concluded that around 5% of abused children attempted suicide ten years after they were first admitted to a hospital. Finally, over 25% of the patients had a record of repeating suicide attempts 20 years after their initial admission to a hospital. These rates show that those who underwent adverse childhoods increase their likelihood of suicide and suicidal ideations (Wong et al., 2020).

There are more general reasons as to why suicide tends to be overlooked. People who have suicidal ideations usually do not talk about it since they tend to think it is embarrassing and are ashamed to think that way. Other times, people do not feel like they have anyone to talk to who will understand and see them. They keep their feelings to themselves, and many of the victim's loved ones fail to recognize the problem until it is too late and the victim has committed suicide. There are many subtle signs of suicide that people tend to ignore, such as making small changes in their behavior like withdrawing from friends, giving away essential items, eating and sleeping more or less, turning to drugs and alcohol more often, having extreme mood swings, and talking as if they are a burden to others or have a ton of emotional or physical pain that seems unbearable to them. These are simply a few of the main signs that suicidal children and adults tend to show (*Warning Signs of Suicide - National Institute of Mental Health (NIMH)*, n.d.). The aforementioned research displays that since suicide is often overlooked, it is underdiagnosed and mistreated, causing an abused child's risk for suicide to increase significantly, further strengthening my argument that abused children's mental health often declines. Therefore, the abuse that children have experienced has a strong correlation to face various mental health consequences, such as anxiety.

Finally, in the section on depression, I mentioned one study that also applies to suicide. To quickly summarize, the psychologists conducted a study where they researched 10,000 randomly selected respondents and concluded that the people who faced four types of abuse as children were 4 to 12 times more likely to have depression and/or suicidal ideations than those who never had an abusive childhood (Felitti et al., 1998). Again, this illustrates the role that childhood abuse may play in leading to suicide later in life because it demonstrates the strong correlation between abused children having an increased risk of suicidal ideations and suicide.

Conclusion

In this paper, I first discussed how two main types of childhood abuse, physical and emotional, are highly detrimental to children. So, I conclude that childhood physical and emotional abuse is extremely destructive psychologically and has a strong correlation with various consequences either in the present or later in life regarding the victim's mental health, such as depression, anxiety, and suicide. Friends and family often overlook both of these types of abuse, and the children suffer as a result. These mental health consequences are extremely taxing on the brain, and they are usually undiagnosed and untreated or mistreated for a variety of reasons, leading to the victim's mental health deteriorating even further.

Depression is best represented in this scenario by a biopsychosocial model. Numerous biological, environmental, and psychological factors impact depression (*Depression - National Institute of Mental Health (NIMH)*, n.d.). Furthermore, a study was conducted where researchers found that those who experience more abuse are more likely to have depression than those who never experienced childhood maltreatment, demonstrating the significant risk abused children have for depression (Felitti et al., 1998). Many major disorders in adults usually begin with anxiety as children (*Depression - National Institute of Mental Health (NIMH)*, n.d.). When abused, many children often associate it with shame and guilt (EndCAN, 2021), leading to an increased amount of worry and panic, which takes a toll on their minds and their bodies. Relating to suicide, one study researched the correlation between childhood abuse and suicide rates. They concluded that the rate of suicide attempts was two and a half times more likely for people who experienced either emotional or physical abuse as a child than for people who did not. Furthermore, children who experience multiple types of abuse, such as physical and emotional, are five times more likely to attempt suicide (*Child Abuse Linked to Risk of Suicide in Later Life*, n.d.).

As a whole, society should care about child abuse victims and their mental health because children are the future generation of society that will be the leaders and have positions of power and influence over others one day. If we do not help them before they get to this position, it may reflect in their work and harm others. Without treatment and help, this problem can and will increase, and many future people will be affected. Finally, if no one helps these children, they may grow up to think that this is "normal," causing them to treat their children this way and create further generational trauma, severely impacting society as a whole.

There is also another correlation between childhood abuse and its consequences. Child abuse does not simply correlate with mental health consequences but also criminal activity, which damages a child's social standing and prevents them from receiving a good education and job. Children who are abused usually have poor mental health and some resort to violence to help them cope, ultimately landing them in prison. Some statistics clearly show this relationship. In the USA, 14% of the population of men in prison and 36% of the women in prison were exposed to child maltreatment, which is two times as much as in the general population of America. Additionally, mistreated children are approximately nine times more likely to participate in criminal activities compared to children who are not mistreated (*Child*

Maltreatment & Neglect Statistics, n.d.). This research displays that abused children not only experience depleted mental health but also affect their behavior as well, which worsens their reputation and affects others who may have been victims of their criminal activity.

There are numerous limitations when it comes to studying this topic. For instance, there is a conceptual difference between cause and correlation. Throughout this paper, I do not use phrases such as “childhood maltreatment causes depression in children.” This is because, although there is considerable data that shows a relationship between maltreatment and mental illness, there is little research that can demonstrate a causal relationship due to ethical limitations. So, I use the phrase “correlation” instead, showing that there is a strong connection between childhood maltreatment and depression. One way to prove that childhood maltreatment causes mental health issues would be to conduct some unethical experiments that would be more suitable for performing on animals instead. However, there may be other ways to prove causation in the future. There is another limitation in this field because, since many families overlook childhood maltreatment and mental health, it is underreported, causing much of the research to be limited and, possibly, inaccurate.

One article explains in detail how, although there are limitations, further research could and should be conducted on how to solve the issue of abuse. They explain that clinics helping abuse victims with their mental health should individualize treatment for each patient and help them based on the type of trauma they experienced and their specific type of abuse. It would be beneficial if there were methods enacted to prevent the factors of abuse, such as poverty and drug rates, instead of solely focusing on treating abused patients. Also, the type of abuse, whether physical or emotional, has a different influence on a person’s brain and also depends on the person as a whole due to various factors such as genetics (Radell et al., 2021). This further stresses the importance of individualizing the treatment each person is given. However, the limitation of the fact that there is a lack of research in individualizing treatment makes it extremely difficult to do so (Radell et al., 2021).

When discussing future research, I believe that the best direction to further understand this issue is to develop solutions. Because of the severity of childhood maltreatment on the brain and body, it is critical to find ways to prevent family trauma, which includes physical and emotional abuse and generational trauma. I suggest that we study how people have helped abuse victims in the past, how these victims have responded to it, what worked well and what did not, and how we can fix what did not work well so it may work better in the future. Furthermore, the limitations that I discussed in the previous paragraph could be bypassed because we could conduct studies on animals, which would give us a better idea of how humans are affected by abuse. For instance, one group of psychologists conducted research on rats. They observed that when rats are born, they have maternal care, and their mother takes care of them during the first few days of life. One example of this is through licking and grooming them. They conducted an experiment where they took one group of rats and had their mother take care of them like normal and another group of rats where they lacked maternal care and studied the two. They found that there were some differences in their brain. Specifically, the rats who underwent maternal

deprivation had an increased level of stress, displayed distress-like behaviors, and a memory deficit (Murgatroyd et al., 2009). This connects to abuse because it shows that rats who faced adversity and trauma when they were young had a declined mental health than the rats who did not face adversity. So, if this same understanding is applied to humans, abused children may have a causal relationship between abuse and declining mental health.

There are also various implications for this field and for society. In this field of abuse, there are issues that numerous people believe that abuse is okay because of how normalized it is in different cultures, such as how spanking children and domestic violence is acceptable in some areas of the world and not in others. This is another factor that causes abuse to become overlooked. When it comes to society, many people fail to discuss their family life as they think it is too personal for others to know about, causing a stigma around the topic. The same reasoning also applies to mental health. So, because of the stigma that society creates, many people fail to discuss the abuse they face and how vulnerable their mental health is causing them to fail to receive proper medical treatment and assistance. As a result, their mental health will further decline, showing how large of an issue it is.

Maltreated children are at a high risk of deteriorating mental health along with numerous other consequences, which should be discussed more, and society needs to find a solution to help them.

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Analyzing Student and Teacher Understanding and Curriculum Gaps in Indigenous History Education By Isaac He

Abstract

In the 2020 census, 9.6 million individuals across the United States claimed indigenous American heritage, yet 87% of highschool curricula “includes only pre-1900 context.” The gap in the current research analyzing indigenous history education consists of a lack of research on indigenous history education’s availability, areas of coverage, and the academic community’s placed importance on indigenous history. This paper addresses students’ confidence they have in indigenous history education, identifies the events through indigenous history which students and teachers cover less comprehensively, and quantitatively measures the percentage of the academic groups that values indigenous history. A survey to students and teacher interviews were conducted which generated the result that students had an average confidence in indigenous history education, but with limited coverage. Furthermore, the study finds that certain events were especially omitted in most standardized curricula, and have low coverage in advanced curricula, which was confirmed by both the survey and teacher interviews. 42.9% of students did not believe that a specialized indigenous history course was beneficial to their school, while 100% of teachers believed in the contrary, indicating the presence of stereotypes in the current student populace that decreases with education on the subject. The results indicate a need for increased indigenous history education that specializes in lesser-taught events, as well as action to increase sentiment for indigenous history as a subject.

Introduction

History is not a study of bygone events, but the pieces that build the puzzles of modern culture. As Houston Family Magazine describes, “History learning exposes children to diverse cultures, traditions, and perspectives worldwide” (Houston Family). In particular, studies have found that students who are exposed to different cultures through education are more “safe with the differences later in life” (“Diversity & Multicultural Awareness in Education”). The University of Kansas states that multicultural education creates “a sense of unity and understanding among classmates” (The University of Kansas). Indigenous culture is no different, as 9.6 million Americans in 2020 claimed indigenous heritage (Dam). Yet, in a 2015 study conducted by researchers at Pennsylvania State University, it was found that 87 percent of highschool curriculum content “includes only pre-1900 context” and 27 states did not even mention a Native person in their history curriculum standards (Shear et.al 68). Even in California, one of the most progressive states when it comes to indigenous history education, there exists a shortage of education on the subject. As California Assemblymember James C. Ramos states, the state “lacks high-quality curriculum materials that highlight the history, culture, and government of local tribes,” demonstrating the severity of this deficit (Uyeda). With the rising importance in cultural awareness, it is imperative that society takes a step back and

looks at education for a solution to the deficit of empathy towards indigenous individuals (Guzman et.al).

Historical Context

Since the first contact between indigenous peoples and white settlers, programs such as the Residential Schools program have been directed towards a mission of “kill the Indian and save the man” (Pratt). As such, lessons on indigenous history or culture were sparse, as efforts were poured into stamping out these aspects of indigenous societies.

With the American Indian Residential School program established in the mid 19th century, many relics and oral traditions were lost to time (Waxman). Other parts of recent indigenous history were also kept secret from the general public by different codes and laws. Charles Burke’s Religious Crimes Code of 1883 is one of these, which made the practice and spread of the Ghost Dance illegal in an effort to suppress indigenous culture and a religion that the government deemed threatening (Irwin). A combination of these programs, as well as the American Imagination’s fixation on the “vanishing red men” stereotype have further perpetuated this loss of indigenous history (Edmunds et.al).

Some states, like California, have laws that encourage schools to work with local Native Tribes to create curricula for public school students. Laws such as the California Indian Education Act, signed by Governor Gavin Newsom, serve as existing literature that encourages the spread of indigenous history (“Recommendation One”). Likewise, Alaska with the Alaska Native Education Program, Oklahoma, and Montana, etc. have similar programs. However, states without a significant native population lack these laws, and thus education on Native history differs vastly between these states.

Literature Review

The literature review portion of this paper was used to pinpoint gaps in the current research, of which the survey will answer. This paper examines existing studies, articles on indigenous education to analyze the gaps within the research of indigenous history. The keywords used for this search include “Native American History,” “Indigenous Pedagogy,” “Culture,” “AP United States History,” and “Common Core History Education.” Using these search words on Google Scholar and Jstor to obtain articles, this paper utilizes multiple articles on both indigenous education as a subject, and potential causes of this drought on education.

Current Articles Analyzing Indigenous History Education

In a study conducted by Michael McNally, Associate Professor at Carleton College, most existing education on indigenous history within native tribes is passed through mostly oral tradition. This oral storytelling culture, such as within the Ojibwe tribe, relies heavily upon the existence of “elders over book knowledge,” which faces the threat of extinction if no one is there to hear the stories (McNally 1). Additionally, McNally states that an effective course on indigenous knowledge must involve methods differing from traditional pedagogy. Professor

Donald Warren from the University of Indiana critiques the existing studies on Indigenous History education by stating that most current literature and academia on Indigenous Peoples fail to take the perspective of natives into account (Warren). The Organization of American Historians doubles down on this perspective, stating that the best way to teach indigenous history is via “diverse texts that demonstrate the multitude of perspectives that exist but are usually excluded from mainstream texts” (Meyers).

A study conducted in the Monterey Peninsula Unified School District in California was conducted primarily on 11th grade students and elementary school teachers. Kite found that 88% of students were unaware of the treatment of Natives during colonization. The paper found that “Sixty-six (66.7%) of students have heard of the Indian Removal Act of 1830... 35.6% of students have heard of the Indian Reorganization Act of 1834... only 11.1% have heard of Dawe’s Act” (Indian Allotment Act of 1887) (20). Through an analysis of existing literature, indigenous history education seems to be underrepresented in current educational standards, as well as incomprehensive in the nature of education.

Current Studies on Common Core United States History

The common core program that was launched in 2010 was a “shift away from disparate content” within the United States (Porter et.al 1). The seeming issue with common core is not only a sparse coverage of indigenous history, but of history in general, as common core lacks “any mention of what might be called a “public history” skill or competency” (Kelly 209). A review of the California Common Core Social Science & History curriculum reveals that the term “american indian” was only mentioned once in the content standards” (History Social-Science Framework). These sources indicate that common core or standardized history education lacks strict guidelines on indigenous history education.

Current Studies on AP US History

AP US History (APUSH), a college-level course on history for highschoolers, represents a college board standard for all highschoolers nationally on accelerated college level history content. When APUSH attempted to make changes to their curriculum in 2015, critics responded to the changes that highlight indigenous suffering during World War II with comments that the curriculum was too dark or negative. As assistant professor Suneal Kolluri highlights, the following year the curriculum reverted into a state “more amenable to defenders of American Society and less relatable for members of marginalized groups” (Kolluri 701). As evident in this criticism of the APUSH board and curriculum, often progressive changes fail to manifest due to conservative pushback. Additionally, these reversions demonstrate how the current APUSH curriculum is unable to fully encapsulate indigenous history, despite being a course of higher education on the subject. Kite also covers the AP Curriculum as a teacher in this survey stated AP students were “exposed to [indigenous history] but we don't spend a great deal of time on it as it is not really tested on the AP exam” (17). These findings indicate that advanced American

history classes, such as APUSH, are still insufficient in comprehension of indigenous history education, though there have been previous efforts to improve coverage.

Gaps in the Research

Across the literature review, there is a general lack of comprehensive research on the availability of indigenous history education. The studies that cover the general knowledge of indigenous history are limited in scope, such as being confined to the Monterey Peninsula Unified School District. For example, Kite's research methodology follows a yes/no style format, surveying respondents on whether they had heard of certain events.

Additionally, there is sparse research on which areas of indigenous history curricula tend to favor, as well as the student and educator base's placed importance level on indigenous history education.

RESEARCH DESIGN AND METHODOLOGY

Purpose Statement and Research Question

The purpose of this research paper was to define 1) what level of confidence American students have in indigenous history education, 2) how does indigenous history education differ between topics and curricula, and 3) what importance does the American student and teacher populace place on indigenous history in schools. Thus, the paper aims to solve the questions: "How comprehensive are current indigenous history programs and what areas of improvement lie in curricula?" and "How do teachers' opinions of indigenous history education differ from those of students?"

Definition of Terms

The definition of education places priority on "the process of acquiring knowledge and life skills, including values and attitude" while preserving the unique culture of a society (Fox and Tippeconnic III 30). For the sake of a controlled research environment, this paper will focus solely on formal education, defined as education mandated and targeted to acquire skills. The definitions of common terms used in this paper will be used in the context of the following:

Likert Scale: (Batterton et.al 32) defines the Likert Scale as an attitude scale built on "the premise that groups of related questions measure a subject's attitude about some issue addressed by those questions." For the sake of this paper, the Likert Scale is implemented to measure respondents' self-assessment on indigenous historical event competency.

Indigenous Peoples/Figures: Indigenous peoples will be defined as per Harvard University's Professor James Anaya: "living descendants of pre-invasion inhabitants of lands now dominated by others" (Anaya 3). In this instance - the term indigenous peoples will be used to refer to the

indigenous peoples of North America. The term indigenous figures will be defined as an indigenous person who took a role of importance in a historical event.

High/Low Comprehension and Coverage (HCC/LCC): For this paper, events will be categorized into two categories that the researcher defined — High Comprehension and Coverage (HCC) and Low Comprehension and Coverage (LCC). HCC shall be defined as any topic with a combined average score on the Likert Rating Scale greater than or equal to a rating of 5. LCC shall be defined as any topic with a Likert Rating Scale average score less than 5. This metric accounts for individuals who did not learn the subject — in which case they reported a score of 0. Figure 3 details each of the events with their combined average Likert Rating Score.

Data Collection Method

This research was conducted with two methods: a survey of students and interviews of High School History teachers.

An anonymous Google Form survey was used for data collection. To determine what aspects of indigenous history to focus on in order to reach a competent level of understanding, the APUSH curriculum was consulted. Table 1 below demonstrates the Khan Academy summary of the APUSH curriculum, as well as the research questions respondents received.

Theme #	American/ national identity	Politics and power	Work, tech, exchange	Culture and society	Migration and settlement	Geography/environment	America in the world
Period 1 1492-1607	-No connection among Native American groups. -Europeans did not intend to stay	Spanish dominated French/ Dutch were more interested -First No Contact w/ Native Americans	-New crops and trade goods into Europe, new tech into Americas -Medieval world (Native American)	-Banning of indigenous and European culture & education driven by art of religion	-Humans came to America on. Starting Land Bridge -Europeans came to extract resources	-Gold in Latin America drove exploration -Discovery from Europeans killed 95% of Native people	-Competition between European powers vs. well off Native American groups led to alliances, conflict
Period 2 1607-1754	-English settlers independent -Native American largely identity based on existing tribes	Settler government of local power gradually democratic in New England -Colonial New France -Colonial South, aristocracy by planters	-Emergence of towns in New England, Rising and falling tides in New England -South: slavery, indenture, cash crops	-New England: life centered around Puritan religion -Border castle system so land in the south -First Great Awakening	-Settlers and traders went to Europe, came to North & South, adventurers looking for wealth -1700s: enslaved persons	-Cherokee Indians refused to ally themselves with Native Americans in South, instead, in many cases killed captured persons	-Conflicting interests on what Native Americans own land, as well between European powers to get territory and goods
Period 3 1754-1800	-Development of independent national identity leading to Revolution -American colonists still writing under their rule despite British laws	-UK's interest in American UK's virtual representation, taxes led to war -Loss of Colonization (break) -Constitution (central govt) -First Party System (Hamilton v. Jefferson)	-End of "feudal" society as English colonists recognized own American goals, a strong local economy -Slavery continued to grow in South, helped by invention of cotton gin	-Influence of Enlightenment thought on Revolution -War men played role in Rev but not consider slaves	-Continued push against western frontier for land -Continual expansion of America	-End of freely available land in West + push west, conflict b/w cowboys, whites and backwoods farmers	-Emergence of USA as independent power -Alliance with France helps win Rev, but withdraws
Period 4 1810-1840	-Growing American identity, included original identity -Development of Native American societies	-Expansion of suffrage to all white men in North & South Democracy spread to South -South had its own government in new territories -Democrats vs. Whigs (Second Party)	-Expansion of infrastructure, markets, railroads, canals, telegraph, cities -Emergence of New England -Emergence of factories (Lower Mill), textile mills -Slave code had to grow in South	-Second Great Awakening -Reform movements to better, temperance, women suffrage, prison reform	-Americans push west -Native Americans forced West -Westward movement of people -1850s: gold strike, internal state conflicts	-Expansion of cotton in the South, slaves heavily worked -1860s: Civil War, Union vs. Confederacy -Treaty annexation	-After of 1812 and Britain's withdrawal in North America, ends 1865 for Native Americans to practice -Modest 1861 + territory
Period 5 1845-1877	-Increasing fracture along sectional lines + Civil War -Northern victory led to the United States, not the US United States -Using racism to control black men in South were citizens	-Brief period of sectionalism, Compromise of 1850, Fugitive Slave Act, Dred	-End of slavery in 1865, move toward system of sharecropping in South -African Americans freed, white Civil War based on factory power -Industrial cities and the country	-Emergence of technological progress of society and industry -Industrial revolution in 1870s -New technologies: steel, iron	-New immigrants coming from Ireland, Germany -Allow widespread continues, especially after gold strike in California -Indian Reservation	-Discovery of gold in CA leads to gold rush -Large population in North, industrial states help win Civil War	-Mid 1800s: largely homestead in the West, railroads that connect West w/ 100,000s on behalf of South are not needed
Period 6 1885-1898	-Increasing American national identity as US becomes global -Native American	-Brief period of American's fight for independence in South with -Jim Crow segregation becomes law -Regulation of power	-USA becomes world's leading Industrial power thanks to steel, oil -Lewis and Clark expedition to St. Louis -Women suffrage 1920 -Socialism, class struggle, socialism -New era of federal government intervention in economy, like trusts	-"Social Darwinism" - believe that some people are inherently better than others due to evolution	-Many new immigrants from S & E Europe -American Bechtel company, "Mother" of	-Cities are polluted, bad working conditions in 1900s -World War I -Colonization starts before Great Migration of 1900s -Southerners to cities in N	-Indian Wars, Native Americans nearly gone -End of American isolationism
Period 7 1890-1945	-New European immigration to US considered not American, because of WWI and connected "Europe"	-Major area of production and innovation, inc. phone, electricity, radio, car, media	-Belief in meritocracy, immigrants coming to USA each year until 1924, first census -Great Migration of 1900s -Southern cities to cities in N	-Many new immigrants coming to USA each year until 1924, first census -Great Migration of 1900s -Southern cities to cities in N	-New immigrants settle in smaller towns -Conservation starts before Great Migration of 1900s -Great Depression	-Spanish-American War -WWI -World War II 20s, 30s -WWII aftermath leads US to communism, isolationism	
Period 8 1945-1980	-Period of expanding Federal power and expanding power of corporations into 1980s -Impact of one USA culture vs. other cultures	-Growth in power until 1980s, when Nixon takes charge -Civil Rights Movement (1950s, 60s) -Women's rights movement, media	-Major economic boom from 1950s -Social movements (Civil Rights, Women's rights, etc.) -Invention of computer, info communications recession	-Religious aware of 1950s -Social movements (Civil Rights, Women's rights, etc.) -Emergence of protest against US going by students	-Move from cities to suburbs, age of cars -Many immigrants with family members with illegal status, mostly from Mexico -Urban sprawl	-Cold War at peak, most US foreign policy commitment to containment -Lead to Vietnam War, Vietnam covered extensively in conflict in the Media best in 70s	
Period 9 1980-	-Period of increasing conservatism, improvements after a movement to reduce size of govt -Construction of USA as world's leading superpower	-End of globalization has connected markets and people all over the world -Affirmative action, the women and minority movements, gay rights movement -Conservatism and inflation -Decline of unions, migration of wages	-Period of "American Syndrome" -Culture West over changing gender, race, family structure increasing diversity	-Increased immigration of people from Latin America and Africa -Movement to South and West for jobs	-Wors in Middle East led to efforts to reduce dependence on oil -Global movements of people -US-Germany deal in energy, food	-US-Soviet collapse, ending Cold War -USA involved in conflict in Middle East over culture, i.e. Gulf War, Sept 11, War on Terror -Age of globalization	

Table 1: AP United States History Curriculum via Khan Academy and Survey Questions (Khan Academy)

The survey consisted of 25 questions, including 8 highlighted events throughout indigenous history, as well as corresponding Likert Scale questions to determine the aptitude of different history curricula. The survey defined different indigenous history events, and if

respondents indicated that they had learned of this event, a corresponding Likert Scale question was generated to measure the respondent's self-defined understanding on the subject. 42 responses were obtained from highschool students varying in socio-economic status, age, and education level.

The interviews were conducted with 4 highschool history teachers, each spanning between 30 minutes - 1 hour. The teachers were asked similar questions as the students when applicable, but were allowed the opportunity to give open-ended responses. The interviews consisted of 10 open ended questions, where teachers were encouraged to elaborate on their justifications for their answers. Instead of a Likert Scale number, teachers were asked to state how long they spent in class on a certain subject or event.

Reason for Survey Design

The reason for conducting an anonymous survey was to preserve the integrity of the research by mitigating the amount of bias introduced. In a study conducted in 2023, it was found that the confidentiality and anonymity in survey processes not only stem from ethical research practices, but emphasize a relationship of trust between researcher and subject. Additionally, anonymous surveys push the survey results towards a more objective stance, eliminating a certain degree of social biases that stem from non-anonymous surveys (Kang).

The rationale for utilizing a Likert Scale lies in the variability of the definition of "comprehensive" and "limited" per different respondents' understanding. The Likert Scale allows respondents to quantitatively measure their understanding of historical events per their relative understanding of history as a subject in order to gauge the significance of indigenous history in curricula relative to other areas of historical study (Sullivan, Anthony).

Reason for Interview Design

The rationale behind conducting open-ended interviews was to obtain detailed statements from professionals, generating salient items with a limited sample size (Weller). Additionally, interviews also allowed the opportunity to clarify statements, recertifying the legitimacy and meaning behind certain statements. The opportunity to go further in depth on certain subjects when required was also a benefit of this research design.

Scope

The scope of this survey was limited to highschool students (ages 14-17), varying from those without a plan to receive a diploma to those who already had received one, and students who had recently completed their highschool diploma, but have yet to undergo college education. The scope of this survey was to establish a standard of education established by common high school history curricula. The scope of this survey was not extended towards Graduate students, as results found that curricula vary greatly between different higher-level education institutions.

The scope of the interview was confined to highschool history teachers, or teachers with a history background. The delimitations were also created prior to the interviews, as teachers were only interviewed within the United States.

Results and findings

Survey

Forty-Two Respondents completed this survey — 50% of which were APUSH students, the other 50% of which were regular US History students. 52.4% of respondents indicated that their school had a unit on indigenous history, 35.7% indicated that there were only a few lessons, 4.8% stated that their school offered an entire course. 7.2% chose “Other” with varying answers, ranging from “not at all,” to “A unit in middle school,” or “It’s covered throughout AP US History when relevant” (Appendix). Of these courses offered, 52.4% took the aforementioned course, 28.6% did not, and 19% stated that there was no course offered. When asked to rate their history course’s coverage of indigenous history as a whole from a scale of 1-10, the average response rate was 6.28. Figure 2 details the exact spread among these answers.

If you took your school's history course, how would you rate the material you learned from it from 1-10?

42 responses

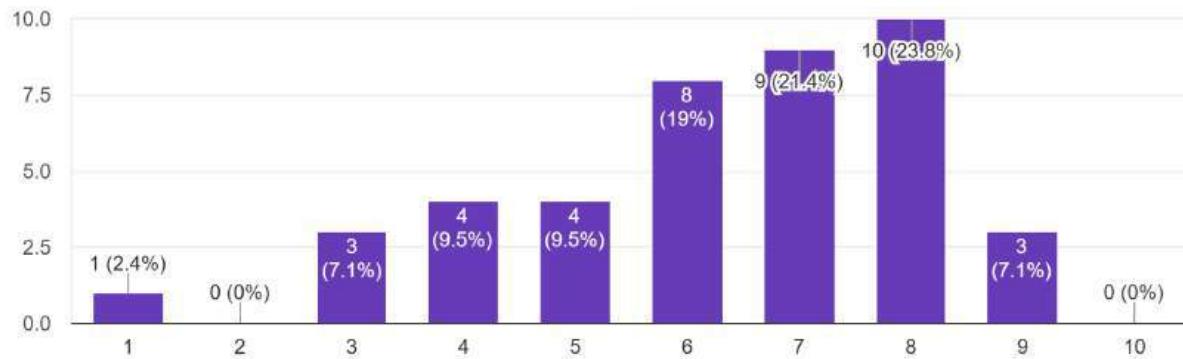


Figure 2: Survey Results on Competency of Indigenous History Curricula

The following questions on the survey assessed respondent’s knowledge on certain events throughout indigenous history, and had them rate their understanding of each event.

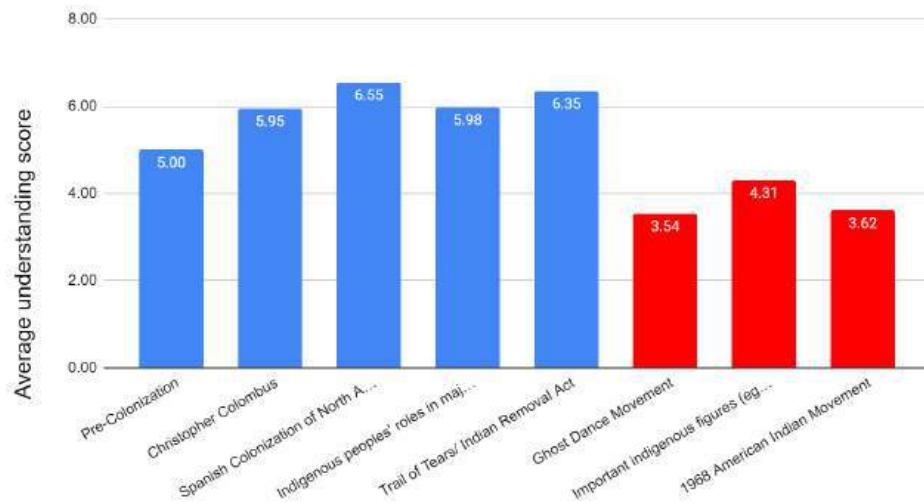


Figure 3: Survey Results of Respondent Knowledge on Indigenous Historical Events

The HCC events are the following: Native American History Pre-Colonization (5.00), Christopher Columbus (5.95), Spanish Colonization of North America (6.55), Native American Roles in Major Wars (5.98), and The Trail of Tears/Indian Removal Act (6.36).

The LCC events are the following: The Ghost Dance Movement (3.54), Important Indigenous Figures (4.31), and The 1968 American Indian Movement (3.62).

Figure 4 illustrates respondents' belief whether or not their school would benefit greatly from a specialized indigenous history course. Of the 42 respondents, 57.1% believed that their school would greatly benefit from such a course, whereas 42.9% disagreed with this statement.

Do you believe your school would benefit greatly from a specialized indigenous history course?
42 responses

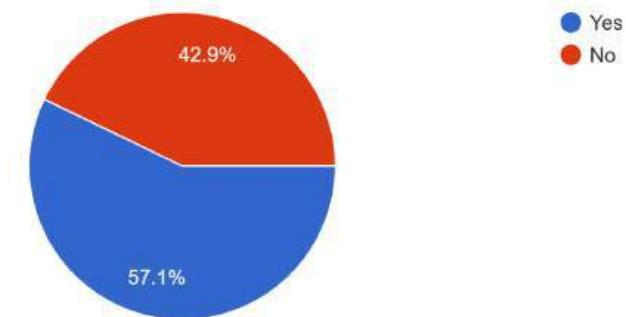


Figure 4: Survey Results on Opinions on the Benefit of a Specialized Course Teacher Interviews

4 teachers were interviewed, ranging from common core to APUSH teachers, and were asked to review the amount of time they spent on the events listed in the survey, the responses varied below.

For HCC events, teacher interviews generated data with the following ranges: Native American history Pre-Colonization- A Unit, Christopher Columbus A Week or Two Weeks, Spanish Colonization of North America - Two to Three Weeks, Native American Roles in Major Wars - A Week to Two Weeks , and The Trail of Tears/Indian Removal Act - A Week.

For LCC events, teacher interviews generated data with the following ranges: The Ghost Dance Movement - One Lecture or Equivalent, Important Indigenous Figures - No Focus and Spread Out Throughout The Curriculum to One Lecture, and The 1968 American Indian Movement - One Lecture of Equivalent Amount.

Additionally, when asked whether they believed their school would benefit greatly from a specialized indigenous history course, all 4 unanimously answered yes. This paper will expand on additional insights about these findings in the discussions section.

DISCUSSION

Results and their Significance

What level of confidence American students have in indigenous history education

The study collected survey results to fulfill its purpose of discovering the average student's understanding of different events in indigenous history, how curriculum differs across schools, as well as the level of importance the American student populace places on indigenous history. The survey demonstrated that the average student's confidence in indigenous history curricula was average (6.28/10). As Figure 2 demonstrates, most respondents went into the survey with a relatively medium confidence level about their course's comprehension of indigenous history. However, the range of responses were from a 1 to a 9, indicating a large imbalance between different students. This could indicate that there is a large disparity across curricula between different school districts or education levels. Additionally this metric contrasts with an earlier figure where 52.4% reported that their curriculum only had a unit and 35.7% reported a couple of lessons on indigenous history. As such, Figure 2 demonstrates that students have relatively high confidence for limited subjects that they were taught, but were not able to extend beyond a few topics.

How does indigenous history education differ between topics and curricula

The results shown within Figure 4 further demonstrated LCC events such as The Ghost Dance Movement, Important Indigenous Figures, and the 1968 American Indian Movement were less covered in most curricula. This disparity is likely explained by the fact that these events are considered higher learning, and are not included or covered comprehensively in most Common Core history curricula (History-Social Science Framework). However, even events that the

majority seemed to be aware of (such as important indigenous figures which 73.8% of respondents indicated they had covered), LCC events also saw a significant decrease in the Likert Rating Scale Average Score. For the Ghost Dance Movement and the 1968 AIM Movement in particular, scores dropped from the 5-6 range down to a 3-4 range.

These findings are reinforced by the teacher interviews results, as on average, HCC topics are covered by one unit or one to three weeks of lectures and LCC topics are covered by one lecture or equivalent. As such, LCC topics are covered significantly less in most indigenous history curricula. Due to the less coverage of LCC topics, it is possible to infer that students' retention of these events are worse compared to HCC topics.

A reasonable explanation for this drop in Likert Score and coverage lies within the historical context of each event and the difference in education between common core and APUSH. As the literature review indicates, there is a significant difference in coverage between common core and APUSH curricula, which may also contribute to this drop. Furthermore, The Ghost Dance Movement lies heavily within the connotation of an American Tragedy — the Wounded Knee Massacre. With deep religious connotation, as well as the fear that most Americans had of a Native population that refused to disappear, The Ghost Dance Movement is not only a sensitive topic, but a convoluted one that requires students to learn from the perspective of the Lakota tribes involved. As assistant professor at Ohio State University, Hasan Kwame Jeffries, highlights "It is hard to comprehend the inhumanity that defined it... It is hard to teach the ideology of white supremacy that justified it." (Turner). While this statement was in reference to another American historical tragedy — the period of Slavery, this statement still applies towards indigenous history. The confidence in teachers and their ability to teach sensitive topics is low, as 47% of American adults state they do not trust public school teachers to teach such topics (Mahnken). As such, these topics may be generally avoided in curriculum due to teachers and school boards avoiding conflict with parents and the general public. Additionally, the movement faced direct opposition from the United States government at the time in the form of the Religious Crimes Code ("Religious Crimes Code 1983"). As an integral piece of one of the last armed resistances to U.S army advances, and one of the most widespread indigenous religions within the modern era, highschool curricula fail to encapsulate the movement and its significance on indigenous history. With a Likert Average Rating Score of 3.54, it is evident that even within the AP Curriculum, the Ghost Dance is not being taught sufficiently. Likewise the Important Figures (eg. Tecumseh and Wovoka) are undertaught due to their roles lying within such events. The following 1968 AIM Movement, one of the biggest and oldest Native American civil rights movements, addresses these events, such as with the occupation of Wounded Knee. This event is possibly still under taught as its effects have not been resolved to this day. Leonard Peltier, an AIM activist arrested and charged with assisting in murder, still lies in prison today (Messerschmidt).

What importance does the students and teachers place on education of indigenous history in schools

The survey also analyzes the student belief in the benefits of a specialized indigenous history course. As seen in Figure 4, 42.9% of respondents indicated that they did not believe their school would greatly benefit from a specialized indigenous history course. In contrast to other historical tragedies, such as slavery, almost 90 percent of 1,800 surveyed students agreed that "teaching and learning about slavery is essential to understanding American history," (Turner). The reason for this measurement, as seen in Figure 4, on students who believe their school would greatly benefit from a specialized indigenous history course is largely due to historical stereotypes and context. A commonly attributed factor to the decline of indigenous history and culture is the belief in the "vanishing red man" stereotypes (Edmunds et.al 718). This stems from the belief that due to their differing way of life, indigenous peoples were either destined to die out, or conform to western civilization. Additionally, modern textbooks mostly portray indigenous peoples as two stereotypes — the "good Indian" and the "bad Indian" (Hirschfelder et.al). This portrayal of indigenous peoples as a side-show to colonial history further perpetuates this dying race stereotype. This metric demonstrates that this stereotype is still prominent within today's students, and there has to be a greater significance placed on indigenous history and its values.

Comparing students survey results to the teacher interviews, the findings are consistent that HCC events had more focus placed on them and more comprehensive coverage compared to LCC events. However, one noticeable difference between the survey and teacher interviews lies in the finding that 100% of teachers believed their school would greatly benefit from a specialized indigenous history course. In particular, one teacher stated "every school would benefit from it, if not for a lack of interest from students or parents." Other teachers elaborated on this idea, stating "this subject is something that we pretty much ignored [in the past], so every school would go about benefiting from that." As such, there is a difference in the level of importance teachers place on indigenous history education when compared to highschool students. One reason that may contribute to this finding is that stereotypes are destigmatized as an individual learns more about a subject ("Reducing Stereotype Threat").

Fulfillment of Gaps in the Research

This research provides one more study on the availability on indigenous history to the average American high school student by serving a broader student body with diverse backgrounds. This research also provides a deeper and quantitative analysis of coverage on specific events by defining events into HCC and LCC categories, providing insights into the coverage of indigenous history education. This survey proves that there is a significant gap between these two categories, which also contributes to a difference of coverage between different curricula (such as standardized vs advanced). The research further addresses this gap through teacher interviews, finding results consistent with previous understanding on the coverage of different events. This paper sufficiently contrasts student and teacher opinion via a survey and interviews to discover the differences in the level of importance that different academic groups place on indigenous history education.

Conclusion

This paper sufficiently accomplishes the goal and answers research questions. Via a student questionnaire, this study establishes that students had an average confidence in the indigenous history education curricula, though they had a large range in responses (ranging from 1-9). The study confirms there is a gap in indigenous history education knowledge within the LCC category via the student survey and the teacher interviews. The survey and teacher interviews demonstrate a difference in viewpoint on the importance of indigenous history education, with all teachers emphasizing the benefits of a specialized course, while student opinion on the subject remains largely split. This research develops on the understanding that there exists a lack of representation of indigenous history in curricula for important subjects. While existing studies focused on a general lack of education, this study pinpoints areas in which curricula can focus on and improve.

Implications

The results of the survey and interviews demonstrate that history curricula, especially those non-advanced, require increased coverage of indigenous history. Furthermore, it highlights events that include tragedies or sensitive topics that require the most attention. This paper also reaffirms the need for indigenous history education as a means of ridding the next generation of generational and harmful stereotypes.

Limitations

One limitation of the survey was the cultural diversity of those involved. For example, 40% of individuals interviewed were Chinese-identifying. 64.3% of those surveyed self-identified as middle class. The findings indicate that both the Chinese community and the Middle Class may have been overrepresented in these findings. As schools in low socioeconomic standing do not receive as much funding, students attending these institutions have their education process hindered (Aikens & Barbarin). This indicates that the findings in these papers are not indicative and may vary across different socioeconomic ranges, and may differ depending on education funding in an area. Another limitation of this paper lies in the subjectivity of the grading scale that responders used to rate their understanding on certain subjects. Without sufficient context to the event, respondents may have underestimated/overestimated their comprehension on a subject. Additionally, respondents may have had different gauges on the values of different numbers on the Likert Scale, therefore introducing an uncertainty on the values of the average comprehension and coverage found in the results portion of this research.

A major limitation lies in the sample size of the teachers interviewed. Since only 4 teachers were considered in the interview portion of this research project, the results may not be comprehensive and represent opinions of other history professors or teachers. As all teachers interviewed were from California-based districts, the interviews also do not account for the differences in curricula between state borders. This geographical distinction also means that teacher data does not account for different curricula standards in different states.

Future Studies

Future studies should interview individuals with indigenous descent or living on Native reservations to better focus on the individuals impacted by these studies. Studies should be performed on curricula specifically within reservations, or in heavily indigenous-populated schools, to measure the extent of which education differs depending on ethnic representation. Additionally, another study can identify how many courses within different curricula cover NAS (Native American Studies) in their curricula. Researchers Mary Jo Tippeconnic Fox and John W. Tippeconnic III define Native American Studies (NAS) as a subject where “the Indian education experience from a Native perspective can be told in authentic and meaningful ways” (Fox and Tippeconnic III 31). Additionally, more studies covering the benefits of learning history from differing perspectives allows for more possibilities of diving deeper into this subject. Future studies may also extend to higher education, such as undergraduate to graduate history courses. To address limitations in data sampling, future studies can control the spread of respondents to vary based on ethnicity, wealth, and profession. Studies developing curricula or the impacts of specialized NSA/ indigenous history courses can also either validate or analyze the benefits/detrimental effects that such a course presents with student experiences. These studies can massively impact the landscape of indigenous education, representation, and racial equity for the next generations.

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The Implications of Targeting EpCAM (CD326) in Breast Cancer Treatment By Lina Elfadil Hamid* and Mohammad S. Hossain**

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Abstract

Epithelial cell adhesion molecule (EpCAM), or CD326, plays a crucial role in breast cancer and has recently become a focus for both researchers and clinicians. This paper explores how EpCAM influences breast cancer development, its potential as a diagnostic and prognostic marker, and its promise as a target for new treatments. Overexpressed in many breast cancers, EpCAM is linked to increased cell growth, metastasis, and traits like cancer stem cells, often leading to worse outcomes for patients. Moreover, EpCAM's expression on cancer cells but limited presence in normal tissues presents an attractive target for therapeutic interventions. Given these associations, targeting EpCAM could be a game-changer in breast cancer therapy. I review the latest research and approaches—including monoclonal antibodies, EpCAM-based vaccines, and T-cell therapies—discussing how they work, the results from clinical trials, and their effectiveness. I also delve into the challenges faced, such as overcoming resistance to these therapies and ensuring they specifically target cancer cells without affecting healthy ones. By integrating findings from molecular biology, clinical studies, and therapeutic development, this review aims to provide a comprehensive overview of EpCAM's role in breast cancer and its promise as a focal point in advancing treatment strategies.

Introduction

EpCAM (Epithelial Cell Adhesion Molecule, CD326) is a glycoprotein prominently expressed on the surface of epithelial cells, consisting of 314 amino acids with a structure integral to its function and role in oncogenesis. The protein includes an extracellular domain, a single transmembrane domain, and a short intracellular domain. The extracellular domain features two key regions initially identified as epidermal growth factor (EGF)-like domains; however, recent studies have indicated that the second region is, in fact, a thyroglobulin (TY)-like domain, capable of inhibiting cathepsins—proteases involved in tissue remodeling and metastasis. This inhibition potentially allows EpCAM to protect tumor cells from their own proteolytic environment, facilitating metastatic progression (Baeuerle and Gires 2007). The transmembrane domain anchors EpCAM to the cell membrane, which ensures stability and proper positioning for cell signaling and adhesion. The intracellular domain, with 26 amino acids, interacts with intracellular molecules, influencing pathways that regulate proliferation and differentiation.

EpCAM is overexpressed in various carcinomas, including breast cancer, and is associated with poor prognosis and malignancy. Functionally, EpCAM mediates cell-cell adhesion, which, in cancer, supports tumor cell proliferation and survival. By maintaining tight cell-cell contacts, EpCAM helps create a microenvironment conducive to tumor growth and protects cancer cells from detachment-induced cell death (*anoikis*) (Imrich, Hachmeister et al.

2012). This adhesion also facilitates the formation of multicellular tumor spheroids, which are known to be more resistant to chemotherapy (Stickler, Rath et al. 2023).

Its involvement in signaling pathways, such as the Wnt pathway, promotes cell cycle progression and oncogenic transformation. EpCAM can act as a signaling molecule that activates the Wnt/β-catenin pathway, leading to increased transcription of the genes involved in cell proliferation and survival (Munz, Baeuerle et al. 2009). This pathway is exceptionally significant when considering cancer stem cells (CSCs), where EpCAM is a marker associated with self-renewal and tumorigenicity. CSCs are a subpopulation of cancer cells that can self-renew and differentiate, driving tumor growth and recurrence. By supporting CSC properties, EpCAM contributes to tumor heterogeneity and resistance to conventional therapies (Gires, Klein et al. 2009).

Aberrant glycosylation of EpCAM in tumor cells enhances invasive properties and immune evasion, affecting its stability, localization, and function. In cancer, abnormal glycosylation patterns can amplify the adhesive properties of EpCAM, promoting cell migration and invasion. This modification can also mask epitopes recognized by the immune system, allowing cancer cells to evade immune surveillance. Moreover, the altered glycosylation can facilitate interactions with other cell surface molecules and the extracellular matrix, further supporting metastatic dissemination (Barkeer, Chugh et al. 2018).

Given its role in CSC maintenance and therapeutic resistance, EpCAM is crucial for understanding breast cancer progression. The structural and functional attributes of EpCAM play a pivotal role in carcinogenesis, making it a critical focus for understanding the mechanisms of tumor growth and metastasis. EpCAM's multifaceted functions in cell adhesion, signaling, and immune evasion collectively enhance the malignant potential of cancer cells, contributing to the complexity and aggressiveness of breast cancer (Liu, Wang et al. 2022).

EpCAM Monoclonal Antibodies as Potential Immunotherapy Effective Against Several Types of Breast Cancer

The use of monoclonal antibodies to target EpCAM is emerging as a promising immunotherapy method to target breast cancer, including ductal carcinoma, lobular carcinoma, and triple-negative breast cancer. These antibodies specifically bind to EpCAM, which is overexpressed in many types of breast cancer, disrupting its cell adhesion, proliferation, and signaling functions, making the cancer cells more prone to apoptosis (Kaneko, Ohishi et al. 2020). In addition, monoclonal antibodies can trigger immune responses through mechanisms like Antibody-Dependent Cellular Toxicity (ADCC) and Complement-Dependent Cytotoxicity (CDC), in which immune cells are recruited to attack the flagged cancer cells. A notable example of this is Catumaxomab, which recruits T-cells and accessory cells to the tumor site, or MT110 (Solitomab), a bispecific T-cell engager (BiTE) which directs T-cells to cancer cells that express EpCAM, demonstrating significant antitumor activity (Hubert and Amigorena 2012). Due to EpCAM's function as a marker for cancer stem cells, antibodies can target them and reduce the risk of relapse, improving long-term outcomes. The specificity of monoclonal antibodies to

EpCAM minimizes unwanted damage to healthy tissue and allows for combination with other cancer therapies to enhance efficiency (Macdonald, Henri et al. 2018).

Ductal Carcinoma, including Ductal Carcinoma In Situ (DCIS) and Invasive Ductal Carcinoma (IDC), is the most common type of breast cancer, accounting for over 80% of all breast cancer diagnoses (Kerlikowske 2010). EpCAM targeting is particularly effective in this type of cancer for multiple reasons. Many ductal carcinomas exhibit abnormally elevated levels of EpCAM expression compared to other types of cancer, most likely due to the crucial role it plays in cell adhesion within the ducts. Monoclonal antibodies targeting EpCAM disrupt this adhesion, breaking down the tumor's structural integrity and making the cells more vulnerable to other treatments. This disruption also prevents metastasis by reducing the risk of tumor cells detaching and spreading to other areas of the body, a primary concern with invasive ductal carcinoma (Gires, Klein et al. 2009).

Invasive Lobular Carcinoma (ILC) is the second most common type of breast cancer. It often presents unique challenges due to its diffuse growth pattern. ILC cells tend to spread in a single-file pattern which makes them difficult to detect and treat. However, EpCAM can specifically bind to the cells regardless of their spread pattern, allowing for faster and more accurate treatment (Mouabbi 2024). EpCAM targeting can also be used in combination with other treatments, such as hormone therapy, to enhance the overall therapeutic effect. This is especially important for ILC, which often responds well to hormone-based treatments.

Triple-negative breast cancer (TNBC) is exceedingly difficult to treat with conventional therapies due to its lack of estrogen receptors, progesterone receptors, and excess HER2 protein. EpCAM-targeted therapies offer a novel mechanism that can be effective against these resistant cancer cells. Monoclonal antibodies targeting EpCAM can induce direct cell killing by recruiting immune cells. Through Antibody-Dependent Cellular Cytotoxicity, natural killer (NK) cells recognize the antibodies bound to EpCAM and release cytotoxic substances to kill the cancer cells. Similarly, Complement-Dependent Cytotoxicity occurs when the binding of monoclonal antibodies to EpCAM activates the complement system, leading to the formation of membrane attack complexes that lyse and kill cancer cells (Hosono, Ohishi et al. 2020). Since TNBC is often treated with chemotherapy, adding EpCAM-targeting agents can provide a synergistic effect which improves the overall response to treatment.

EpCAM-Based Vaccines Against Breast Cancer

The use of EpCAM-based vaccines is an emerging strategy in breast cancer treatment, aiming to harness the immune system to target and eliminate cancer cells that express EpCAM. These vaccines are engineered to provoke a specific immune response against tumor cells, which could potentially offer both therapeutic and preventive benefits. Various approaches to developing EpCAM-based vaccines include peptide vaccines, which use short fragments of the EpCAM protein; protein vaccines that incorporate larger portions of the protein; DNA/RNA vaccines that use genetic material to induce cells to produce the EpCAM antigen; and dendritic

cell (DC) vaccines, which employ antigen-presenting cells to initiate a targeted immune response (Choi, Park et al. 2018).

The mechanisms by which EpCAM-based vaccines operate involve the activation of different components of the immune system. These vaccines aim to stimulate cytotoxic T-cells (CTLs), which are adept at recognizing and killing cancer cells presenting EpCAM-derived antigens. Dendritic cells play a crucial role in this process by presenting these antigens to CTLs, thereby initiating the immune attack. Additionally, the vaccines enhance the activity of helper T-cells (Th cells), which boost the overall immune response by activating both CTLs and B-cells. The activation of B-cells leads to the production of antibodies against EpCAM, which bind to the cancer cells and mark them for destruction by other immune cells like natural killer (NK) cells and macrophages (Mellman 2013). A significant advantage of these vaccines is their potential to create long-lasting immune memory, ensuring that the immune system remains vigilant against cancer recurrence.

EpCAM-based vaccines hold significant promise in treating various subtypes of breast cancer. They are particularly beneficial for targeting cancer stem cells (CSCs), a subset of cells within tumors responsible for initiating and sustaining cancer growth and recurrence. By targeting EpCAM, these vaccines can effectively reduce the CSC population, potentially decreasing the likelihood of relapse and improving long-term survival rates (Gires, Klein et al. 2009). Furthermore, EpCAM-based vaccines can be integrated with existing therapies such as chemotherapy and radiation, enhancing the overall treatment efficacy through a multifaceted approach. Another promising application is in prophylactic settings for individuals at substantial risk of developing breast cancer, such as those with genetic predispositions. Vaccination could prime the immune system to recognize and eliminate EpCAM-expressing cells early, preventing tumor development. Unlike monoclonal antibodies, which require repeated administration and do not induce immune memory, EpCAM-based vaccines aim to provide a prolonged and durable response, reducing the frequency of treatments needed and maintaining ongoing protection against cancer recurrence (Chaudry, Sales et al. 2007).

EpCAM Enhances T-cell Mediated Immune Response to Eradicate Breast Cancer Cells

EpCAM (Epithelial Cell Adhesion Molecule, CD326) plays a crucial role in enhancing the T-cell mediated immune response against breast cancer cells. This glycoprotein, prominently expressed on the surface of many epithelial cancers, serves as a potent target for T-cell-based immunotherapies. EpCAM-specific targeting strategies, including the use of EpCAM-based vaccines and bispecific T-cell engagers (BiTEs), leverage the immune system's cytotoxic T lymphocytes (CTLs) to recognize and destroy cancer cells. EpCAM-based vaccines introduce EpCAM-derived antigens to the immune system, prompting antigen-presenting cells, such as dendritic cells, to process and present these antigens on their surface (Macdonald, Henri et al. 2018). This antigen presentation activates CTLs, which are then primed to identify and kill EpCAM-expressing breast cancer cells. Furthermore, bispecific T-cell engagers like MT110 (Solitomab) simultaneously bind to EpCAM on cancer cells and CD3 on T-cells, physically

bringing T-cells into close proximity with the cancer cells and facilitating targeted cell killing (Haas, Krinner et al. 2009). This interaction not only enhances the direct cytotoxic activity of T-cells but also induces the release of cytokines, amplifying the overall immune response. By harnessing the body's own immune system, EpCAM targeting effectively directs T-cells to eliminate breast cancer cells, offering a promising therapeutic approach to improve treatment outcomes and reduce recurrence rates in patients with breast cancer.

Detection of EpCAM as a Diagnostic and Prognostic Biomarker

The utilization of EpCAM (Epithelial Cell Adhesion Molecule, CD326) as a diagnostic marker in breast cancer offers significant promise due to its elevated expression in epithelial-derived tumors compared to normal tissues. This differential expression makes EpCAM a valuable biomarker for identifying cancerous cells, particularly in early-stage disease. Diagnostic tests leveraging EpCAM can detect circulating tumor cells (CTCs) in the blood, which is crucial for early diagnosis, monitoring disease progression, and evaluating treatment efficacy (Hiraga, Ito et al. 2016). Techniques such as immunohistochemistry (IHC), flow cytometry, and PCR-based assays capitalize on EpCAM's presence to accurately identify and quantify CTCs. This facilitates a less invasive diagnostic approach, allowing for real-time tracking of tumor dynamics. Moreover, EpCAM's expression correlates with tumor aggressiveness and poor prognosis, providing valuable prognostic information. By integrating EpCAM detection into routine diagnostic protocols, clinicians can achieve more precise and timely interventions, tailor treatment strategies to individual patient profiles, and potentially improve overall survival rates (Awasthi, Kumari et al. 2017).

In breast cancer specifically, EpCAM serves as a critical marker due to its overexpression in most breast carcinoma cells. This overexpression is particularly notable in ductal carcinoma, which accounts for many breast cancer cases. Detecting EpCAM in breast tissue biopsies helps pathologists differentiate between benign and malignant lesions, thereby aiding in accurate diagnosis (Gostner, Fong et al. 2011). Additionally, the presence of EpCAM in breast cancer cells can help distinguish between different subtypes, such as ductal and lobular carcinomas, which is crucial for determining the most effective treatment approach. For instance, higher EpCAM levels are often associated with more aggressive forms of breast cancer, which might necessitate more intensive therapeutic interventions (Soysal, Muenst et al. 2013).

Furthermore, EpCAM's role as a marker for cancer stem cells (CSCs) in breast cancer adds another layer of diagnostic utility. Identifying CSCs within a tumor through EpCAM expression can help predict the likelihood of recurrence and metastasis, guiding decisions on the intensity and type of adjuvant therapy required (Osta, Chen et al. 2004). The ability to monitor CSC populations via EpCAM expression can also inform the effectiveness of ongoing treatments, allowing for timely adjustments to therapeutic strategies to better combat the disease (Mohtar, Syafruddin et al. 2020).

The integration of EpCAM into liquid biopsy platforms represents a significant leap forward in breast cancer diagnostics. Liquid biopsies, which analyze CTCs, cell-free DNA

(cfDNA), and exosomes from blood samples, offer a non-invasive alternative to traditional biopsies. EpCAM-based capture and analysis of CTCs from liquid biopsies can provide a dynamic picture of tumor evolution and treatment response over time. This real-time monitoring capability is essential for adapting treatment plans quickly to counteract resistance mechanisms and disease progression. By enabling frequent and less invasive assessments, liquid biopsies enhance patient comfort and compliance, contributing to better overall management of breast cancer (Ring, Mineyev et al. 2015).

Current and Future Challenges for Overcoming Resistance Related to EpCAM Mediated Breast Cancer Immunotherapy

Despite the promising potential of EpCAM-mediated immunotherapy in treating breast cancer, several challenges remain in overcoming resistance and improving treatment efficacy. One of the primary obstacles is the heterogeneity of EpCAM expression among different tumor cells and even within the same tumor. This variability can lead to incomplete targeting and survival of EpCAM-negative cancer cells, which contributes to disease relapse and progression. Additionally, tumor cells can develop adaptive resistance mechanisms, such as downregulating EpCAM expression or altering glycosylation patterns to evade immune recognition. These adaptive responses can diminish the effectiveness of EpCAM-targeted therapies over time (Mal, Bukhari et al. 2020).

Another significant challenge is the immunosuppressive tumor microenvironment, which can inhibit the activity of cytotoxic T lymphocytes (CTLs) and other immune effector cells. Factors such as regulatory T cells (Tregs), myeloid-derived suppressor cells (MDSCs), and inhibitory cytokines like TGF- β and IL-10 can create a hostile environment for immune-mediated tumor eradication. The tumor microenvironment often promotes the expression of immune checkpoint molecules, such as PD-L1, which interact with PD-1 receptors on T-cells, leading to their functional exhaustion and reduced anti-tumor activity. This immunosuppressive milieu presents a significant barrier to the success of EpCAM-targeted immunotherapies (Takeuchi and Nishikawa 2016).

Moreover, the development of antigen loss variants, where cancer cells mutate or lose EpCAM expression, further complicates the efficacy of immunotherapies. These antigen loss variants can arise under selective pressure from immune attacks, leading to the outgrowth of tumor cell populations that are no longer recognized by the immune system. This phenomenon necessitates the exploration of strategies that can target multiple antigens or pathways simultaneously to prevent tumor escape (Yang, McCloskey et al. 2021).

To address these issues, future strategies may involve combination therapies that include immune checkpoint inhibitors, cytokine therapy, or other agents that modulate the tumor microenvironment to enhance T-cell activity and sustain immune pressure on the tumor. For example, combining EpCAM-targeted therapies with PD-1/PD-L1 inhibitors could potentially overcome T-cell exhaustion and restore robust anti-tumor immune responses. Additionally,

incorporating agents that deplete Tregs or MDSCs, or that block their suppressive functions, could further enhance the efficacy of EpCAM-targeted treatments (Chen, Liang et al. 2020).

Advances in personalized medicine, such as identifying and targeting patient-specific mutations and leveraging next-generation sequencing, could also help tailor EpCAM-targeted treatments to individual patients' tumor profiles, reducing the likelihood of resistance. Personalized approaches might include developing patient-specific vaccines that incorporate a broader array of tumor antigens, thereby minimizing the risk of antigen-loss variants. Furthermore, the integration of bioinformatics and machine learning could improve the prediction of resistance mechanisms and guide the design of more effective combination therapies.

Emerging technologies, such as CRISPR/Cas9 gene editing, could also play a role in overcoming resistance by enabling precise modifications of tumor cells or the immune system to enhance therapeutic efficacy. For instance, gene editing could be used to enhance the expression of co-stimulatory molecules on T-cells or to knock out inhibitory pathways that limit T-cell function.

Overcoming these challenges requires a multifaceted approach that integrates our growing understanding of tumor biology, immunology, and therapeutic innovations to enhance the long-term success of EpCAM-mediated breast cancer immunotherapy. Collaborative efforts across research disciplines, clinical trials, and technological advancements will be essential in developing more effective and durable treatments for breast cancer patients facing resistance to current immunotherapies.

Conclusion

In summary, EpCAM (CD326) is a pivotal glycoprotein in the context of breast cancer, with its overexpression linked to increased tumor growth, metastasis, and poor patient outcomes. Its role as a diagnostic and prognostic marker highlights its importance in cancer biology. Therapeutic strategies targeting EpCAM, including monoclonal antibodies and EpCAM-based vaccines, have shown promise in disrupting cancer cell functions and enhancing immune-mediated destruction. These approaches leverage the specificity of immune responses to improve treatment efficacy and reduce recurrence rates. However, challenges such as tumor heterogeneity, adaptive resistance, and the immunosuppressive tumor microenvironment necessitate ongoing research and the development of combination therapies and personalized medicine strategies. By advancing our understanding and application of EpCAM-targeted therapies, we can enhance breast cancer treatment outcomes and provide new hope for patients.

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Awasthi, N. P., et al. (2017). "EpCAM-based Flow Cytometric Detection of Circulating Tumor Cells in Gallbladder Carcinoma Cases." Asian Pac J Cancer Prev **18**(12): 3429-3437.

Purpose: Liquid biopsy has entered the arena of cancer diagnostics in the past decade and detection of circulating tumor cells (CTC) is one diagnostic component. CTCs in gallbladder cancer (GBC) have hitherto not been comprehensively analysed. **Methods and Results:** The current study focused on the diagnostic role of CTCs in 27 cases of treatment-naïve GBC and 6 normal controls as well as 6 cases of cholecystitis. An EasySep kit featuring negative immunomagnetic bead separation and flow cytometric detection of EpCAM positive and CD45 negative cells revealed CTCs in 25 of the 27 cases. At a cut-off point of ≥ 1 , the CTC count discriminated GBC from controls with a sensitivity, specificity and diagnostic accuracy of 92.6%, 91.7% and 92.3%, respectively. CTC levels in turn correlated significantly with clinico-pathological parameters of cases in terms of known prognostic indicators, with significant diagnostic potential at a cut-off point of >4 , to discriminate disease stage I and II vs. III and IV GBC. With a cut-off of >3 , the CTC count discriminated tumor stages I and II vs. III and IV and at >6 CTCs could discriminate metastatic vs. non metastatic GBCs with a sensitivity, specificity and diagnostic accuracy of 55.6%, 100.0% and 85.2, respectively. A review of CTC in pancreatico-biliary malignancies is included. **Conclusion:** Detection and quantification of CTCs may serve as a non-invasive biomarker for GBC diagnosis in correlation with radiological studies.

Baeuerle, P. A. and O. Gires (2007). "EpCAM (CD326) finding its role in cancer." British Journal of Cancer **96**(3): 417-423.

Barkeer, S., et al. (2018). "Glycosylation of Cancer Stem Cells: Function in Stemness, Tumorigenesis, and Metastasis." Neoplasia **20**(8): 813-825.

Chaudry, M. A., et al. (2007). "EpCAM an immunotherapeutic target for gastrointestinal malignancy: current experience and future challenges." British Journal of Cancer **96**(7): 1013-1019.

Chen, H.-N., et al. (2020). "EpCAM Signaling Promotes Tumor Progression and Protein Stability of PD-L1 through the EGFR Pathway." Cancer Research **80**(22): 5035-5050. Although epithelial cell adhesion molecule (EpCAM) has previously been shown to promote tumor progression, the underlying mechanisms remain largely unknown. Here, we report that the EGF-like domain I within the extracellular domain of EpCAM (EpEX) binds EGFR, activating both AKT and MAPK signaling to inhibit forkhead transcription factor O3a (FOXO3a) function and stabilize PD-L1 protein, respectively. Treatment with the EpCAM neutralizing antibody, EpAb2-6, inhibited AKT and FOXO3a phosphorylation, increased FOXO3a nuclear translocation, and upregulated high temperature requirement A2 (HtrA2) expression to promote apoptosis while decreasing PD-L1 protein levels to enhance the cytotoxic activity of CD8+ T cells. In vivo, EpAb2-6 markedly extended survival in mouse metastasis and orthotopic models of human colorectal cancer. The combination of EpAb2-6 with atezolizumab, an anti-PD-L1 antibody, almost completely eliminated tumors. Moreover, the number of CD8+ T cells in combination-treated tumors was increased compared with atezolizumab alone. Our findings suggest a new combination strategy for cancer immunotherapy in patients with EpCAM-expressing tumors. This study shows that treatment with an EpCAM neutralizing antibody promotes apoptosis while decreasing PD-L1 protein to enhance cytotoxic activity of CD8+ T cells.

Choi, Y. J., et al. (2018). "EpCAM peptide-primed dendritic cell vaccination confers significant anti-tumor immunity in hepatocellular carcinoma cells." PLOS ONE **13**(1): e0190638.

Gires, O., et al. (2009). "On the abundance of EpCAM on cancer stem cells." Nature Reviews Cancer **9**(2): 143-143.

Gostner, J. M., et al. (2011). "Effects of EpCAM overexpression on human breast cancer cell lines." BMC Cancer **11**(1): 45.

Recently, EpCAM has attracted major interest as a target for antibody- and vaccine-based cancer immunotherapies. In breast cancer, the EpCAM antigen is overexpressed in 30-40% of all cases and this increased expression correlates with poor prognosis. The use of EpCAM-specific monoclonal antibodies is a promising treatment approach in these patients.

Haas, C., et al. (2009). "Mode of cytotoxic action of T cell-engaging BiTE antibody MT110." *Immunobiology* **214**: 441-453.

Hiraga, T., et al. (2016). "EpCAM expression in breast cancer cells is associated with enhanced bone metastasis formation." *Int J Cancer* **138**(7): 1698-1708.

Epithelial cell adhesion molecule (EpCAM) has been implicated in multiple cellular functions including cell adhesion. EpCAM has also recently been identified as a marker for cancer stem cells (CSCs). Here, we examined the roles of EpCAM in the development of bone metastasis of breast cancer by using well-characterized animal models. Morphological and real-time reverse transcriptase-polymerase chain reaction data showed that the EpCAM-negative and -positive (EpCAM(neg) and EpCAM(pos)) cell populations isolated from breast cancer cell lines exhibited mesenchymal and epithelial phenotypes, respectively. Flow cytometric analysis revealed that EpCAM(pos), but not EpCAM(neg), cells possessed self-renewal and differentiation potentials. Tumorsphere formation in suspension cultures and tumorigenicity in the orthotopic mammary fat pad of mice were significantly greater in EpCAM(pos) cells than in EpCAM(neg) cells. The development of bone metastases induced by an intracardiac injection was markedly increased in mice inoculated with EpCAM(pos) cells. Furthermore, intracardiac inoculations of parental cells demonstrated that the EpCAM(pos) population in cancer cells that colonized in bone was significantly higher than that in parental cells. However, stable transduction of EpCAM into EpCAM(neg) cells failed to reproduce the phenotypes of EpCAM(pos) cells. These results suggest that the expression of EpCAM in breast cancer cells is associated with CSC-like phenotypes, which contribute to the promotion of bone metastases by enhancing tumorigenicity. Our results also support the possibility that the epithelial phenotypes of EpCAM-expressing cells confer advantageous properties for the development of bone metastases, at least after entering the circulation, while EpCAM is likely not solely responsible for the phenotypes of EpCAM(pos) cells.

Hosono, H., et al. (2020). "The anti-epithelial cell adhesion molecule (EpCAM) monoclonal antibody EpMab-16 exerts antitumor activity in a mouse model of colorectal adenocarcinoma." *Oncology Letters* **20**(6): 1-1.

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Liu, Y., et al. (2022). "Understanding the versatile roles and applications of EpCAM in cancers: from bench to bedside." *Experimental Hematology & Oncology* **11**(1).

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Mal, A., et al. (2020). "EpCAM-Mediated Cellular Plasticity Promotes Radiation Resistance and Metastasis in Breast Cancer." *Front Cell Dev Biol* **8**: 597673.

Substantial number of breast cancer (BC) patients undergoing radiation therapy (RT) develop local recurrence over time. During RT therapy, cells can gradually acquire resistance implying adaptive radioresistance. Here we probe the mechanisms underlying this acquired resistance by first establishing radioresistant lines using ZR-75-1 and MCF-7 BC cells through repeated exposure to sub-lethal fractionated dose of 2Gy up to 15 fractions. Radioresistance was found to be associated with increased cancer stem cells (CSCs), and elevated EpCAM expression in the cell population. A retrospective analysis of TCGA dataset indicated positive correlation of high EpCAM expression with poor response to RT. Intriguingly, elevated EpCAM expression in the radioresistant CSCs raise the bigger question of how this biomarker expression contributes during radiation treatment in BC. Thereafter, we establish EpCAM overexpressing ZR-75-1 cells (ZR-75-1(EpCAM)), which conferred radioresistance, increased stemness through enhanced AKT activation and induced a hybrid epithelial/mesenchymal phenotype with enhanced contractility and invasiveness. In line with these observations, orthotopic implantation of ZR-75-1(EpCAM) cells exhibited faster growth, lesser sensitivity to radiation therapy and increased lung metastasis than baseline ZR-75-1 cells in mice. In summary, this study shows that similar to radioresistant BC cells, EpCAM overexpressing cells show high degree of plasticity and heterogeneity which ultimately induces radioresistant and metastatic behavior of cancer cells, thus aggravating the disease condition.

Mellman, I. (2013). "Dendritic Cells: Master Regulators of the Immune Response." Cancer Immunology Research **1**(3): 145-149.

Mohtar, M. A., et al. (2020). "Revisiting the Roles of Pro-Metastatic EpCAM in Cancer." Biomolecules **10**(2).

Epithelial cell adhesion molecule (EpCAM) is a cell surface protein that was discovered as a tumour marker of epithelial origins nearly four decades ago. EpCAM is expressed at basal levels in the basolateral membrane of normal epithelial cells. However, EpCAM expression is upregulated in solid epithelial cancers and stem cells. EpCAM can also be found in disseminated tumour cells and circulating tumour cells. Various OMICs studies have demonstrated that EpCAM plays roles in several key biological processes such as cell adhesion, migration, proliferation and differentiation. Additionally, EpCAM can be detected in the bodily fluid of cancer patients suggesting that EpCAM is a pathophysiological relevant anti-tumour target as well as being utilized as a diagnostic/prognostic agent for a variety of cancers. This review will focus on the structure-features of EpCAM protein and discuss recent evidence on the pathological and physiological roles of EpCAM in modulating cell adhesion and signalling pathways in cancers as well as deliberating the clinical implication of EpCAM as a therapeutic target.

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Osta, W. A., et al. (2004). "EpCAM is overexpressed in breast cancer and is a potential target for breast cancer gene therapy." Cancer Res **64**(16): 5818-5824.

EpCAM (epithelial cell adhesion molecule) is a cell surface molecule that is known to be highly expressed in colon and other epithelial carcinomas. EpCAM is involved in cell-to-cell adhesion and has been the target of antibody therapy in several clinical trials. To assess the value of EpCAM as a novel target for breast cancer gene therapy, we performed real-time reverse transcription-PCR to quantify the level of EpCAM mRNA expression in normal breast tissue and primary and metastatic breast cancers. We found that EpCAM is overexpressed 100- to 1000-fold in primary and metastatic breast cancer. Silencing EpCAM gene expression with EpCAM short interfering RNA (siRNA) resulted in a 35-80% decrease in the rate of cell proliferation in four different breast cancer cell lines. EpCAM siRNA treatment decreased cell migration by 91.8% and cell invasion by 96.4% in the breast cancer cell line MDA-MB-231 in vitro. EpCAM siRNA treatment was also associated with an increase in the detergent-insoluble protein fraction of E-cadherin, alpha-catenin, and beta-catenin, consistent with the known biology of EpCAM as a regulator of cell adhesion. Our hypothesis is that modulation of EpCAM expression can affect cell migration, invasion, and proliferation by enhancing E-cadherin-mediated cell-to-cell adhesion. These data provide compelling evidence that EpCAM is a potential novel target for breast cancer gene therapy and offer insights into the mechanisms associated with EpCAM gene silencing.

Ring, A., et al. (2015). "EpCAM based capture detects and recovers circulating tumor cells from all subtypes of breast cancer except claudin-low." Oncotarget **6**(42): 44623-44634.

Purpose: The potential utility of circulating tumor cells (CTCs) as liquid biopsies is of great interest. We hypothesized that CTC capture using EpCAM based gating is feasible for most breast cancer subtypes. **RESULTS:** Cancer cells could be recovered from all intrinsic subtypes of breast cancer with IE/FACS, however, claudin-low cell lines showed very low capture rates compared to the four other groups ($p = 0.03$). IE/FACS detection of CTC mimic cells was time sensitive, emphasizing controlling for pre-analytic variables in CTC studies. Median fluorescent intensity for flow cytometry and RNA flow cell type characterization were highly correlated, predicting for CTC isolation across molecular subtypes. RNA-Seq of IE/FACS sorted single cell equivalents showed high correlation compared to bulk cell lines, and distinct gene expression signatures compared to PB. **MATERIALS AND METHODS:** Ten cell lines representing all major subtypes of breast cancer were spiked (as CTC mimics) into and recovered from peripheral blood (PB) using immunomagnetic enrichment followed by fluorescence-activated cell sorting (IE/FACS). Flow cytometry and RNA flow were used to quantify the expression of multiple breast cancer related markers of interest. Two different RNA-Seq technologies were used to analyze global gene expression of recovered sorted cells compared to bulk cell lines and PB. **CONCLUSIONS:** EpCAM based IE/FACS detected and captured a portion of spiked cells from each of the 10 cell lines representing all breast cancer subtypes, including basal-like but not claudin-low cancers. The assay allows for the isolation of high quality RNA suitable for accurate RNA-Seq of heterogeneous rare cell populations.

Soysal, S. D., et al. (2013). "EpCAM expression varies significantly and is differentially associated with prognosis in the luminal B HER2(+), basal-like, and HER2 intrinsic subtypes of breast cancer." Br J Cancer **108**(7): 1480-1487.

BACKGROUND: Epithelial cell adhesion molecule (EpCAM) is frequently expressed in breast cancer, and its expression has been associated with poor prognosis. Breast cancer can be subdivided into intrinsic subtypes, differing in prognosis and response to therapy. **METHODS:** To investigate the association between EpCAM expression and prognosis in the intrinsic subtypes of breast cancer, we performed immunohistochemical studies on a tissue microarray encompassing a total of 1365 breast cancers with detailed clinicopathological annotation and outcomes data. **RESULTS:** We observed EpCAM expression in 660 out of 1365 (48%) cases. EpCAM expression varied significantly in the different intrinsic subtypes. In univariate analyses of all cases, EpCAM expression was associated with a significantly worse overall survival. In the intrinsic subtypes, EpCAM expression was associated with an unfavourable prognosis in the basal-like and luminal B HER2(+) subtypes but associated with a favourable prognosis in the HER2 subtype. Consistently, specific ablation of EpCAM resulted in increased cell viability in the breast cancer cell line SKBR3 (ER(-), PR(-), and HER2(+)) but decreased viability in the breast cancer cell line MDA-MB-231 (ER(-), PR(-), and HER2(-)). **CONCLUSION:** The differential association of EpCAM expression with prognosis in intrinsic subtypes has important implications for the development of EpCAM-targeted therapies in breast cancer.

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Takeuchi, Y. and H. Nishikawa (2016). "Roles of regulatory T cells in cancer immunity." *Int Immunol* **28**(8): 401-409.

CD4(+) regulatory T cells (Tregs) expressing the transcription factor FoxP3 are highly immune suppressive and play central roles in the maintenance of self-tolerance and immune homeostasis, yet in malignant tumors they promote tumor progression by suppressing effective antitumor immunity. Indeed, higher infiltration by Tregs is observed in tumor tissues, and their depletion augments antitumor immune responses in animal models. Additionally, increased numbers of Tregs and, in particular, decreased ratios of CD8(+) T cells to Tregs among tumor-infiltrating lymphocytes are correlated with poor prognosis in various types of human cancers. The recent success of cancer immunotherapy represented by immune checkpoint blockade has provided a new insight in cancer treatment, yet more than half of the treated patients did not experience clinical benefits. Identifying biomarkers that predict clinical responses and developing novel immunotherapies are therefore urgently required. Cancer patients whose tumors contain a large number of neoantigens stemming from gene mutations, which have not been previously recognized by the immune system, provoke strong antitumor T-cell responses associated with clinical responses following immune checkpoint blockade, depending on the resistance to Treg-mediated suppression. Thus, integration of a strategy restricting Treg-mediated immune suppression may expand the therapeutic spectrum of cancer immunotherapy towards patients with a lower number of neoantigens. In this review, we address the current understanding of Treg-mediated immune suppressive mechanisms in cancer, the involvement of Tregs in cancer immunotherapy, and strategies for effective and tolerable Treg-targeted therapy.

Yang, Y., et al. (2021). "Bispecific CAR T Cells against EpCAM and Inducible ICAM-1 Overcome Antigen Heterogeneity and Generate Superior Antitumor Responses." *Cancer Immunol Res* **9**(10): 1158-1174.

Adoptive transfer of chimeric antigen receptor (CAR) T cells has demonstrated unparalleled responses in hematologic cancers, yet antigen escape and tumor relapse occur frequently. CAR T-cell therapy for patients with solid tumors faces even greater challenges due to the immunosuppressive tumor environment and antigen heterogeneity. Here, we developed a bispecific CAR to simultaneously target epithelial cell adhesion molecule (EpCAM) and intercellular adhesion molecule 1 (ICAM-1) to overcome antigen escape and to improve the durability of tumor responses. ICAM-1 is an adhesion molecule inducible by inflammatory cytokines and elevated in many types of tumors. Our study demonstrates superior efficacy of bispecific CAR T cells compared with CAR T cells targeting a single primary antigen. Bispecific CAR T achieved more durable antitumor responses in tumor models with either homogenous or heterogeneous expression of EpCAM. We also showed that the activation of CAR T cells against EpCAM in tumors led to upregulation of ICAM-1, which rendered tumors more susceptible to ICAM-1 targeting by bispecific CAR T cells. Our strategy of additional targeting of ICAM-1 may have broad applications in augmenting the activity of CAR T cells against primary tumor antigens that are prone to antigen loss or downregulation.

**Evaluating the Potential of Decentralized Finance to Address Financial Challenges,
through Machine Learning tools, in Areas with Limited Access to Banking Services
Post-COVID-19 By Tarush Garg**

1 Research Question

To what extent can Decentralized Finance (DeFi) solve the challenges faced by residents in areas with limited access to financial and banking services post-COVID-19?

2 Abstract

The financial sector has undergone a radical transformation as the COVID-19 crisis unfolded, and today many of the world's most economically distressed rural and underserved urban areas are being cut out from traditional banking services. This paper analyzes the prospect of Decentralized Finance (DeFi) in alleviating financial stress and addressing banking issues for residents living far from ATMs, cashpoints post COVID-19 pandemic via this research paper. COVID-19 has severely exacerbated financial exclusion in rural and underserved urban areas. DeFi — using blockchain technology is a new paradigm that provides decentralized banking. This paper will see if DeFi can help solve the problem of financial exclusion by reviewing the benefits, opportunities, risks, and regulatory challenges. A surge in DeFi adoption can be seen with users increasing from 3,000 to over 1 million between 2018 and 2020, and the total value locked in DeFi protocols reaching approximately \$70 billion in 2022(Ozili). The paper draws on a comprehensive analysis of existing data on DeFi adoption and its impact on financial inclusion. The research method involves using machine learning models such as Linear Regression, K-Nearest Neighbors (KNN), Support Vector Regressor to model their relation with DeFi adoption and financial inclusion. The results provide insights into the viability of DeFi as a solution for financial exclusion and offer recommendations for policymakers and stakeholders on harnessing DeFi's potential while mitigating its risks.

Keywords Decentralized Finance (DeFi), Financial exclusion, COVID-19 pandemic, Rural areas, Blockchain technology, Financial services, Financial inclusion, Machine learning models, Linear Regression, K-Nearest Neighbors, Support Vector Regressor, DeFi adoption, Financial challenges, Regulatory challenges, Policymakers, Stakeholders.

3 Introduction

Decentralized Finance is a revolutionary technology that has the potential to reshape the financial landscape by making financial services accessible to everyone regardless of their location or economic status. The COVID-19 crisis exposed the weaknesses of traditional banking systems, exacerbating access to financial services by citizens in remote and poorly developed urban areas. Using the blockchain technology allows it to offer a variety of decentralized financial services like lending, borrowing, and investing without any interference. This paper investigates the ability of DeFi to offer as a financial solution for unbanked populations in

regions that lack proper banking access after COVID-19. With the issue of financial exclusion burned into sharp relief by the pandemic and new urgent need for innovative solutions, getting good research on this question is more critical than ever. The research on the question is critical in the current context, where financial exclusion has been exacerbated by the pandemic, and innovative solutions are urgently needed. The study focuses on understanding how DeFi could reduce financial exclusion by providing an inclusive, efficient, and transparent alternative to conventional banking. Recent studies highlight the transformative potential of DeFi, suggesting it could play a crucial role in democratizing access to financial resources. The hypothesis is that DeFi can significantly reduce financial exclusion in areas lacking traditional banking services, offering a more inclusive, efficient, and transparent alternative. By analyzing datasets from the Global Findex Database and Chain Analysis, to understand DeFi adoption rate vs unbanked population, this study provides insights into the feasibility of DeFi as a solution for financial exclusion.

4 Background

4.1 Decentralized Finance (DeFi)

Decentralized Finance, commonly known as DeFi, is an emerging financial technology that leverages blockchain to create an environment without the need of traditional intermediaries such as banks and brokers. At heart, DeFi operates on decentralized networks like Ethereum, enabling peer-to-peer financial transactions through smart contracts. These self-executing contracts with terms written directly into code ensure transparency, security, and automation(Ozili). The decentralization of financial services aims to offer open access to financial instruments such as lending, borrowing, and trading to anyone with an internet connection. Existing literature highlights the potential of DeFi in reducing costs, enhancing efficiency, and broadening financial inclusion, particularly for the unbanked populations(Ozili). However, as DeFi grows, it raises fundamental questions about its role in the existing financial institutions and regulatory frameworks(Zetsche et al). This study seeks to explore these challenges, focusing on how DeFi can address financial exclusion and what the broader implications are for global financial stability.

4.2 DeFi Tools and Platforms

The DeFi ecosystem comprises various tools and platforms that facilitate decentralized financial activities. Key among these are decentralized exchanges (DEXs) like Uniswap and Sushiswap, which allow direct cryptocurrency trading without intermediaries. These platforms use automated market-making algorithms to set prices, challenging traditional exchange models. Additionally, decentralized lending platforms such as Aave and Compound offer innovative solutions for lending and borrowing, using smart contracts to automate agreements and minimize counterparty risk. Stablecoins like DAI and USDC provide a means of mitigating the volatility inherent in cryptocurrencies by pegging digital assets to traditional currencies. These

innovations, along with yield farming and liquidity mining protocols, have drawn significant attention in academic and industry discussions, with researchers exploring their implications for financial stability and user behavior(Qin et al.). The diverse range of DeFi tools represents both opportunities and challenges, as they push the boundaries of traditional finance while posing new risks that require careful consideration.

4.3 Financial Inclusion

Financial inclusion is a critical goal in global development, aiming to make financial services accessible to all individuals and businesses, regardless of their socio-economic status(Demirgüç-Kunt et al.). Traditional banking systems often exclude large segments of the population, particularly in developing countries, due to barriers such as high fees, lack of documentation, and geographic limitations.DeFi has been proposed as a solution to these challenges, offering decentralized, borderless financial services that can be accessed via smartphones, bypassing the need for traditional banking infrastructure. By facilitating access to savings, loans, and investment opportunities, DeFi has the potential to transform financial inclusion, especially for underserved groups like women, rural communities, and small businesses. However, the success of DeFi in achieving these goals depends on overcoming significant barriers, including digital literacy and regulatory uncertainty, which remain underexplored in the current literature.

4.4 COVID-19's Impact on Financial Inclusion

The COVID-19 pandemic has accelerated the adoption of digital financial services, exposing the vulnerabilities of traditional financial systems and underscoring the importance of financial inclusion(Ozili). As lockdowns and social distancing measures disrupted physical financial services, digital platforms became essential for conducting transactions, accessing credit, and managing finances. This shift highlighted the divide between those with access to digital financial tools and those without, exacerbating existing inequalities.In this context, DeFi emerged as a potential alternative, offering resilient financial services that operate independently of traditional banking infrastructure. Studies have shown that DeFi platforms played a crucial role during the pandemic by facilitating peer-to-peer lending, providing liquidity through DEXs, and enabling secure digital transactions(Chen and Bellavitis). This has prompted a reevaluation of the role of DeFi in promoting financial inclusion, particularly in times of crisis. However, the pandemic also exposed challenges related to the scalability and security of DeFi platforms, which must be addressed to ensure their long-term viability.“Our research indicates that individuals who are elderly or less economically-advantaged are not accessing to the same extent the digital financial services that many take for granted, and have benefitted from during the COVID-19 pandemic”(London School of Economics and Political Science). This quote highlights the limitations of traditional digital banking services in reaching disadvantaged groups, revealing a gap that DeFi can potentially fill. By offering decentralized, accessible financial services without the need for traditional infrastructure, DeFi could play a crucial role in

reducing financial exclusion, particularly for those underserved by conventional banking systems.

4.5 Opportunities with DeFi

The opportunities presented by DeFi are vast, with the potential to redefine the financial landscape by making it more inclusive, efficient, and transparent. One of the most significant opportunities is its ability to provide banking services to unbanked and underbanked populations globally. By removing the need for traditional banking infrastructure, DeFi enables anyone with internet access to participate in the global financial system, potentially bridging the gap in financial inclusion. Moreover, DeFi fosters financial innovation by enabling the creation of new financial products and services, such as decentralized lending, automated market-making, and yield farming. These innovations not only enhance access to financial services but also introduce new paradigms of transparency and trust, as all transactions are recorded on a public, immutable ledger. However, realizing these opportunities requires addressing significant risks and challenges, particularly in terms of regulatory compliance and technological robustness.

4.6 Risks and Challenges with DeFi

While DeFi holds great promise, it also presents substantial risks and challenges that must be carefully managed. One of the primary risks is the vulnerability of smart contracts to bugs and exploits, which can lead to significant financial losses, as evidenced by high-profile incidents in the DeFi space. Regulatory uncertainty also poses a major challenge, as the decentralized nature of DeFi complicates traditional regulatory oversight and raises concerns about money laundering, financial crime, and consumer protection. Additionally, scalability issues remain a significant hurdle, with current blockchain infrastructures struggling to handle large volumes of transactions, leading to network congestion and high fees. The lack of consumer protection mechanisms, such as deposit insurance and legal recourse, further exposes users to risks that are typically mitigated in traditional financial systems. Addressing these challenges requires a concerted effort from developers, regulators, and stakeholders to create a secure, scalable, and compliant DeFi ecosystem that can fulfill its potential for financial inclusion and innovation.

5 Methodology

5.1 Research Design and Data Sources

The research is designed to explore the potential of Decentralized Finance (DeFi) in addressing financial exclusion, particularly in regions underserved by traditional banking services. To achieve this, multiple datasets were utilized, each contributing unique insights into various aspects of financial inclusion and DeFi adoption. The primary datasets include those from the World Bank and Chainalysis, covering financial inclusion metrics from 2017 and 2021, as well as DeFi adoption rates in 2021. These datasets allow for a longitudinal analysis of financial behaviors and the impact of DeFi across different countries. Additionally, the Merchant

Machine dataset provides crucial data on the unbanked population in 2021, highlighting regions where DeFi could have the most significant impact. By using these data sources, the study aims to create a comprehensive picture of the global financial landscape, focusing on areas where DeFi can bridge gaps in financial inclusion. This holistic approach ensures that the research is grounded in empirical evidence, providing a robust foundation for analyzing the potential of DeFi.

5.2 Data Processing and Preparation

The data processing phase was carefully designed to ensure that the datasets were in an optimal format for analysis, aligning with the study's research objectives. Initially, the raw data from the World Bank was cleaned(removing missing values) to address inconsistencies, a crucial step for maintaining the integrity of the analysis. The data was then organized into a table by country and year, focusing on key financial indicators that are directly relevant to the research question. To address the issue of missing data, mean imputation(filling in the values with the average) was employed, particularly for the target variable, 'Digital Payment (2021).' This approach minimized potential biases and ensured that the analysis remained comprehensive. Additionally, a method called Principal Component Analysis (PCA) was used to simplify the data while keeping most of the important information, retaining 95% of the variance. This step was essential for simplifying the feature space, thereby improving the efficiency and interpretability of the models used in the study.

5.3 Machine Learning

Machine learning (ML) is a branch of artificial intelligence (AI) that focuses on the development of algorithms and statistical models that enable computers to perform tasks without explicit programming. It involves training models on large datasets to recognize patterns, make decisions, and predict outcomes. The learning process is categorized into three main types: supervised, unsupervised, and reinforcement learning. In supervised learning, the model is trained on a labeled dataset, meaning the input comes with corresponding correct outputs, allowing the algorithm to learn the mapping function. Unsupervised learning, on the other hand, deals with unlabeled data, and the model tries to identify inherent structures or patterns within the data. Reinforcement learning is based on a system of rewards and punishments, where an agent learns to make decisions by interacting with an environment to maximize cumulative rewards. The power of machine learning lies in its ability to improve automatically through experience, making it a important feature of modern AI applications, ranging from natural language processing and computer vision to robotics and data analytics(Loy).

5.4 Model Selection and Justification

Given the complex and multi-dimensional nature of financial inclusion, a diverse set of machine learning models was selected to explore different facets of the research question. These models were chosen for their ability to handle varying types of data and their proven

effectiveness in financial prediction tasks. The models include Linear Regression, K-Nearest Neighbors (KNN), Random Forest Regressor, Gradient Boosting Regressor, XGBoost Regressor, Support Vector Regressor (SVR), Ridge Regression, and Lasso Regression.

- **Linear Regression** served as a baseline model, providing a straightforward interpretation of the relationship between the predictors and the target variable. Its simplicity allows for an initial understanding of how DeFi adoption might influence financial inclusion(Swaminathan).
- **K-Nearest Neighbors (KNN)** was employed to capture non-linear relationships in the data, offering insights into complex patterns that traditional linear models might miss(Srivastava).
- **Random Forest Regressor** was selected for its robustness to overfitting (which is when a model works well on training data but poorly on new data) and its ability to handle a large number of input variables. This model's feature importance measure was particularly valuable for identifying key drivers of financial inclusion and DeFi adoption(Sruthi).
- **Gradient Boosting Regressor** and **XGBoost Regressor** were included for their ability to model non-linear relationships and their effectiveness in reducing bias and variance, respectively. XGBoost, in particular, was chosen for its speed and performance in handling large datasets, making it suitable for this study's comprehensive analysis(Singh).
- **Support Vector Regressor (SVR)** was utilized to explore complex interactions between features, providing a deeper understanding of how various financial indicators relate to DeFi usage.
- **Ridge and Lasso Regression** were used so they could manage issues when predictors are too similar to each other (multicollinearity). They also simplify the model by reducing the influence of less important factors, focusing on the most impactful ones.These models helped in refining the analysis by focusing on the most impactful predictors

Each of these models was not just selected for their individual strengths but was also integrated into a broader strategy to answer the central research question: How can DeFi be leveraged to improve financial inclusion in areas with limited access to traditional banking services?

5.5 Model Training and Evaluation

The models were trained and evaluated using a rigorous approach that aligns with the study's objectives. Key evaluation metrics included R-squared, Mean Absolute Error (MAE), and Mean Squared Error (MSE), each providing a different perspective on the model's performance.

- **R-squared** was used to assess how well the independent variables explained the variability in the target variable, 'Digital Payment (2021)', providing insights into the overall fit of each model(Fernando).
- **MAE** offered a measure of the average prediction error, ensuring that the models were accurately capturing the relationship between DeFi adoption and financial inclusion(Ahmed).
- **MSE** was particularly useful for highlighting models that made larger errors, guiding the selection of models that balanced error distribution effectively(Agarwal).

Additionally, **Grid Search with Cross-Validation (GridSearchCV)** was employed for hyperparameter tuning, ensuring that each model was optimized for the best possible performance. This process not only refined the models but also provided a robust estimate of their generalizability to unseen data, further strengthening the study's findings(Shah).

6 Results

6.1 Model Training and Dataset Utilization

The model training was conducted on both the datasets using a Nvidia T4 GPU within the Google Collaboratory platform running the Jupyter Notebook environment. Training took roughly 2-3 minutes on average on both the datasets.

6.2 Correlation Analysis

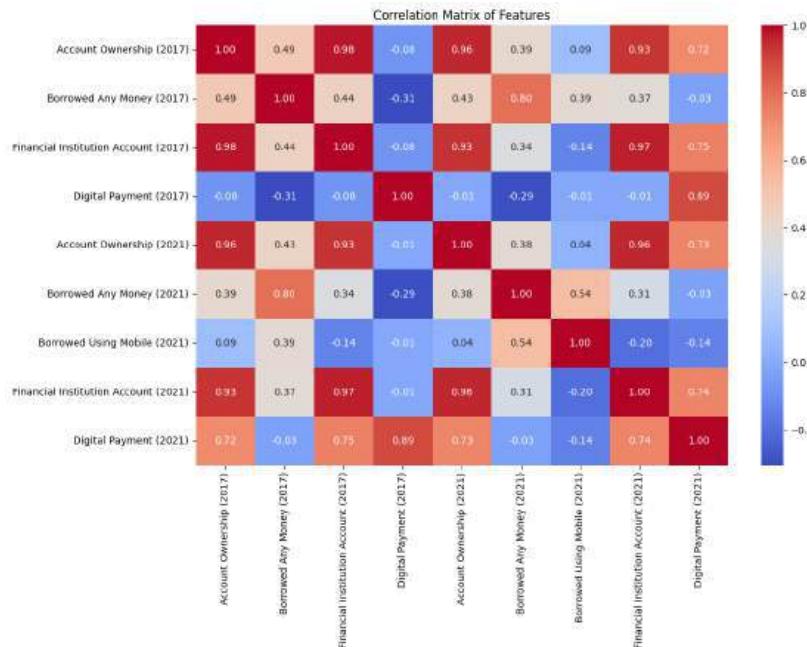


Figure 1: Correlation heatmap to show the accuracy of the model comparing different variables in the Global Findex Dataset

In this model, we utilized the Global Findex dataset to generate a correlation heatmap, aiming to see the relationships between key financial variables such as account ownership, digital payment usage, and borrowing habits across various countries. The correlation heatmap visually represents the strength and direction of these relationships, where color intensity indicates the correlation's magnitude. Red showing higher correlation and blue showing weaker correlation. The results revealed several significant positive correlations, particularly between account ownership and digital payment usage in 2021. This strong correlation suggests that countries with higher rates of account ownership also tend to exhibit higher adoption of digital payments. Another notable correlation was observed between financial institution accounts and borrowing through mobile platforms, indicating that access to formal financial institutions is often associated with the use of mobile borrowing technologies. The effects of these findings are substantial, as they highlight the interconnectedness of different financial behaviors and the potential impact of financial inclusion initiatives. These findings are directly relevant to the adoption of decentralized finance (DeFi) as a tool for financial inclusion. The strong link between account ownership and digital payment usage suggests that foundational access to formal financial systems can serve as a stepping stone for DeFi adoption. Furthermore, the correlation between financial institution access and mobile borrowing indicates that traditional financial systems can create familiarity and trust, reducing barriers to adopting decentralized solutions. This analysis highlights that countries with robust financial infrastructure and higher digital payment adoption are better positioned for DeFi integration, while those lacking such infrastructure may require targeted interventions, such as mobile banking expansion and digital literacy programs. Overall, the correlation heatmap provides a framework for identifying readiness and challenges in promoting DeFi adoption, reinforcing its potential to complement traditional financial inclusion efforts and bridge the gap for underserved populations.

6.3 Regression Model Results

Table 1: Model Performance between DeFi adoption rate(2021) and Unbanked Population(2021)

	Best Alpha	CV Mean Score
Model		
Ridge Regression	10	-0.0247
Lasso Regression	0.01	-0.0273
Best Model Coefficient	[0.0628, -0.0326, -0.0369, -0.0303, 0.0155, -0.0300]	

In this analysis, Ridge and Lasso regression techniques were used to identify the best-fit model, with alpha serving as a key hyperparameter controlling regularization. For Ridge regression, an alpha of 10 indicates a moderate level of regularization, resulting in a cross-validated mean score of -0.0247, which reflects a slight negative average prediction error. The Ridge model's coefficients reveal that as the log of total population(0.0628) increases, the predicted outcome also increases, while higher percentages of the unbanked population(-0.0326), cash transactions(-0.0369), card transactions(-0.0303), and internet penetration(-0.0300) are associated with lower predicted outcomes. In contrast, more ATMs per 100,000 people(0.0155) is linked to a higher predicted outcome. The Lasso model, with an alpha of 0.01 and a cross-validated mean score of -0.0273, had a slightly worse performance, indicating less accuracy in its predictions compared to Ridge. Overall, the Ridge model was chosen for further analysis due to its marginally better performance and its coefficients' insights into the relationships between predictors and the response variable.

The negative coefficients in the model provide significant insights into the factors influencing DeFi adoption rates. The Unbanked Population (%) had a coefficient of -0.0326, indicating that higher DeFi adoption could lead to lower unbanked population. Similarly, Cash Transactions (%) had a coefficient of -0.0369, showing that economies with higher DeFi adoption rate would have lower cash transactions. This aligns with the notion that reliance on cash signifies lower digital financial integration. Additionally, Card Transactions (%) had a negative coefficient of -0.0303, suggesting that if countries were to increase DeFi adoption rate then the number of card transactions will eventually decrease.

The choice of an alpha value of 10 in the Ridge regression model indicates a significant regularization effect, meaning that the model is penalizing large coefficients to prevent overfitting. This level of regularization suggests that the model is attempting to balance complexity and accuracy by smoothing out the influence of any one predictor variable. In practical terms, this means the model considers all variables, but none are allowed to dominate excessively, which is important for generalizing the findings to other datasets or future data. The results underscore the complexities of promoting DeFi adoption as a means to address financial exclusion. While larger populations and a robust traditional banking infrastructure, as indicated by the number of ATMs, correlate positively with DeFi adoption, other socio-economic factors present challenges.

6.4 Model Evaluation

Table 2: Model Evaluation Metrics

Model	Mean Squared Error	R-Squared	Mean Absolute Error
Linear Regression	10.3746	0.9440	2.0927
K-Nearest Neighbors	8.6214	0.9535	1.5128
Random Forest	35.0625	0.8107	3.1486
Gradient Boosting	26.3740	0.8576	2.8840
XGBoost	40.1098	0.7835	3.2381
Support Vector Regressor	7.9523	0.9571	1.9344

Note: Mean Squared Value is calculated by $\frac{1}{n} \sum_{i=1}^n (y_i - \hat{y}_i)^2$

R-squared value is calculated by $1 - \frac{\sum_{i=1}^n (y_i - \hat{y}_i)^2}{\sum_{i=1}^n (y_i - \bar{y})^2}$

Mean Absolute Error is calculated by $\frac{1}{n} \sum_{i=1}^n |y_i - \hat{y}_i|$

y_i = actual value

\hat{y}_i = predicted value

n = number of observations

$|y_i - \hat{y}_i|$ = absolute error for each observation

In this research, various machine learning models were applied to the Global Findex dataset to investigate the potential of Decentralized Finance (DeFi) in addressing financial exclusion. The dataset provides critical insights into financial behavior across different countries, including account ownership, digital payment usage, and borrowing patterns. These variables are key indicators of financial inclusion and are used to model the relationship between DeFi adoption rates and the unbanked population. By employing models such as Linear Regression, K-Nearest Neighbors, Random Forest, Gradient Boosting, XGBoost, and Support Vector Regressor, this study aims to predict digital payment usage proxy for DeFi adoption based on

financial variables from 2017 and 2021. The use of Principal Component Analysis (PCA) to reduce dimensionality and StandardScaler for feature standardization ensures that the model inputs are well-prepared for accurate predictions.

The results from the different models provide a comprehensive overview of their predictive capabilities. The Linear Regression model, which produced a high R-squared value of 0.944, indicates that 94.4% of the variance in digital payment usage can be explained by the independent variables in the model. This high R-squared value suggests that the model fits the data well, meaning the selected financial indicators are strong predictors of DeFi adoption. Additionally, the K-Nearest Neighbors (KNN) model, with an R-squared of 0.953 and the lowest Mean Absolute Error (MAE) of 1.51, outperformed Linear Regression in terms of predictive accuracy, highlighting the potential of non-linear relationships in the data. The Support Vector Regressor (SVR) also demonstrated strong performance, with an R-squared value of 0.957 and a MAE of 1.93, indicating its effectiveness in capturing complex patterns in the data. However, more complex models like Random Forest and Gradient Boosting, despite their ability to capture non-linearities and interactions among features, showed lower performance with R-squared values of 0.810 and 0.857, respectively. This could be due to dimensionality or overfitting issues, especially given the large number of features in the dataset. XGBoost, another powerful ensemble method, further highlighted this trend with an even lower R-squared of 0.783, suggesting that the simpler linear relationships captured by Linear Regression, KNN, and SVR are more effective for this specific dataset.

6.5 DeFi Adoption Trends

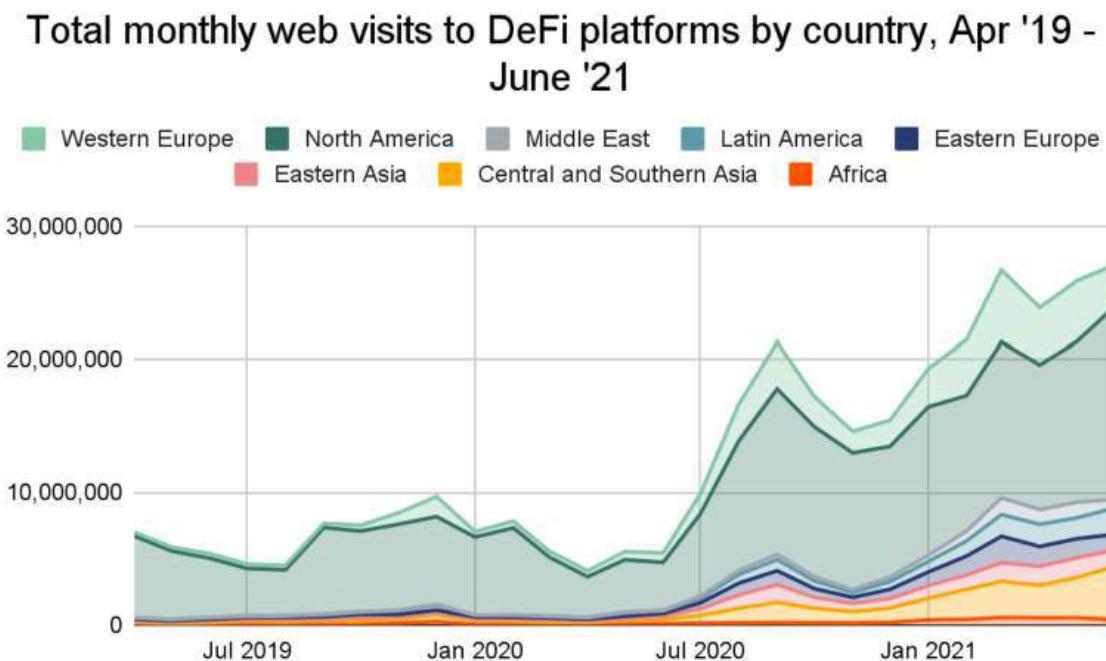


Figure 2: A graph showcasing the increase in DeFi adoption rate in different countries(Ozili, 2021)

The chart depicting the increase in DeFi adoption from April 2019 to June 2021 across various countries highlights a significant global trend toward decentralized finance. The rapid growth observed during this period, particularly in regions such as North America and Western Europe, underscores the rising interest in DeFi as an alternative to traditional financial systems. This surge in adoption can be attributed to DeFi's ability to provide accessible financial services without the need for traditional intermediaries, making it particularly appealing in regions with underdeveloped banking infrastructure. The post-COVID-19 era has amplified the demand for inclusive financial solutions as the pandemic has increased financial exclusion, especially in rural and underserved urban areas. The widespread adoption of DeFi across diverse regions suggests its potential to bridge the gap left by conventional banking, offering a decentralized, accessible, and transparent alternative that can play a crucial role in addressing financial exclusion in the aftermath of the pandemic.

7 Evaluation

The evaluation of the various machine learning models applied to the Global Findex dataset and the Chain Analysis Dataset highlights the significant impact and relevance of DeFi adoption in addressing financial exclusion. By employing models such as Linear Regression, K-Nearest Neighbors (KNN), Random Forest, Gradient Boosting, XGBoost, and Support Vector Regressor, this study sought to uncover the factors that influence DeFi adoption and its relationship with financial inclusion. Feature preparation using Principal Component Analysis (PCA) and StandardScaler ensured an effective methodology, minimizing gaps in data handling.

The results demonstrated that simpler models like Linear Regression and K-Nearest Neighbors (KNN) exhibited high predictive accuracy, with R-squared values of 0.944 and 0.953, respectively. KNN, with the lowest Mean Absolute Error (MAE) of 1.5128, showed particular strength in capturing non-linear relationships. Similarly, Support Vector Regressor (SVR) performed well, achieving an R-squared value of 0.957 and MAE of 1.9344, reflecting its ability to handle complex data patterns. In contrast, more sophisticated models such as Random Forest, Gradient Boosting, and XGBoost underperformed, with lower R-squared values (0.8107, 0.8576, and 0.7835, respectively). This underperformance may be attributed to overfitting or the dimensionality of the dataset, despite these models' capacity to capture non-linearities and feature interactions.

The Ridge regression model provided further insights into the factors influencing DeFi adoption. Positive coefficients for variables such as Log_Total_Population and Log_ATMs_Per_100k underscore the importance of traditional financial infrastructure and population density in facilitating DeFi adoption. Conversely, negative coefficients for Unbanked Population (%) and Cash Transactions (%) highlight DeFis potential to address financial exclusion by reducing the reliance on cash and decreasing the unbanked population. This dual insight - showing both enablers and barriers - emphasizes the complex relationship between existing financial systems and DeFi adoption.

This evaluation highlights specific relationships between financial behaviors and DeFi adoption, emphasizing their implications for addressing financial exclusion. For instance, the strong performance of simpler models like Linear Regression and KNN reveals robust and interpretable relationships between variables such as account ownership, digital payment usage, and DeFi adoption rates. These findings provide policymakers with actionable insights, such as the significant role of traditional financial infrastructure (e.g., ATMs per capita) in facilitating DeFi adoption and the inverse relationship between unbanked population percentages and DeFi usage.

The challenges faced by complex models, such as Random Forest and XGBoost, suggest that there is potential to improve predictive accuracy by refining methodologies. Incorporating hybrid approaches or additional socio-economic variables, such as income inequality and mobile internet penetration, could enhance understanding of the nuanced dynamics between financial inclusion and DeFi adoption. Ultimately, this evaluation underscores the transformative potential of DeFi, advocating for the development of a scalable, data-driven approach to building an inclusive financial ecosystem. This approach would enable DeFi to address financial exclusion while complementing traditional banking systems effectively.

8 Conclusion

This research aimed to explore the role of Decentralized Finance (DeFi) in addressing financial exclusion, particularly in regions with limited access to traditional banking services. Leveraging machine learning models and comprehensive datasets, the study sought to quantify the relationship between DeFi adoption and financial inclusion metrics, uncovering key insights with far-reaching implications.

The findings reveal that DeFi adoption has a significant and measurable impact on improving financial inclusion. Models such as Ridge regression demonstrated that higher DeFi usage correlates with a reduction in unbanked populations and reliance on cash transactions, signaling a shift toward more inclusive financial systems. This relationship, though minor in magnitude, aligns with the notion that higher DeFi adoption can contribute to reducing the number of unbanked individuals. Such findings highlight DeFi's potential to complement traditional banking systems by bridging gaps, reducing reliance on cash, and expanding access to credit and other financial tools. The strong correlation between digital payment adoption and account ownership further highlights the interconnectedness of traditional financial infrastructure and DeFi solutions. These results validate the potential of DeFi to complement traditional banking systems, particularly in underserved regions where centralized banking infrastructure remains limited.

The implications of this research are profound. DeFi offers an alternative to traditional financial systems by providing decentralized, accessible, and transparent services, particularly in areas where financial exclusion is most acute. The results show that DeFi can bridge critical gaps left by centralized systems, offering tools to reduce reliance on cash, expand access to credit, and empower individuals through greater financial autonomy. However, challenges such as

regulatory uncertainties, technological vulnerabilities, and the need for widespread digital literacy remain significant hurdles to its broader adoption.

The importance of this research lies in its demonstration of DeFi's dual role as both a disruptor and a complement to traditional financial systems. By integrating DeFi with existing infrastructure, stakeholders can create a hybrid model that leverages the strengths of both systems to drive financial inclusion. Policymakers and innovators must work together to address regulatory and technological barriers, ensuring the development of a secure and scalable DeFi ecosystem.

In conclusion, this study reinforces the potential of DeFi in reshaping the financial landscape. It highlights the need for strategic investments in digital infrastructure, education, and regulatory frameworks to fully realize DeFi's promise. By addressing these challenges and building on the insights from this research, DeFi can play a pivotal role in creating a more equitable and inclusive global financial system, offering new opportunities for millions of underserved individuals worldwide.

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The Symbiotic Relationship Between Keyboard Instrument Development and Composers By Kailun Ma

Abstract

The interplay between instruments and composers serves as a cornerstone for the evolution of music. There is extensive literature focused on the history of various instruments and composers, but there is a notable gap in sources that discuss the interdependent relationship between them. This paper includes a literature review and investigates the symbiotic relationship between the composers and the keyboard instruments, which are important for musical composition. Based on both historical and theoretical frameworks, the paper explores the transformation of string sound through methods such as rubbing, touching, plucking, and hammering in six musical periods: the Middle Ages, Renaissance, Baroque, Classical, Romantic, and Modern. The paper traces the history and development of the dulcimer, clavichord, harpsichord, pianoforte, and modern piano through these periods. The findings demonstrate that the enhanced range, structural innovations, timbre variations, and increased accessibility of keyboard instruments influence composers. Conversely, composers will point out the direction for the development of keyboard instruments. Furthermore, the development pattern follows a recurring cycle consisting of four periods: interactivity, adaptability, complementarity, and co-creativity. And the upward spiral trend of development is driven by the symbiotic relationship. This positive feedback loop emphasizes cooperative progress between science and art. By adopting a cyclical perspective, the study not only explains the historical patterns but also offers insights for predicting future developments in music. Understanding these historical interdependencies is important for anticipating the next era of musical innovation.

Keywords music history, keyboard instruments, composers, symbiotic, harpsichord, clavichord, pianoforte, musical evolution, compositional techniques.

Introduction

The musical development has been influenced by the special relationship between composers and keyboard instruments. There are various keyboard instruments, the dulcimer with rubbing and touching, the clavichord with touch springs, the harpsichord with plucking springs, the pianoforte with hammering action, and the modern piano without springs. Each instrument possesses a unique structure, range, timbre, and accessibility (Montagu, 2007). While there is extensive research on the keyboard instruments and biographies of composers, there is only a limited focus on exploring their special relationship and interaction model. By exploring dynamic mode models, it can help explain and predict the future of music civilization.

Although there is a lot of literature on musical instruments and composers, there is still a significant gap in the study of their relationships. This study solves this gap and aims to clarify this symbiotic relationship by studying how the evolution of keyboard instruments affects composer practice and how the composer's innovation is promoted. The interaction model is very

important because it highlights the continuous feedback circuit between the instrument and the composer, namely, the development relationship between science and art. Unfortunately, there is almost no literature to discuss this model in existing research. These findings have an impact on historical music science and contemporary musical instruments, and they can provide continuous interaction between the future development of music and technology.

The study focuses on the historical development of five key keyboard instruments: the dulcimer, the clavichord, the harpsichord, the pianoforte, and the modern piano (Matthews, 1972). The study also analyses the changes in different parts such as range, structure, timbre, accessibility, etc. to understand their influence on the composer's creation (Libin, 1989). However, even after composing using these instruments, music composers still struggled to find ways to explore structural evolution. Due to its long history, this study may be limited in interpretation by the availability of historical data and potential biases.

There are two frameworks for studying this relationship: a historical framework that traces the evolution of keyboard instruments and a theoretical framework that explores the symbiotic relationship. First, this study uses a historical framework to explore how the structural development of keyboard instruments was influenced by composers. This exploration is anchored by sound-making techniques from six musical periods, including friction, touch, plucking, and hammering, spanning the Medieval, Renaissance, Baroque, Classical, Romantic, and Modern periods (Nadirova & Aliyeva, 2024). The timeline outlines the evolution of keyboard instruments and highlights the cyclical patterns of interaction between composers and instruments. Then, with the support from the theoretical framework, this research focuses on four stages, the idea for the frame structure came from a paper on composers and performers (Mus, 2020), through which the relationship between composers and keyboard instruments progresses: interactivity, adaptability, complementarity, and co-creativity. These stages illustrate the dynamic nature of their interrelationships, forming a spiral relationship that evolves over time. This paper finds that advances in the range, structure, timbre, and ease of use of keyboard instruments have provided new opportunities for composers, and conversely, composers' innovative works have stimulated the development and progress of keyboard instruments. The analyzed data reveal a feedback loop that has promoted both the art of music and the science of musical instruments. This study is based on a historical and theoretical framework and aims to explore the model regularities of the interaction between keyboard instruments and composers. The cyclical perspective of this study suggests that the observed historical patterns are crucial for understanding past trends and predicting future developments in music.

The research method focuses on literature review, integrating existing research on the evolution of keyboard instruments and composer biographies to study the symbiotic relationship between keyboard instruments and composers, and further uses it to explore the relationship model and development pattern between the two.

Methods

The search strategy for relevant literature focused on consulting library resources, including books, papers, and other scholarly materials. Subsequently, an internet search was conducted using scholarly databases such as Google Scholar and Music Index. Boolean searches were conducted using keywords including “keyboard instruments,” “instrument evolution,” and “music composers.” This dual approach ensured a comprehensive collection of research materials. Initially, the selection criteria for the studies included relevance to the history of keyboard instruments, historical development of these instruments, publications in peer-reviewed or reputable scholarly sources, and biographies of composers. Data extraction then involved gathering information from the selected studies using standardized forms. Key details included author names, publication dates, research focus, and key findings. In addition, the collected information was synthesized through thematic analysis. The aim of the synthesis was to organize the findings into coherent categories, highlighting the mutual influence and historical progression of the symbiotic relationship between keyboard instrument development and compositional practice. Finally, the quality assessment of the studies was based on relevance, methodological rigor, and credibility. The studies were evaluated for their contribution to the understanding of the interaction between keyboard instruments and composers, with a focus on the validity and reliability of the findings.

Results

Keyboard Instruments

The chart (Chart 01) is divided into six historical periods, highlighting the main musical genres of each period and showing their styles and characteristics as well as the structure, range, timbre and accessibility of contemporary keyboard instruments.

Historical Periods	Music		Keyboard Instrument				
	Music Style	Music Characteristics	Keyboard Instrument	Structure	Range	Timbre	Accessibility
Middle Ages (500 – 1400)	*gregorian chant *monophonic music *early polyphonic music *liturgical compositions	*vocal lines *sacred focus *modal	Dulcimer	trapezoidal soundboard; strings struck by mallets	limited range diatonic scales	soft resonant metallic tone	widely accessible secular and sacred music not a primary instrument
Renaissance (1400 – 1600)	*polyphonic textured vocal music *secular music	*interwoven melodic lines *smooth voice leading *balanced harmonic structures	Clavichord Harpsichord	clavichord small, rectangular, metal tangents striking strings; harpsichord large, quills plucking the strings;	clavichord moderate range expressive dynamics harpsichord more fixed dynamics	clavichord soft, intimate, expressive; harpsichord bright, clear, percussive,	clavichord popular for private practice harpsichord widely used in both sacred and secular music
Baroque (1600 – 1750)	*instrumental music *suites *sonatas *concertos	*elaborate musical lines *contrast in dynamics and texture *strong sense of rhythm	Clavichord Harpsichord	clavichord more refined mechanics; harpsichord larger, with manual keyboards	more expanded range suite for more complex music	clavichord - more expressive, suitable for intimate settings harpsichord - bright, resonant;	clavichord a tool for composition and private use harpsichord dominant in public performances
Classical (1750 – 1820)	*sonata form *symphonies *string quartets	*clear, singable melodies *structured forms *dynamic contrasts	Pianoforte	hammer-striking mechanism wooden frame lighter action	expanded range greater dynamic expression	dynamic nuances from soft to loud more delicate tone than the modern piano.	primary keyboard instrument accessible to composers and performers central to domestic
Romantic (1820 – 1900)	*programmatic music	*rich harmonies *lyrical melodies *expanded orchestration *individual expression	Modern Piano	iron frame heavier action larger soundboard powerful strings	fully expanded range (up to 88 keys)	rich, resonant wide dynamic range pianissimo - fortissimo	widely accessible in concert halls and homes a central instrument in Romantic music.
Modern (20th Century and Contemporary)	*atonality *serialism *neoclassicism *minimalism *electronic music	*experimentation scales/rhythms/forms *incorporation folk music/ jazz/ non-Western influences	Modern Piano, Electronic, and Digital Pianos	modern pianos iron frames precise action; electronic pianos synthesized sampled sounds	standard range of 88 keys any range	modern pianos acoustic pianos rich, dynamic timbres; electronic pianos from traditional piano sounds to entirely new synthesized tones	acoustic pianos widely accessible. electronic pianos accessible to a broad audience

Chart 01. Development of the Keyboard Instruments across the Historical Periods by author

This chart presents the characteristics of each keyboard instrument in different periods from four aspects: structure, range, timbre, and accessibility. First, it demonstrates the structure of the keyboard instruments and the way to make the spring sound. Also, the chart indicates the range of octaves available, showing an expansion from limited ranges in early instruments to the broad span of modern pianos. Furthermore, the evolution of the timbre quality is explored, starting from simple sounds in the past to more complex tonal qualities today. Finally, as accessibility is addressed, demonstrating its steady improvement throughout history.

Music in the Middle Ages was characterized mainly by Gregorian chant and monophonic music (Smith, 1986), which included polyphonic music and liturgical compositions (Norlind, 1936). The music was simple and unaccompanied, prioritizing vocal church music. During this period, the dulcimer was prevalent and a trapezoidal soundboard with strings struck by hammers. It had a moderate range with diatonic tuning and a soft, resonant timbre. The dulcimer was widespread for minstrels and merchants (Norman, 1979).

There is polyphonic texture, vocal music and secular music in the Renaissance period. The characteristics are interwoven melodic lines, smooth voice leading and balanced harmonic structures. At that time the clavichord and harpsichord appeared, the clavichord is more popular

for private practice, while the harpsichord is widely used in both sacred and secular music (Neupert, 1965).

The Baroque period was rich with instrumental music (Kerman et. al., 2011). It involved elaborate musical lines with consistent rhythm and complex harmony. The clavichord was used for private use. The harpsichord, known for its keyboard plucking mechanism, valued for its expansive range and bright, metallic timbre (Kenyon, 1949). The instrument became more widely used among high society and skilled musicians.

Classical music was defined by sonatas, symphonies, and string quartets. The characteristics of the music are clear melodies, structured forms and dynamic contrasts. The pianoforte used a hammer-striking method that allowed for dynamic expression (Isacoff, 1994). The instrument had an expanded range and was increasingly accessible to the educated middle class for domestic compositions.

Romantic music emphasized on the programmatic music which included the rich harmonies, lyrical melodies, expanded orchestration and individual expression (Sumner, 1971). It offered thematic transformation and expressive modulation. The piano could make a further expanded range and resonant timbre with its hammer action. It was highly accessible, becoming a central feature in households and music education.

Modern music covers diverse genres, including classical, jazz, and experimental styles (Palmieri, 2004). It emphasizes modernist and experimental sounds, tonal and atonal structures. Digital pianos and acoustic pianos dominate, featuring advanced keyboards with varied sound capabilities (Gil et. al., 2020). They offer a comprehensive range and versatile timbres. Also they are widely accessible for professional and amateur musicians.

Composers

This chart (Chart 02) illustrates the famous composers throughout six historical periods, demonstrating how composers utilized contemporary keyboard instruments to create unique musical expressions and their demands for the playing technology.

Historical Periods	Composers	Keyboard Instrument	Music Expression of Composers	Playing technology	Famous Compositions
Middle Ages (500 – 1400)	Guillaume de Machaut (1300–1377)	Dulcimer	more isorhythm complex polyphony melodic lines counterpoint	focused on melody vocal music polyphony	• Messe de Notre Dame • Douce dame jolie
Renaissance (1400 – 1600)	Gioffredo Caccini (1551–1618)	Clavichord Harpsichord	the monodic style emphasized the vocal line	harmonic structure clarity expressive nuances of vocal line	• Le Nuove Musiche • Euridice
Baroque (1600 – 1750)	Johann Sebastian Bach (1685–1750)	Clavichord Harpsichord	complex counterpoint rich harmonies	finger independence precision technical mastery expression	• The Well-Tempered Clavier • Brandenburg Concertos
	Domenico Scarlatti (1685–1757) Baroque/Classical Transition	Clavichord Harpsichord	bold harmonic shifts rapid arpeggios hand-crossing repeated notes	rapid arpeggios contrasting registers	• Sonata in E major, K. 380 • Sonata in D minor, K. 141
	Carl Philipp Emanuel Bach (1714–1788) Baroque/Classical Transition	Clavichord Harpsichord	sensitive style individual expression	a nuanced touch emotional depth	• Symphonies, Wq. 182 • Keyboard Sonatas, Wq. 55/6
Classical (1750 – 1820)	Wolfgang Amadeus Mozart (1756–1791)	Pianoforte	clarity balance elegance	fast scales swift arpeggios more ornamentation	• The Magic Flute • Symphony No. 40 in G minor, K. 550
	Ludwig van Beethoven (1770–1827) Classical/Romantic Transition	Pianoforte	dynamic contrasts motivic development emotional intensity structural innovation personal expression	powerful playing sudden dynamic shifts extensive pedal wide leaps	• Choral Symphony • Moonlight Sonata • Fidelio
Romantic (1820 – 1900)	Frédéric Chopin (1810–1849)	Modern Piano	expressiveness legato line rich harmonic textures	delicate ornamentation complex rhythms cantabile playing refined touch	• Nocturnes, Op. 9 • Études, Op. 10 • Ballade No. 1 in G minor, Op. 23
	Franz Liszt (1811–1886)	Modern Piano	dramatic contrasts virtuosic demands use full keyboard range more expressive range	technical brilliance rapid arpeggios complex textures strength and dexterity	• Hungarian Rhapsodies • Piano Sonata in B minor, S. 178
Modern (20th Century and Contemporary)	Igor Stravinsky (1882–1971)	Modern Piano Electronic Piano Digital Piano	rhythmic complexity sharp contrasts certain percussive quality	precise control unconventional techniques irregular rhythms shifting moods and textures	• The Rite of Spring • Petrushka • Symphony of Psalms
	Jean-Michel Jarre (b. 1948)	Modern Piano Electronic Piano Digital Piano	layered textures blending melodic lines ambient soundscapes electronic effects	understanding design technical proficiency live manipulation	• Oxygène • Equinoxe

Chart 02. Development of the Music with Composers across the Historical Periods by author

The Keyboard Instruments column shows the primary keyboard instruments associated with each period. The Music Expression of Composers section provides details on their specific musical styles or expressions. The Playing Technology column discusses the playing techniques and technological advancements in keyboard instruments. Finally, the Famous Compositions column lists some of their most well-known works.

Initially, in the Middle Ages, Guillaume de Machaut led the way in complex polyphony and rhythmic innovation. His music was with more isorhythm, complex polyphony, melodic lines, and counterpoint. The players must focus on melody and vocal music polyphony.

During the Renaissance, Gioffredo Caccini emphasized the vocal line and the monodic style. The players need to demonstrate clarity in the harmonic structure and expressively convey nuances of the vocal line.

The Baroque era, led by Johann Sebastian Bach, featured complex counterpoint and rich harmonies (Neupert, 1960). The players require finger independence and technical mastery to express themselves effectively. Domenico Scarlatti introduced bold harmonic shifts, rapid arpeggios, hand-crossing, and repeated notes. These compositions need the performance of rapid

arpeggios and contrasting registers. Carl Philipp Emanuel Bach played a key role in the transition from Baroque to Classical music, he emphasized sensitivity and individual expression (Neupert, 1965). His works need a nuanced touch and depth emission.

During the classical period, Wolfgang Amadeus Mozart exemplified clarity, balance, and elegance with exclusive masterpieces (Montagu, 2007). The players need the ability of precision touch, fast scales, swift arpeggios and demonstrate ornamentation. Ludwig van Beethoven added dynamic contrasts and personal expression in the works and the players need the ability of powerful playing, sudden dynamic shifts, extensive pedal and wide leaps (Matthews, 1972).

In the Romantic period, Frédéric Chopin demonstrated the legato line and rich harmonic textures of the melody, which demanded the players to manage the delicate ornamentation, complex rhythms, cantabile playing and refined touch (Sumner, 1971). Franz Liszt demonstrated the dramatic contrasts, virtuosic demands and more expressive range, which demanded the players to handle the technical brilliance, rapid arpeggios, complex textures, strength and dexterity (Sumner, 1971).

In the modern period, Igor Stravinsky demonstrated rhythmic complexity, sharp contrasts and certain percussive qualities, which demanded the players to handle precise control, unconventional techniques, irregular rhythms, and shifting moods. Jean-Michel Jarre showcases layered textures, mixed melodic lines, ambient soundscapes, and electronic effects, which require the performer to master an understanding of musical design, technical proficiency and live manipulation of sound parameters, making the performance an integral part of the compositional process.

Keyboard Instruments and Composers

This chart (Chart 03) explores the dynamic interaction between composers and the development of keyboard instruments in six musical periods: Medieval, Renaissance, Baroque, Classical, Romantic, and Modern. It highlights how composers influenced the evolution of keyboard instruments by demanding greater complexity, dynamic range, and expressiveness in their music. In turn, these evolving instruments shaped the composers' musical styles, offering new possibilities while also imposing certain limitations. The chart illustrates how this interrelationship drove technical advances in keyboard instruments and innovation in music composition.

Historical Periods	Composers Influence the Instruments		Keyboard Instruments Influence the Composers		
	Composers	Influence on Instrument	Instruments	Benefits	Limitations
Middle Ages (500 – 1400)	Guillaume de Machaut (1300–1377)	the harmonic support more complex polyphony	Dulcimer	resonant sound melodic lines	in folk melodies dance tunes
Renaissance (1400 – 1600)	Gioffredo Caccini (1551–1618)	harmonic and rhythmic support	Harpsichord	harmonic and rhythmic	less dynamic flexibility
Baroque (1600 – 1750)	Johann Sebastian Bach (1685–1750)	action mechanisms dynamic control	Clavichord Harpsichord	harpsichord: bright, articulate clavichord: expressive dynamics	harpsichord: lacked dynamic control clavichord: too quiet for large venues
	Domenico Scarlatti (1685–1757) Baroque/Classical Transition	greater dynamic range more expressive capabilities	Harpsichord	bright and precise attack crafting sonatas rapid scales	less rhythmic limited harmonic variations
	Carl Philipp Emanuel Bach (1714–1788) Baroque/Classical Transition	subtle changes in touch dynamic capabilities	Clavichord Harpsichord	subtle dynamics nuanced expression	limited dynamic range less reliable of tuning weak durability
Classical (1750 – 1820)	Wolfgang Amadeus Mozart (1756–1791)	more robust construction wider range better dynamic control	Pianoforte	nuanced dynamics subtle articulations expressive challenging high technical	limited range weak power
	Ludwig van Beethoven (1770–1827) Classical/Romantic Transition	cast-iron frame increased string tension extended range		greater sustain more power dynamic contrast	fell short of demands unrealize the dramatic contrasts
Romantic (1820 – 1900)	Frédéric Chopin (1810–1849)	refinement of action touch sensitivity convey subtle emotional shifts	Modern Piano	expressive capabilities: wide dynamic range strong sustain singing tone	individual tonal qualities
	Franz Liszt (1811–1886)	more robust frames: improved action greater durability		full range powerful sound sustain notes	physical limits widen the boundaries
Modern (20th Century and Contemporary)	Igor Stravinsky (1882–1971)	timbre exploration percussive potential electronic enhancements	Modern Piano Electronic Piano	wide range percussive qualities rhythmically complex	can't achieve desired effects
	Jean-Michel Jarre (b. 1948)	greater polyphony sound fidelity ease of use	Digital Piano	unprecedented control expanding the palette	limited technological less polyphony weak sound quality

Chart 03. The Interplay of Keyboard Instruments and Composers across the Historical Periods by author

Initially, in the Middle Ages, the works of Guillaume de Machaut were primarily vocal, which led to the development of keyboard instruments designed for more complex polyphony (McGrady, 2012). At the time, there was a folk dulcimer that provided a rich, resonant sound, reinforcing the melody line and supporting the vocals. The dulcimers are used mostly in folk melodies and dance tunes.

Moving into the Renaissance, the harpsichord provided harmonic and rhythmic support crucial for Gioffredo Caccini's vocal compositions (Hammond, 1983). But the harpsichord lacked the dynamic flexibility, so it restricted the types of articulation and tone colors. Meanwhile the clavichord is just a practice instrument and intimate setting at home. His basso continuo highlighted the development of harpsichord in providing harmonic and rhythmic support.

Then comes the most flourishing Baroque Period. First, J. S. Bach's intricate polyphony and complex counterpoint demanded advancements in keyboard instruments, particularly in their action mechanisms and ability to handle polyphony. His work directly influenced the development of clavichord and harpsichord. The nuanced dynamic clavichord and the harpsichord with its bright and articulate sound, greatly influenced Bach's compositional style. However, their limitations in dynamic range and volume constrained their use.

The Baroque period is a golden age for keyboard instruments, with Johann Sebastian Bach at the forefront (Neupert, 1960). The harpsichord is proud of its bright and articulate sound,

while lacking expressive and dynamic control. And despite the clavichord for its expressive dynamics, it was too quiet for large venues. Bach's demands for instruments capable of handling complex polyphony and articulation directly pushed the keyboard instruments for improvements in action mechanisms and dynamic control that would later be realized in the forte piano.

Alongside J. S. Bach, Domenico Scarlatti's sonatas are characterized by rapid register changes, sudden rhythm shifts, and dynamic bass variations (Bogianckino, 1967). The rapid scales, hand crossings, and arpeggios reflected the harpsichord's unique layout and range. While the limitation of dynamic control restricted emotional expression to rhythmic and harmonic variations rather than volume changes. Scarlatti emphasized the need for greater dynamic range and expressive capabilities of the forte piano. From the Baroque to Classical period, Carl Philipp Emanuel Bach is a titan composer in keyboard evolution, and he was a key figure in both the harpsichord and the pianoforte (Neupert, 1965). While the early pianofortes had a limited dynamic range, they could constrain performance because of weakness in tuning and durability. C.P.E. Bach's emphasis on emotional expression in keyboard music highlighted the need for instruments. His guidance shows the way of the development of subtle changes in touch and dynamic capabilities.

During the Classical period, the forte piano allowed Wolfgang Amadeus Mozart to explore nuanced dynamics and articulations; he could create music that was both expressive and technically challenging (Montagu, 2007). But the pianoforte was still evolving in range and power, which slightly restricted the scope of the compositions. Mozart's piano concertos and sonatas, pushed the forte piano's capabilities, driving the demand for instruments with more robust construction, wider range, and better dynamic control. Also, Beethoven's compositions demanded greater sustain, power, and dynamic contrast, which the piano gradually provided. While the evolving instruments couldn't fully realize the dramatic contrasts he envisioned, the instrument he left at his death seems to have been a wreck due to the strong power when he played it (Sumner, 1971). Beethoven's intense, emotionally charged music directly influenced the development of the modern piano, pushing for innovations like the cast-iron frame, increased string tension, and extended range that would become standard.

In the Romantic period, Frédéric Chopin's music fully exploited the modern piano's expressive capabilities: wide dynamic range, everlasting sustain, and ability to produce a singing tone (Sumner, 1971). By Chopin's time, the modern piano was highly developed, and people preferred certain brands of pianos for their unique sound. Chopin's lyrical melodies and expressive nuance influenced the refinement of the piano and the ability to convey emotional shifts. Franz Liszt, a contemporary of Chopin, his magic music demanded the utmost from the modern piano. His compositions took advantage of the full range, powerful sound, and ability to sustain notes (Matthews, 1972). Furthermore, the masterpieces often pushed the boundaries of what was technically possible. His demands led to further refinements in piano construction, including more robust frames, improved action, and greater durability.

Transitioning to the 20th century, modern pianos can offer a wide range and percussive qualities, especially in rhythmically complex works. This is ideal for Igor Stravinsky's

explorations of rhythm and dissonance (Straus, 2004). Nevertheless, his desired effects in sounds led him to play with other instruments and even orchestration. Stravinsky also encouraged instrument makers to continue experimenting with the piano's timbre and percussive potential, leading to the development of piano techniques and electronic enhancements. Jean-Michel Jarre was a pioneer of modern electronic music. The electronic piano gave him unprecedented control over sounds, timbres, and effects, expanding the range of timbres available for keyboard instruments (Rideout, 2011). While the main limitations were technical, early synthesizers had limited polyphony, sound quality, and reliability compared to modern digital instruments. Jarre also pushed for more advanced technology to achieve higher polyphony, sound fidelity, and ease of use.

Discussion

Symbiotic Relationship

The study comprehensively examines the evolving relationship between composers and keyboard instruments, highlighting how this interaction has influenced music creation and the development of instruments. On the one hand, keyboard instruments have expanded their range and developed richer timbres, prompting composers to innovate. On the other hand, composers have pushed stylistic boundaries, establishing a feedback loop with instrument manufacturers that guides future keyboard instrument development.

This symbiotic relationship goes through four cyclical stages: interactivity, adaptability, complementarity, and co-creation. The term "symbiotic relationship" in the chart (Chart 04) emphasizes the interdependence between composers and keyboard instruments. There is also a feedback loop structure between them, which promotes each other.

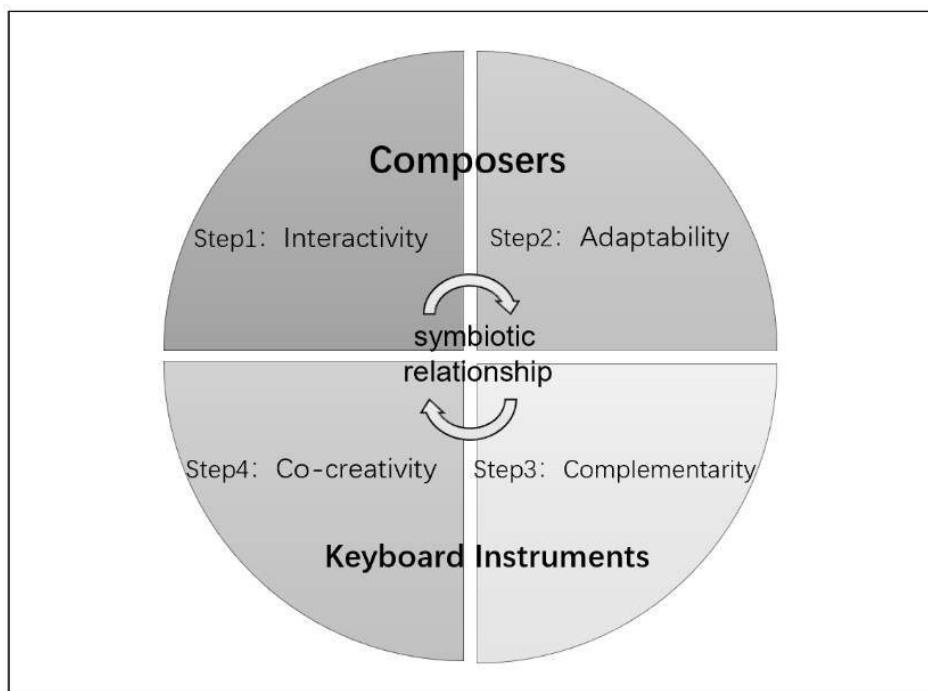


Chart 04. Symbiotic Relationship between Composers and Keyboard Instruments by author

The interactive phase initially allowed composers to explore fresh keyboard instruments for their range and sound qualities, sparking musical experimentation. Additionally, composers would contact instrument makers or even make changes themselves to better suit their needs.

As keyboard instruments advanced, the period shifted to adaptability. Composers began adjusting their compositions techniques and styles to meet with the evolving capabilities of the instruments. The development of the new keyboard instruments marked significant milestones, as these new features expanded the expressive possibilities. This reciprocal adaptation led to enhancements in instrument design, which followed the changing request for innovative approaches from the composers.

Then, in the third period, the concept of complementarity, also called synergy, emphasizes the combination of the composer's intention and the characteristics of the instrument, complementing each other's missing parts to create a more harmonious and beautiful piece. For example, the composer deliberately added trills to the harpsichord melody that were more suitable for the harpsichord pronunciation.

Finally, the phase of co-creation emphasized collaborative innovation between composers and instrument makers, resulting in mutual advances. This continuous feedback loop also promotes the development of both sides, both musical expression and instrument design are beginning to achieve self-breakthrough, and when they reach a certain height, they will break through the bondage, and more advanced keyboard instruments will be invented, and the relationship between the two will enter the next cycle of symbiosis.

All in all, each phase contributed to a continuous feedback loop. In the symbiotic theoretical framework the composers' innovations and demands influenced the design and capabilities of keyboard instruments, while these advancements, in turn, opened new creative possibilities for composers. Both of the keyboard instruments and composers influence each other, develop and make breakthroughs together.

Cyclical Spiral Trend

By superimposing the symbiotic framework onto a historical timeline, the result shows a continuous upward spiral of development, in which each stage of interaction, adaptation, complementarity, and co-creation promotes the continuous development of keyboard instruments and composers. This cyclical relationship highlights how the mutual influence between composers and instruments shapes the trajectory of music and provides a basis for predicting future trends in this symbiotic development model.

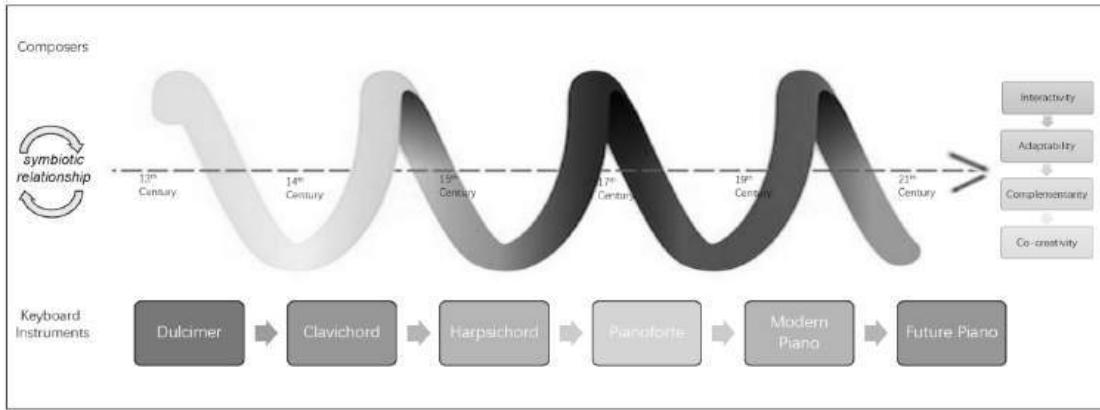


Chart 05. Evolutionary Timeline Model by author

The chart (Chart 05) illustrates a continuous upward spiral, the trend symbolizes the progressive and mutually beneficial interaction between composers and keyboard instruments. The spiral's ascent trend reflects the continuous development and refinement of both musical composition and instrument design. Furthermore, the development will progress through the four key cyclical phases over time.

The four methods of sounding a string on a keyboard evolved sequentially as rubbing, touching, plucking, and hammering in six musical periods. This paper uses the corresponding keyboard instrument representing the dulcimer, clavichord, harpsichord, pianoforte, and modern piano as the framework for analysis. The horizontal time axis marks significant centuries, from ancient times through the 21st century, indicating the historical progression of this relationship. The advance of time aligns with key developments in both composers' approaches and the evolution of keyboard instruments. The arrows connecting these keyboard instruments illustrate the progress and transformation of historical keyboard technology and design.

The symbiotic relationship on the right goes through four cyclical stages: interactivity, adaptability, complementarity, and co-creativity. Collaborative innovation between composers and instrument makers would shape future advances in both fields at each critical period. Also, the stages are connected by arrows that show the progression from one stage to the next, forming a continuous cycle of development. Furthermore, after another new keyboard instrument is invented, the cycle would start over again.

This chart summarizes the upward spiral of development driven by the symbiotic relationship between composers and keyboard instruments. It shows how, over the centuries, this relationship has evolved through four stages into a constant cycle. The diagram suggests that this dynamic interplay will continue to shape the future of both artistic music and scientific keyboard instrument design. The sequence of developments followed by this symbiotic relationship has not only shaped the history of music, but also provides insights into future developments in musical expression and instrument technology. By understanding this interconnected history, we can better predict and guide the ongoing co-evolution of composers and their instruments.

Conclusions

The results of this study indicate that the relationship between composers and keyboard instruments rises and develops in the form of a spiral. This evolving interaction demonstrates how each interactivity, adaptability, complementarity, and co-creativity stage drives the continued evolution of music composition and instrument design. Understanding the role of the dulcimer illustrates how ancient folk and classical traditions intertwined over the centuries to influence musical literacy across civilizations. The contributions of the clavichord and harpsichord marked a key step in the evolution of keyboard instruments, shaping compositional techniques of the time and extending to modern keyboard music. The shift to the pianoforte heralded a new era in music, as the instrument's enhanced expressive and dynamic capabilities offered composers new opportunities to express emotion and complexity. These developments have impacted on modern musicology and instrument craft, building a bridge between historical and contemporary musical practice.

Recommendations

Future research could delve into specific mechanisms by which compositional techniques influence instrument innovation, or explore the role of other instrumental families to gain a broader understanding of composer-instrument relationships. Practical applications might include using these insights to guide new keyboard instrument designs or inform educational curricula that link historical understanding with modern music creation.

Limitations

This research acknowledges two main limitations. Firstly, the focus was limited to only five major keyboard instruments, which may overlook other influential instruments or regional variations. Secondly, the reliance on existing literature and historical records may introduce biases regarding source availability and interpretation. These factors could affect the generalizability of the findings.

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The Impact of Income Inequality on Growth: A Comparative Analysis of Developed and Developing Economies By Jimith Parekh

Abstract

This research paper examines the complex relationship between income inequality and economic growth, focusing on developed and developing economies. Using recent data from 2010-2023 and advanced statistical analysis, it aims to provide clear insights into how income inequality influences economic performance. The literature review explores key theoretical perspectives and empirical findings, revealing how income inequality interacts with economic growth factors. The analysis considers regional disparities and the unique characteristics of different economic systems. Key findings demonstrate that higher GDPs are often associated with higher Gini coefficients, a measure of income inequality, though the relationship varies across regions. In developed economies, there is a clear correlation between lower inequality and stronger economic growth, indicating the advantages of equitable wealth distribution. In contrast, income inequality is positively linked to growth in many developing economies, particularly in areas where inequality drives investment and consumption, though this pattern differs regionally. The paper emphasizes the importance of accounting for local economic policies, historical contexts, and regional factors when analyzing income inequality's effects on growth. These findings offer valuable insights for policymakers focused on fostering sustainable development while addressing the challenges of rising income inequality.

Keywords Income inequality; GDP growth; cross-country analysis

I.Introduction

Income inequality and economic growth are two fundamental and often interconnected facets of macroeconomics, shaping the socio-economic landscapes of nations worldwide. While economic growth is heralded as a cornerstone of prosperity, income inequality often emerges as a counterbalance, raising questions about equitable wealth distribution and its implications for long-term development. This research investigates the nuanced relationship between these variables, focusing on the dichotomy between developed and developing economies. By exploring regional disparities, it seeks to uncover patterns and mechanisms that explain how income inequality influences, and is influenced by economic growth.

In developed economies, the narrative often revolves around high GDP levels, technological advancement, and capital accumulation. Yet, these nations frequently grapple with persistent income inequality, raising concerns about diminishing returns to growth and social stratification. Conversely, developing economies face different challenges—poverty alleviation, labor market informalities, and limited access to resources—factors that shape a distinct interaction between inequality and growth. Understanding this dynamic is crucial, as policymakers in these regions aim to foster inclusive development while sustaining economic momentum.

This study bridges theoretical frameworks with empirical evidence, using recent data on Gini coefficients and GDP from diverse regions. Through a comparative analysis of the United States and India as representatives of developed and developing economies, the paper delves into the multifaceted nature of income inequality. The case studies illuminate the broader trends, identifying outliers and regional variations that often elude generalized conclusions. Ultimately, this research aims to contribute to the ongoing discourse on the intersection of income inequality and economic growth by offering actionable insights. By analyzing data trends, exploring policy implications, and highlighting unique regional dynamics, the paper underscores the importance of tailored economic strategies that address the dual imperatives of growth and equity.

The rest of the paper is organized as follows: The next section presents a literature review. Then section three presents the data and methods. Section four presents the evidence analysis. Section five presents the conclusion, and finally, section six presents the references.

II. Literature Review

The relationship between economic growth and income disparity has been extensively researched and discussed. This literature overview looks at many perspectives and results from current research. It summarizes important techniques and findings from numerous research publications and incorporates theoretical models and empirical data. Understanding how income disparity impacts economic growth in both wealthy and developing nations is the aim.

Theoretical Perspectives

The connection between economic growth and income disparity is attempted to be explained by several ideas. **The Kuznets Curve** (*Kuznets, 1955*) is a well-known idea that suggests an inverse U-shaped link between inequality and development. This hypothesis holds that inequality increases in the early phases of industrialization when money concentrates among those who can take advantage of new economic opportunities. On the other hand, inequality declines as growth expands.

Neoclassical growth theories also explain this link. For example, according to the Solow-Swan growth model (*Solow, 1956; Swan, 1956*), more inequality may cause low-income households to save less, impeding capital accumulation and economic growth. Furthermore, **Human Capital Models** (*Lucas, 1988*) highlight how educational and skill disparities can impede human capital growth, affecting productivity and overall economic growth.

Models of political economy also draw attention to the possible drawbacks of extreme inequality. According to *Alesina and Rodrik (1994)*, social and political instability brought on by high inequality might raise the likelihood of civil unrest and even jeopardize economic progress. Additionally, *Acemoglu and Robinson (2012)* stress how political power and institutions shape the connection between inequality and growth. The elite may gain disproportionately from economic growth in societies with weak institutions and unequal power distribution, impeding inclusive development.

Empirical Evidence

Mixed findings have resulted from empirical research on the connection between economic growth and income inequality. In his seminal study, *Barro (2000)* discovered a negative correlation between growth and inequality, indicating that more disparity may obstruct economic progress. *Perotti (1996)* discovered a non-linear relationship, nevertheless, with greater inequality possibly promoting growth at low levels but impeding it at high ones.

Methodological Considerations

The outcomes of research on the connection between economic growth and income disparity are largely dependent on the methodologies employed. Numerous methodologies, such as panel data analysis, instrumental variable procedures, and cross-country regressions, have been used in diverse research. Because economic growth may have a simultaneous impact on inequality and other growth-influencing factors, *Durlauf and Johnson (1995)* emphasize the significance of addressing potential endogeneity difficulties in empirical studies.

Data Sources and Limitations

The World Bank, the International Monetary Fund (IMF), and the OECD are frequently used data sources in studies on inequality and growth. These data sources might, however, have drawbacks, including problems with measurement, possible biases in data gathering, and problems with data quality. For example, it can be difficult to evaluate income and wealth distribution accurately, especially in developing nations.

III. Data and Methods

This study utilizes updated data from the World Bank, extending to 2023, to analyze the relationship between income inequality and economic growth across diverse regions and income groups. Key metrics include Gini coefficients, which measure income inequality, and GDP per capita (in current USD), representing economic performance. Data was categorized by regions—such as East Asia & Pacific, Latin America & Caribbean, and Sub-Saharan Africa—and further grouped into low/middle-income and high-income categories. Graphs were created to illustrate GDP disparities across these income groups, while detailed tables provide country-specific Gini and GDP data for each region. This methodological approach ensures a nuanced understanding of regional trends and outliers, emphasizing both macroeconomic patterns and local deviations to offer a comprehensive perspective on the dynamics between inequality and growth.

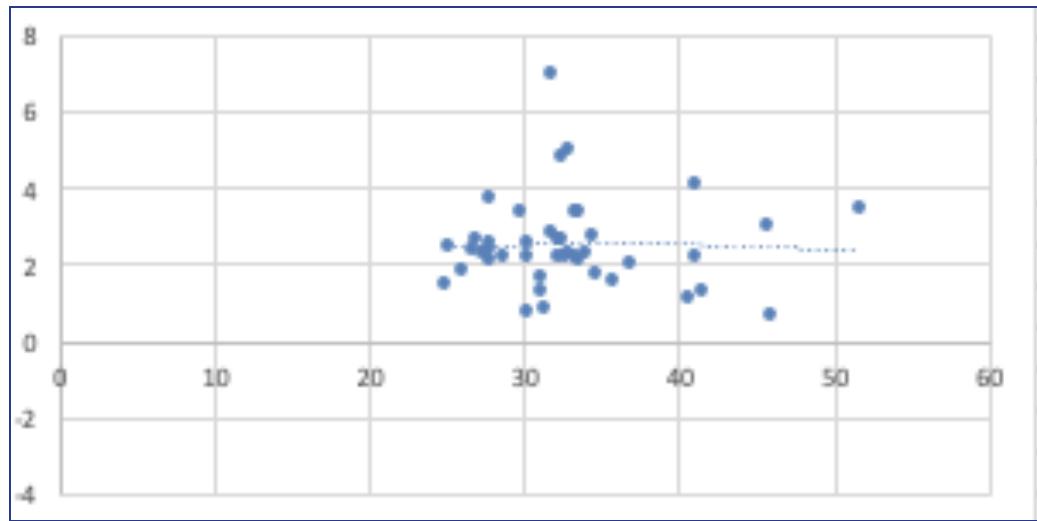


Figure 1. Growth vs. Gini Index: Developed Economies

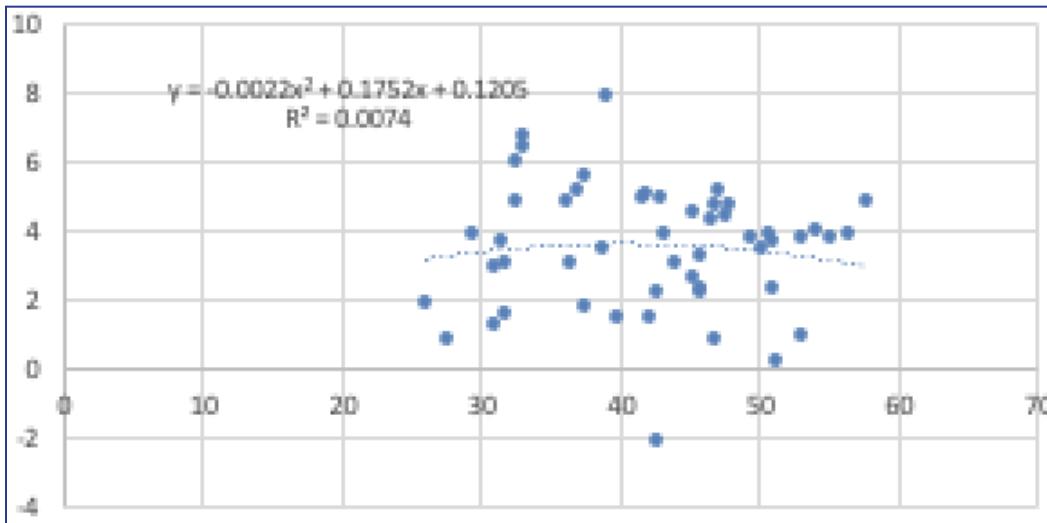


Figure 2. Growth vs. Gini Index: Developing Economies

IV. Evidence Analysis

The relationship between income inequality and economic growth varies significantly between developing and developed economies and is, shaped by distinct structural, institutional, and policy-driven factors. To better understand these dynamics, the analysis is divided into two parts: overall patterns observed in the data and region-specific trends. Figures 1 and 2 illustrate these broader patterns, contrasting the divergent behaviors of developed and developing economies. This section begins by discussing overarching trends before transitioning into a detailed exploration of individual regions.

Figure 2 highlights the weak correlation between income inequality and GDP growth in developing economies, with a low R^2 value (0.0074) signaling a minimal direct relationship. This weak association suggests that external factors such as governance quality, infrastructure development, or reliance on foreign investment play more significant roles in driving growth. Moreover, the erratic growth patterns seen in *Figure 2* reveal a lack of consistency, where

increasing inequality neither guarantees nor inhibits growth predictably. This unpredictability is further complicated by potential non-linear relationships, as external shocks and regional variations often overshadow the influence of inequality. The dispersed data points in *Figure 2* underscore this complexity, suggesting that inequality interacts with external variables in ways unique to each economy, thereby complicating the direct linkage to economic performance. In contrast, *Figure 1* presents the relationship between inequality and growth in developed economies as more variable but still lacking a strong direct correlation. The scattered data points highlight a wide range of growth outcomes, suggesting that inequality's effects are mitigated or amplified depending on the presence of strong institutions and robust social policies. For instance, welfare programs and progressive taxation systems may buffer against inequality's adverse impacts, leading to more stable growth even in the presence of high inequality. Additionally, *Figure 1* hints at a potential threshold effect, where inequality's influence becomes more pronounced only when it crosses certain critical levels. This dynamic illustrates how developed economies, while not immune to inequality's challenges, may be better positioned to manage their economic consequences.

The transition from this broader analysis sets the stage for exploring regional disparities in detail. While developed economies exhibit nuanced outcomes, specific regional factors—such as the role of natural resources, trade partnerships, and cultural norms—add further layers of complexity to the global narrative. These regional distinctions, discussed in the next section, illuminate the diverse ways in which inequality and growth intersect worldwide.

There is a notable variance in the relationship between economic growth and income inequality in different parts of the world. This section compares this relationship across several regions, looking at important causes, noteworthy outliers, and regional trends.

East Asia & Pacific

There is a moderately positive association between GDP and income inequality in East Asia and the Pacific. While nations with relatively low Gini coefficients—Australia and New Zealand, 32.47 and 32.47 respectively—enjoy high GDPs, China, with a higher Gini coefficient—39.06—also demonstrates substantial economic activity, with a GDP of 6.82. This implies that the region's economic performance is mostly driven by elements other than income disparity, such as solid export-oriented growth, technical advancements, and strong economic institutions. However, further research is necessary given the high levels of inequality in nations like China and Hong Kong, which probably contribute to unequal income distribution and social exclusion.

Europe & Central Asia

In general, income inequality is smaller in Europe and Central Asia than in other regions. In this area, there is little relationship between GDP and income disparity. With solid social welfare systems and substantial social safety nets, nations like France and Germany exhibit steady economic development and relatively low inequality (Gini coefficients of 29.0 and 29.5,

respectively). However, Russia stands out with a high Gini coefficient of 37.63 and a lower GDP, which may be the result of economic difficulties and wealth concentration in particular industries. Economic instability and inequality in this region could be made worse by the ongoing crisis in Ukraine.

Latin America & Caribbean

High levels of income disparity are a defining feature of Latin America and the Caribbean, which frequently has modest GDP growth. The GDP and income inequality are strongly positively correlated in this region. For example, Chile and Brazil both exhibit moderate GDP growth and increased inequality, with Gini coefficients of 52.3 and 53.9, respectively. This implies that both high inequality and economic disparities may be caused by elements like unequal access to resources, inadequate social safety nets, and historical legacies of inequality. Although certain nations, such as Uruguay, exhibit reduced inequality concerning GDP (Gini coefficient of 43.58), suggesting the possible efficacy of social programs, the general pattern points to a continuing difficulty in attaining both equitable development and economic progress.

Middle East & North Africa

The correlation between economic growth and wealth disparity is less evident in the Middle East and North Africa. Some nations with greater GDPs, like Qatar, have lesser inequality (Gini coefficient of 27.66); nevertheless, some nations with lower GDPs, such as Egypt (Gini coefficient of 33.9) and Tunisia, have higher inequality. This implies that the relationship between inequality and growth in this region may be greatly influenced by elements like civil discontent, political instability, and the concentration of wealth among small elite groups.

South Asia

High levels of income inequality and comparatively low GDPs are characteristics of South Asia. In this area, there is a discernible positive relationship between GDP and income inequality. India, for instance, has a larger GDP and notable inequality, as indicated by its Gini score of 35.7. The continuation of caste systems, restricted access to healthcare and education, and unequal economic opportunity distribution are some of the causes of this tendency.

Sub-Saharan Africa

With extremely low GDPs throughout the continent, Sub-Saharan Africa has the highest rates of income disparity in the world. In this area, it is unclear how income disparity and economic growth are related. For example, despite notable economic differences, Namibia (Gini coefficient of 59.88) and South Africa (Gini coefficient of 63.0) show exceptionally high levels of inequality. This implies that other elements—like weakened institutions, conflict, and restricted access to essential services—have a greater influence on how the economy develops.

Example: India vs. USA: A Comparative Analysis

Because of their different economic systems, political systems, and historical backgrounds, India and the U.S. exhibit divergent trends in the link between income disparity and economic growth.

United States: A Developed Economy with High Inequality

Despite having one of the biggest economies in the world, the United States has a comparatively high Gini coefficient (~41):

1. **Market-Oriented Policies:** Because of the United States' strong reliance on a free-market system, income inequality results from little interference with pay regulation. Although enormous money is produced in industries like technology and finance, its distribution is still uneven.
2. **Weakened Social Safety Nets:** The United States has very few redistributive policies, such as universal healthcare or subsidized education, in contrast to many other industrialized economies. Wealth disparities therefore continue to exist across populations and geographical areas.
3. **Race and Structural Barriers:** Minority populations are disproportionately impacted by historical and systemic injustices. Access to good-paying jobs and high-quality education is frequently restricted for African-American and Hispanic communities.

The United States continues to thrive economically despite high levels of inequality, indicating that the negative consequences of income inequality are somewhat mitigated by wealth concentration in productive industries like technology. However, since middle-class stagnation reduces overall consumption, this model runs the risk of causing long-term instability.

India: A Developing Economy with Structural Inequality

With a Gini value of ~35.7, India tells a different story. Its disparity has deep origins, even though it is very moderate when compared to the United States:

1. **Caste System and Social Stratification:** Economic chances are still shaped by historical problems like caste prejudice, particularly in rural areas. Upward mobility is restricted by this deeply ingrained inequality.
2. **Urban-Rural Divide:** Rural areas in India have fewer resources and develop more slowly as a result of the country's economic growth being centered in urban centers like Bangalore and Mumbai.
3. **Unequal Access to Education and Healthcare:** Although universal education initiatives like Sarva Shiksha Abhiyan have raised literacy rates, inequalities in quality still exist. Similar disparities in healthcare access exacerbate wealth disparity.

The manufacturing and service industries are major drivers of India's growth trajectory, but the advantages frequently do not reach the country's sizable rural populace. In contrast to the United States, India's disparity prevents a sizable section of the populace from participating in and profiting from economic growth, so directly impeding the country's potential for growth. *Table 1* below presents a comparison between the US and India and lists some implications of this comparison.

Table 1. Comparison and Implications

Factor	United States of America	The Republic of India
Gini Coefficient	~41 (high inequality)	~35.7 (moderate inequality)
Primary Drivers	Market-oriented policies, tech wealth	Urban-rural divide, social stratification
Social Safety Nets	Limited	Improving but inconsistent
Growth Impact	High GDP growth despite inequality	Inequality hinders broad-based growth

Key Takeaways

- Because of sector-specific wealth creation and consumption-driven markets, the United States shows that developed countries can maintain significant inequality while still experiencing robust development. However, the hazards of civil unrest and political polarization make this paradigm less long-term viable.
- India serves as an illustration of how structural obstacles worsen inequality's detrimental consequences on growth, particularly in developing nations. Income inequality has the potential to erode the pillars of economic growth in the absence of inclusive policy.

Policy Reflections

- Progressive taxation and growing social safety nets could reduce inequalities in the US without limiting innovation.
- For India to experience equitable progress, bridging the urban-rural divide through focused investments in infrastructure and education is essential.

V. Conclusion

The data in this analysis shows that there is a complicated and subtle relationship between economic growth and income disparity. Although there is a general trend that greater GDPs are frequently linked to higher Gini coefficients, there are considerable regional variations in this relationship. There is a clearer link between reduced inequality and faster economic growth in industrialized economies, indicating that fair wealth distribution can support long-term economic progress. For example, European nations with substantial social safety nets and comparatively low Gini coefficients frequently exhibit great economic success.

On the other hand, the link is more complicated in many developing economies. Higher GDPs may occasionally be linked to greater inequality, although this is frequently a reflection of underlying structural problems that could impede long-term sustainable growth, such as unequal

access to resources, shoddy institutions, and historical legacies of inequality. This is especially true in places like Sub-Saharan Africa and Latin America, where low economic growth frequently coexists with high levels of inequality.

Policy Implications

The analysis's conclusions have important policy ramifications. Policies that reduce economic inequality through focused social programs, human capital investments, and inclusive growth are essential in developing economies. These regulations could consist of:

- **Expanding access to education and healthcare:** Promoting the development of human capital and lowering inequality requires equal opportunities for all citizens.
- **Strengthening social safety nets:** The detrimental effects of inequality can be lessened by putting in place strong social security systems, unemployment insurance, and initiatives to combat poverty.
- **Promoting inclusive economic growth:** Encouraging equitable access to financing and markets, encouraging entrepreneurship, and supporting small and medium-sized businesses can all contribute to ensuring that the advantages of economic expansion are distributed more widely.
- **Addressing institutional weaknesses:** Encouraging inclusive and sustainable development requires bolstering governance, thwarting corruption, and encouraging accountability and openness in public institutions.

While sustaining economic development is still crucial in industrialized economies, policy should also address the growing inequality. These regulations could consist of:

- **Progressive taxation:** Putting in place progressive taxation schemes will guarantee that individuals with higher earnings make a larger contribution to the general welfare.
- **Strengthening social safety nets:** Granting all citizens greater access to reasonably priced homes, high-quality healthcare, and education.
- Encouraging labor market practices that lessen wage inequality and encourage fair wage growth.

Concluding Remarks

A crucial topic with significant social and economic ramifications is the connection between economic growth and income disparity. This study emphasizes how crucial it is to comprehend the intricate interactions between these two variables as well as the notable geographical differences in their relationship. In addition to being a social justice issue, addressing income disparity is essential to attaining equitable and sustainable economic growth for all.

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What are the Applications and Implications of Open-Source Artificial Intelligence?

By Raed Khanani

Abstract

Open-source software has been a popular software distribution model for both developers and users. Recently, this model has also been applied to artificial intelligence, resulting in a variety of applications and implications. This paper aims to provide the reader with an overview of those applications and implications by looking at the current open-source artificial intelligence landscape, how open-source artificial intelligence compares to proprietary artificial intelligence, the implications of its development and its applications. The research on open-source artificial intelligence is limited but the research on open-source software is not. As such, we have also reviewed the literature on open-source software to supplement our findings. While there is little difference between these two, there may be some nuance in the artificial intelligence aspect that may yield new discoveries. We find that the current landscape of open-source artificial intelligence is new and growing and also providing competition to proprietary artificial intelligence. We also find that there are many intrinsic and extrinsic factors affecting the success of open-source artificial intelligence projects. The literature also shows a wide variety of applications in the healthcare sector.

1. Introduction

Open-source software (OSS), as defined by The Open Source Initiative, is one where the source code is available to analyze, modify and distribute freely (“The Open Source Definition”). OSS is not to be confused with ‘open software’ which is software that does not completely adhere to the OSS standard and overall has a much looser definition that will be discussed further when talking about Meta’s Llama (Touvron et al., 2023; Touvron, Martin, et al., 2023; Grattafiori et al, 2024). OSS has been the catalyst for innovation in many fields. Due to its open nature, the source code can be studied and iterated on by large communities of developers thus pushing the boundaries in their respective fields (Bitzer and Schröder, 2007; Erickson et al., 2005; Pinto-Coelho, 2023). This is no different when it comes to Open-Source Artificial Intelligence (OSAI). OSAI tools like TensorFlow (Abadi et al., 2016; tensorflow) and platforms like HuggingFace (Pol, 2024; Castaño et al., 2024; Kathikar et al., 2023) democratize access to the same resources used by Google, Meta and OpenAI for their own Proprietary AI (PAI) models. This paper aims to understand the current landscape of OSAI, how OSAI compares to PAI, the implications of OSAI development and the applications of OSAI in various fields.

2. The Current OSAI Landscape

Understanding the current OSAI landscape is important as it serves as a base for the ideas that will be explored later on in this paper. In order to grant a holistic overview of the OSAI landscape, this paper will discuss an OSAI model, tool and platform, which are Meta Llama, TensorFlow and HuggingFace respectively.

2.1 Meta LLaMA

Large Language Model Meta AI (Llama) is Meta's line of large language models (LLM) (Touvron et al., 2023; Touvron, Martin, et al., 2023; Grattafiori et al, 2024). An LLM is an AI that is trained on large datasets of text in order to analyze, understand and generate human language (think of ChatGPT). LLMs are designed using advanced machine learning (ML) techniques and transformer based architectures like GPT (Generative Pre-trained Transformer) and BERT (Bidirectional Encoder Representations from Transformers). Meta's LLM is currently in its third generation with Llama 3 which has three models: Llama 3.1 8B, Llama 3.1 70B and Llama 3.1 405B which have 8, 70, and 405 billion parameters respectively (Grattafiori et al, 2024). Meta's flagship Llama 3.1 405B model manages to remain competitive against other leading proprietary models such as OpenAI's GPT-4 Omni across a wide variety of benchmarks such as coding, math and reasoning despite having fewer parameters (Grattafiori et al., 2024). Meta has been able to achieve this performance due to 3 main factors: data, scale and managing complexity. Compared to Llama 2 (Touvron, Martin, et al., 2023), the quality and quantity of pre-training and post-training data has been greatly improved by increasing the selectiveness when curating pre-training data and increasing the rigour and quality assurance of post-training data (Grattafiori et al., 2024). Llama 3 was pre-trained using 15.6 trillion text tokens (Grattafiori et al., 2024), almost 8 times more than Llama 2's 2 trillion text tokens (Touvron, Martin, et al., 2023) and 11 times more than Llama 1's 1.4 trillion tokens (Touvron et al., 2023). Furthermore, Llama 3 uses a standard dense Transformer architecture and a more simplified post-training procedure, allowing the project to scale up more smoothly in the future (Grattafiori et al., 2024).

What makes Meta's Llama stand out is Meta's approach to its development. Meta emphasizes a research-friendly and open approach to AI development. All Llama models are available on HuggingFace with their source code and are approaching a total of 350 million downloads (*Meta-Llama* (*Meta Llama*)). Furthermore, Llama models are trained off public datasets and open-source information, further emphasizing transparency, accessibility and security as no private and/or sensitive data that could potentially be exposed is being used (Grattafiori et al., 2024).

Meta calls their Llama models 'open-source' ("Llama"), however, they are not licensed under a typical OSS license such as Apache (*Apache License*) or MIT. The Llama 3 models are licensed under the Meta Llama 3 Community License, a custom commercial license agreement (*LICENSE · Meta-Llama/Meta-Llama-3-70B at Main*). The aforementioned Apache and MIT licenses allow for complete freedom in how the software is used and distributed, but the Llama 3 Community License has a few restrictions. Under section 2, if the version of the LLaMA 3 model released has greater than 700 million monthly active users, the creator must request a license from Meta (*LICENSE · Meta-Llama/Meta-Llama-3-70B at Main*). Under section 2.v, users are not allowed to train other LLMs using the outputs generated by the Llama 3 model (*LICENSE · Meta-Llama/Meta-Llama-3-70B at Main*). The first restriction prevents users from running large internet services; and while this is only going to affect a small percentage of users, it is still a restriction. The second restriction is more likely to affect a large percentage of users.

By The Open Source Initiative's definition ("The Open Source Definition") the Llama models cannot be considered OSS but rather open software.

2.2 TensorFlow

Developed by Google, TensorFlow is an open-source platform that provides a comprehensive and flexible set of tools and libraries for ML. TensorFlow is one of the most popular platforms for creating deep learning models, especially for production and industrial use cases due to its scalability as well as its compatibility with mobile devices using TensorFlow Lite.

TensorFlow gets its name from the way it handles machine learning. TensorFlow uses tensors: multidimensional arrays that have the capability to operate across different dimensions. These tensors are used to illustrate the data that flows through TensorFlow models (Abadi et al., 2016; Pang et al., 2019).

TensorFlow offers an exhaustive set of features and components for every stage of machine learning: TensorFlow Core, the base library for building and deploying machine learning models; Keras API, a high-level API designed for fast experimentation; TensorFlow Lite, used for deploying machine learning models on mobile devices; TensorFlow Extended, a platform for developing machine learning pipelines in production environments and TensorFlow Hub, a repository for sharing and using pre-trained models (Pang et al., 2019).

TensorFlow's success is attributed not only to its flexibility but also the active open-source community surrounding it and the extensive documentation. Its open-source nature allows for millions of developers worldwide to contribute (tensorflow) (sometimes in the form of add-ons and libraries that extend TensorFlow's capabilities) and consequently improve TensorFlow whilst also amassing a wealth of shared knowledge.

2.3 HuggingFace

HuggingFace is a platform that provides developers with useful open-source libraries, datasets and pre-trained models to help kickstart their projects. It has an extensive transformers library that includes pre-trained models and tools that work with transformer based architectures such as BERT and GPT. HuggingFace also has a wide variety of datasets including text, images and audio allowing developers to quickly train ML models to produce effective results (Pol, 2024).

That being said, many of the AI models on the HuggingFace platform contain security vulnerabilities. A study conducted in 2017 found that across the 110,000 pre-trained models that were parsed, 35.98% had high-severity vulnerabilities and 6.79% had low-severity vulnerabilities (Kathikar et al., 2023). However, when looking at the forked and searched repositories as compared to the root repositories, the majority of the vulnerabilities were of low-severity (Kathikar et al., 2023). This is only possible due to the open-source nature of the platform. When forking the repositories to adapt the models for their own use cases, the users also patched the high-severity vulnerabilities. So while there might be many vulnerabilities in the

pre-trained models on HuggingFace, it still offers a good starting point for most developers (Castaño et al., 2024).

3. OSAI vs. PAI

3.1 Security

One of the main factors that can be taken into consideration when deciding between OSAI and PAI (as well as OSS and proprietary software in general) is security. One might assume that free access to the source code of the software would leave it vulnerable to be exploited by bad actors, and that assumption does hold true in the short-term. When open-sourcing a project, many vulnerabilities become apparent. With many developers in large communities surrounding open-source projects, these vulnerabilities are identified and patched swiftly as many of these developers personally use the software. So, for each bad actor looking to exploit those vulnerabilities, there could be hundreds of developers raising awareness and patching them (Hoepman and Jacobs, 2007).

In the long-run, open-sourcing projects have been shown to increase security (Payne, 2002; Witten et al., 2001; Hoepman and Jacobs, 2007; Al-Kharusi et al., 2024). There are a few social aspects when it comes to security in OSS. Firstly, OSS projects are held to a higher standard as poor code can hurt a developer's credibility (Hoepman and Jacobs, 2007). Secondly, with large communities of developers collaborating together, security updates become faster and more comprehensive (Hoepman and Jacobs, 2007). However, the biggest reason is the increased transparency. With the source code being freely available, it is open to public scrutiny. This allows for vulnerabilities to be identified before they are exploited, unlike closed-source projects where flaws often remain hidden until they are exploited (Hoepman and Jacobs, 2007; Jokonya, 2015).

The security benefits can be seen in the case of HuggingFace in which the transparency allowed users to identify vulnerabilities in the pre-trained models they needed to use and patch those high-severity vulnerabilities in their forks of the root repository (Kathikar et al., 2023). Furthermore, many governments including France, China, Japan and South Korea have started pushing for OSS to be used in their government systems with security being the driving force behind their initiatives. The reason for this being that OSS can be independently audited while proprietary software cannot, potentially leading to mistrust (Jokonya, 2015).

3.2 Customization

A key feature of OSAI is customizability. Meta's Llama has served as a foundation model for many OSAI projects. MGH Radiology Llama is an LLM powered by the Llama 3 70B model and is built off its predecessors Radiology-GPT and Radiology-Llama2. Radiology Llama came about due to the limitations of general purpose proprietary LLMs much like other specialized OSS. Seeing the potential of LLMs in assisting radiologists, researchers trained the Llama 3 70B model on datasets provided by the Massachusetts General Hospital. The result of this was the

creation of the specialized MGH Radiology Llama LLM that had the necessary in-depth domain-specific knowledge needed to effectively assist radiologists (Shi et al., 2024).

Another specialized OSAI model is Meditron. Prior to the release of Meditron, many attempts had been made to improve LLM's medical knowledge and reasoning but the resulting models were either closed-source or limited in scale in terms of their parameters. As a result, Meditron was created. Meditron is a suite of open-source LLMs adapted to the medical domain. It is built off Meta's Llama 3 and comes in 7B and 70B variants. The latest version, MEDITRON-70B, outperforms closed-source models such as Med-PaLM and GPT-3.5 and remains competitive with the newer Med-PaLM-2 and GPT-4 (Chen et al., 2023; Chen, Romanou, et al., 2024).

3.3 Innovation

Innovation is synonymous with open-source. OSAI tools such as MONAI (Medical Open Network for AI) have served as a catalyst for the rapid innovation in the domain of medical imaging (Cardoso et al., 2022; Pinto-Coelho, 2023). Medical imaging uses X-Rays, Ultrasound scans and MRIs (Magnetic Resonance Imaging) to detect and diagnose diseases. This field has been revolutionized by deep learning models trained on large datasets of medical images to learn patterns and help detect diseases that might not be apparent to the human eye (Pinto-Coelho, 2023). MONAI is an open-source framework for deep learning specifically for medical imaging. It is based on PyTorch, a TensorFlow competitor developed by Meta. MONAI serves as the foundation for deep learning medical imaging models by extending the capabilities of PyTorch to support the processing of medical data. MONAI is able to streamline the development and deployment of medical AI models thus paving the way for further innovation (Cardoso et al., 2022).

3.4 Cost

OSS is free to use, modify and distribute; this prevents vendor lock-in and dependence on monopolistic technologies which greatly benefits the governments (Jokonya, 2015; Russo, 2016). While OSS is free, this does not mean that it has no cost. However, the cost of OSS is relatively low compared to proprietary software and this is the greatest benefit for businesses adopting OSS (Spinellis and Giannikas, 2012). Proprietary software is the better option for companies in which the cost of their software does not make a large proportion of their total cost and are also in rapidly-changing demanding environments (Spinellis and Giannikas, 2012).

4. Implications of OSAI Development

4.1 Openness

Openness in AI has many strategic implications. In the short to middle term, openness seems to have net positive consequences such as innovation and the dissemination of existing technologies (Bostrom, 2017). In the long-run, things get a bit more complicated. On one hand,

increased openness in AI would make the ‘AI race’ more competitive, thus creating problems when it comes to implementing control measures due to the fast rate of innovation (Bostrom, 2017). On the other hand, openness could improve the control problem as it will generate wider engagement with the scientific community which may have relatively more interest in the public good of safety (Bostrom, 2017; Bildirici, 2024).

4.2 Collaboration

The OSS development cycle allows anyone and everyone to participate in it. It relies on the incremental contributions and collaborative effort of developers across the globe brought together by a shared goal. With so many contributors, success of the open-source project depends on effective coordination and management. This is where version control systems like Git and platforms like GitHub step in (Ming-Wei Wu and Ying-Dar Lin, 2001). OSS projects are stored as repositories where developers can contribute code through ‘commits’ and bring attention to problems with ‘issues’. Studies show that the most successful OSS projects make full use of these features by labelling and writing detailed descriptions of issues and assigning them to developers (Yang et al., 2023; Midha and Palvia, 2012).

One more thing to consider is the quality of the code that is being contributed. Due to the nature of OSAI development, all contributions are done voluntarily. Furthermore, due to permissive licenses like Apache (*Apache License*) and MIT, developers are not held accountable by external factors for the code they contribute so the quality of contributed code depends on a developer’s perceived code accountability (Bartsch et al., 2024). This personal accountability is influenced by system-related factors such as the legal framework and software license being used, project-related factors like which systems or professional settings the software will be integrated into and individual factors like reputation and career prospects (Bartsch et al., 2024). However, there is an inverse relation between perceived code accountability and code contribution. Higher perceived code accountability discourages participation in OSS projects as it entails a greater effort and responsibility (Bartsch et al., 2024) and so it is important to maintain a balance to achieve success.

4.3 Success Factors

Success of an open-source project can be divided into technical success (developer activity) and market success (project popularity). This success is determined by intrinsic and extrinsic factors. Intrinsic factors consist of complexity and modularity whereas extrinsic factors consist of the user base, license type, developer base and language translations (Midha and Palvia, 2012). The study finds that in the early stages of the OSS development cycle, success is driven by extrinsic factors such as the license type and user base as this attracts early adopters and allows projects to gain some momentum behind them. By using a restrictive license in the early stages of development, the project will attract more committed developers and once a solid foundation is built, the license can be switched to a more open one (Midha and Palvia, 2012). On the other hand, intrinsic factors like lower complexity and increased modularity increase

developer retention which is crucial for long-term sustainable success of OSAI projects (Midha and Palvia, 2012).

5. Applications of OSAI

5.1 Healthcare

The field of healthcare is vast and requires professionals specialized in each domain. Similarly, AI must also be specialized in order to be effective in the healthcare sector. Many PAI models lack the specialized knowledge needed to effectively provide assistance. OSAI on the other hand can be customized for any domain as seen with MGH Radiology Llama (Shi et al., 2024) and Meditron (Chen et al., 2023; Chen, Romanou, et al., 2024). The healthcare sector greatly benefits from this key characteristic of OSAI, especially the domain of Radiology. MGH Radiology Llama opens up the potential for LLM assistants in other fields and MONAI (Cardoso et al., 2022) has played a big role in streamlining the process of training ML models for medical imaging purposes (Pinto-Coelho, 2023).

5.2 Education

Combining both healthcare and education, AnatomyGPT is a customized version of ChatGPT based on OpenAI's GPTs (Collins et al., 2024). AnatomyGPT serves as an intelligent tutoring system for the anatomical sciences. Similarly to Meta's Llamas (Touvron et al., 2023; Touvron, Martin, et al., 2023; Grattafiori et al., 2024), AnatomyGPT is trained on open-source textbooks. In its test against the proprietary ChatGPT on prompts from the National Board of Medical Examiners, Anatomy GPT achieved high scores on sample items for Gross Anatomy, Embryology, Histology and Neuroscience whilst giving multiple citations, whereas ChatGPT gave none (Collins et al., 2024).

Mathpresso, a South Korean startup created MathGPT which is an LLM specialized for math and built off Meta's Llama 2 (Touvron, Martin, et al., 2023) model. It recently beat GPT-4 and Microsoft's ToRA 13B (previous record holder) in the MATH and GSM8K benchmarks (Mathpresso, 2024). It is trained on data collected from Mathpresso's QANDA platform which handles 10 million problem searches every day (Mathpresso, 2024). The data includes detailed learning contexts and user interactions, allowing MathGPT to effectively provide assistance (Mathpresso, 2024).

6. Methodology

In this paper, we attempted to cover a wide range of areas in the OSAI literature in order to provide a general overview. Many OSAI software and tools have research papers published alongside them. These served as the primary source for the technology discussed in section 2. When comparing OSAI to PAI, we chose the 4 most discussed factors in the literature to compare. In section 4, there was especially limited literature on OSAI development but there was a lot on OSS development. As such the OSS literature was used to supplement the findings on

OSAI development. This should not have any implications given the section discusses the method of development (which is common between the two) rather than the subject of development.

7. Concerns and Limitations

Due to the limited literature on OSAI, this paper uses OSS research and extends its findings to OSAI under the assumption that they are very similar. This assumption seems reasonable as many of the OSS and OSAI papers discussed overlap and support each other and so should not have any negative implications on the research. The biggest difference between OSS and OSAI is the subject of development: AI. This nuance may result in findings that are not the same between OSS and OSAI and so that is why we call for more research on the applications of OSAI. As of right now, most of the applications have been in the healthcare sector, more specifically Radiology. There is potential for research on OSAI in the public sector given the existing literature for OSS (Jokonya, 2015; Russo, 2016).

8. Conclusion

The field of OSAI is vast, and this paper only scratches the surface. There are few open-source AI models, the closest we have to that is Meta's Llamas (Touvron et al., 2023; Touvron, Martin, et al., 2023; Grattafiori et al, 2024). Most of the OSAI landscape consists of tools like TensorFlow (Abadi et al., 2016; Pang et al., 2019), PyTorch and MONAI (Cardoso et al., 2022) and platforms like HuggingFace (Pol, 2024; Castaño et al., 2024; Kathikar et al., 2023). The OSAI landscape is overall very developer and research oriented as seen with the healthcare applications (Shi et al., 2024; Chen et al., 2023; Chen, Romanou, et al., 2024; Cardoso et al., 2022) rather than commercially oriented like generalist PAI models such as GPT-4. OSAI development has many implications and factors that affect its success. It is important to try and juggle these variables but before that, the foundation must be strong by having well managed repositories (Yang et al., 2023; Midha and Palvia, 2012; Bartsch et al., 2024).

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The Psychological Cost of Conflict: Examining the Impact of Conflict on Mental Health

By Michael Peng

Abstract

Wars and conflicts affect all people regardless of their status or position, and the prevailing detriment of mental illness knows no jurisdiction. According to estimates, currently, the globe is struggling with the most active conflicts since WWII, and it means that people suffering from mental health deterioration in conflict-affected countries is crucial to comprehensively analyze in the future. Psychiatric disorders are a problem needing treatment for veterans of military operations, but veterans are not the only people exposed to the adverse effects of armed conflicts. The situation with the mental health of people living in areas affected by violence is incredibly critical, and the already existing methods of social rehabilitation often prove to be ineffective. Most such psychiatric disorders have a direct correlation with the presence of wars and violence around, and therefore, highlight the requirement of an overarching framework to solve the issue.

Introduction

According to the Global Peace Index 2024, there are 56 active conflicts around the world. This is the highest number since World War 2. International involvement in wars is also the highest it's been since the GHPI index was created, as there are 92 countries engaged in a conflict beyond their borders (Institute for Economics & Peace). One major impact of conflict is the mental health problems citizens and soldiers can develop. According to new estimates by the WHO, in areas affected by conflict, one in five is living with a mental disorder such as mild depression anxiety or psychosis, as shown in figure 1 below. Even worse, almost one in ten is living with a moderate or severe mental disorder (World Health Organization: WHO). With a large proportion of the world currently experiencing conflict, treatment and prevention of mental health disorders must be a significant priority in global health and peace.

How many people experience mental health conditions in conflict zones and globally?

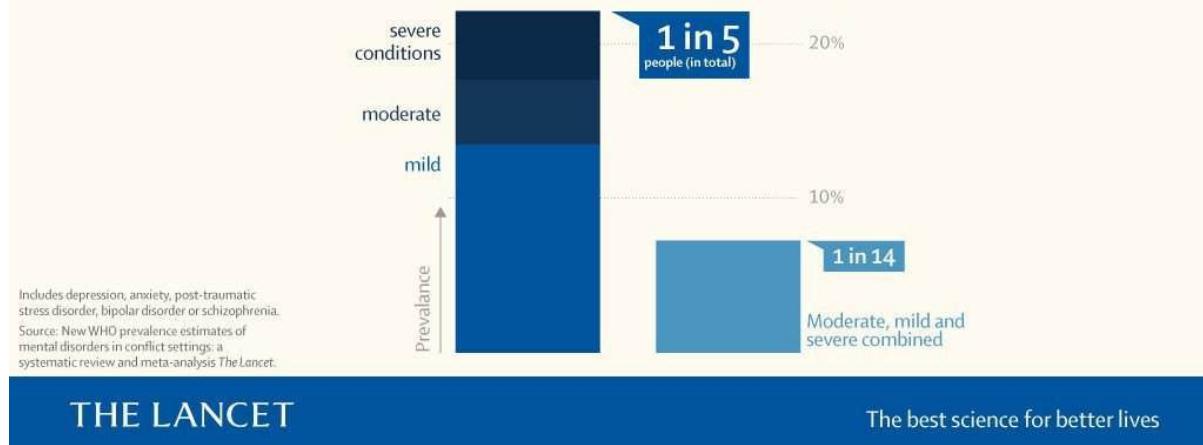


Figure 1: Percentage of people experiencing mental health conditions in conflict zones and globally (United Nations, 2019).

Mental Health in Soldiers

Soldiers are often the most affected by mental health issues in conflict-affected regions. The Israeli-Palestinian conflict has caused devastating mental health impacts on soldiers. According to a statement made in August 2024 by the Israeli defence ministry's rehabilitation division, 35% of the soldiers complained of their state of mind, and 27% developed "a mental reaction or post-traumatic stress disorder (PTSD)." Research finds that this may reflect wider realities wherein 20-30% of soldiers begin facing health challenges following deployment. Long-term effects persist for years in some cases, as noted in research (Nasveld et al.). Reports suggest that mental health treatment is often underutilized, with U.S. veterans showing only a 21.3% current treatment rate, which indicates that most of the soldiers with current mental disorders are not in treatment now (Colpe et al.). Increased exposure to war can also increase mental health problems, which can increase significantly due to cumulative exposure to conflict, as shown in figure 1 (Russell & Figley).

Dosage Effect of Cumulative Exposure to War Stress

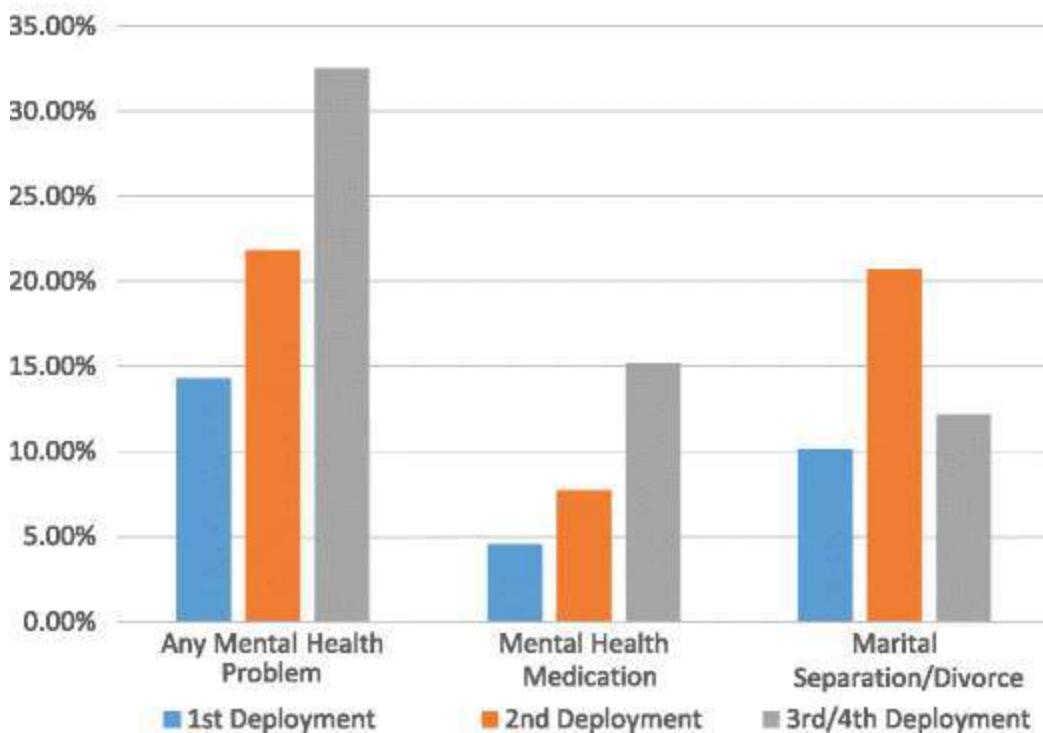


Figure 2: Dosage Effect of Cumulative Exposure to War Stress (Russell & Figley, 2017).

Mental Health in Citizens of Conflict-Affected Regions

While citizens may not be directly involved in fighting, conflicts can severely impact their mental health. The WHO estimated that, in the situations of armed conflicts throughout the world, “10% of the people who experience traumatic events will have serious mental health problems and another 10% will develop behaviour that will hinder their ability to function effectively. The most common conditions are depression, anxiety, and psychosomatic problems such as insomnia or back and stomach aches (Murthy & Lakshminarayana).” In Iran, which has been constantly involved in war, whether directly or indirectly, nearly 25% of citizens have psychiatric disorders (Damari, Sharifi, Asgarood, & Hajebi). Surveys conducted in Afghanistan after two decades of war found that Symptoms of depression were found in 67.7% of respondents, symptoms of anxiety in 72.2%, and PTSD in 42% (Murthy & Lakshminarayana). Studies show that greater exposure to traumatic events causes increasing mental health damage. During the Yugoslav wars, an increasing amount of traumatic events were negatively linearly correlated with mental health status and social functioning in those aged 65 years or older and had previous psychiatric illnesses or chronic health conditions (Murthy & Lakshminarayana). In the current Israeli-Palestinian conflict, Gazan citizens have displayed alarming mental health issues. The Gaza Community Mental Health Programme reports that over 65% of surveyed residents are experiencing symptoms of severe psychological distress, with many, including

children, having signs of PTSD, anxiety, and depression (Gaza Community Mental Health Programme).

Available Rehabilitation Systems That Treat Mental Health Issues

Rehabilitation systems that treat mental health issues are critical in conflict-affected settings. The existing healthcare system and military-based healthcare are the most common platforms involved in trauma and rehabilitation interventions (Jain et al.). However, these systems currently lack the tools necessary to treat patients. The issue with rehabilitation lies in the complexity of the issue it's trying to solve. Studies show that "There is no single methodology that would contribute to a more productive implementation of this process [rehabilitation] (Yukiia Tsurkan-Saifulina)." Rehabilitation is particularly difficult for soldiers because there is a stigma in opening up about their physical and mental injuries, with 43% of US veterans believing that admitting to psychological problems will lead to loneliness and other problems in interpersonal communication (Yukiia Tsurkan-Saifulina). For rehabilitation services to be effective for military personnel and citizens, studies show they need to be accessible, comprehensive, detailed and structured (Colpe et al.) (Yukiia Tsurkan-Saifulina).

Conclusion

Mental health issues can have devastating impacts on the well-being of people globally. The WHO states that "Mental health conditions can cause difficulties in all aspects of life, including relationships with family, friends and community... The economic consequences of mental health conditions are also enormous, with productivity losses significantly outstripping the direct costs of care (WHO)." Mental illnesses have a negative impact on family quality of life, as well as an increase in social exclusion (Walton-Moss, Gerson, & Rose) (Boardman). Anxiety, depression, insomnia, and hallucinations are just a few of the adverse impacts poor mental health can have on the quality of life people enjoy (de Cates et al.). All of these issues are especially pressing in conflict-affected areas, warranting immediate attention and treatment. Having adequate rehabilitation systems that are holistic and accessible is necessary to help military personnel and citizens cope with war and its traumas. At the moment, finding the most effective rehabilitation program remains to be found.

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How Does the Rapid Advancement of the CRISPR-Cas9 Genome Editing Technology Affect the Modern Societal and Scientific Views on the Ethics for the Genetic Testing and Editing of Humans and Other organisms? By Sreeya Nair

ABSTRACT

CRISPR-Cas 9, a genome editing tool, has revolutionized the scientific world and society. It presents many opportunities in medicine, environmental welfare, and commerce. However, the current comprehension of CRISPR technology and its impact on the genome and society is still incomplete. CRISPR risks being a potential environmental hazard, introducing off-target effects to edited organisms, and societal misuse. This paper explores the broad applications, advantages, and optimistic aspirations associated with CRISPR technology, while also acknowledging the ethical considerations that arise alongside its usage. It first addresses the general applications and limitations of CRISPR, followed by how CRISPR affects animals and commerce. Afterward, the paper goes over the testing procedures of CRISPR on non-human primates and ends with editing humans.

Keywords CRISPR, genetic engineering, ethics, gene drive, aquaculture, non-human primates, testing, gene therapy, embryo editing, blastocyst complementation

INTRODUCTION

While gene editing is a relatively new technology, humans have selectively bred animals and plants for centuries.¹⁻⁵ Selective breeding occurs when humans choose which animals should produce offspring because they have more desirable traits. Selective breeding, also known as artificial selection, takes longer and produces less exact results compared to gene editing technology, but humans still depend on selective breeding, mainly for food. For example, common vegetables consumed by humans today, such as cabbage, broccoli, and cauliflower were all selectively bred from wild mustard. Selective breeding also has commercial impacts. Dogs have been selectively bred for maximum popularity and profit, although undesired side effects have occurred for short-faced breeds, such as defects in their neurotomy. Another example of commercial breeding comes with fish, which have been bred to reduce susceptibility to disease and increase profit. However, as technology improves, scientists become less reliant on the genes organisms already possess and shift to creating new genes. Gene editing technologies, notably CRISPR-Cas9, change an organism's genetic code without breeding. It produces desired results quickly and cost-efficiently.

CRISPR-Cas9 technology, introduced in 1987, creates a more efficient, simple, and affordable means of editing genomes.⁶⁻¹¹ Through genome editing, scientists can insert, edit, delete, replace, or modify DNA in the genome of organisms. CRISPR speeds the arduous process of gene editing without physically depending on the animal's traits for desired results. With this gene editing technology, scientists quickly recreate cell and animal models to accelerate research on cancer or mental illnesses. Although other gene editing technologies

existed before CRISPR, scientists could not perform edits as efficiently. For example, CRISPR performs better than previous gene editing tools such as ZFNs (zinc-finger nucleus) or TALENs (Transcription activator-like effector nucleases) due to CRISPR's easy design and ability to modify several genomic sites simultaneously (Table 1). In addition, CRISPR is less complex and more cost-efficient than other genome editing tools. CRISPR presents a myriad of opportunities for scientific and social advancements and has already been used to develop allergy-free foods, eradicate pests, and improve animal breeds.

Table 1¹²

This table compares CRISPR with other gene editing tools such as ZFNs or TALENs.

Feature	ZFNs	TALENs	CRISPR
Length of recognized DNA target (bp)	9–18	30–40	22 (with a PAM sequence)
Mechanism of target DNA recognition	DNA–protein interaction	DNA–protein interaction	DNA–RNA interaction via Watson-Crick base pairing
Mechanism of DNA cleavage and repair	Double-strand break induced by FokI	Double-strand break induced by FokI	Single- or double-strand break induced by Cas9
Design	Challenging. Available libraries of zinc finger motifs with predefined target specificity, but zinc finger motifs assembled in arrays can affect specificity of neighboring zinc finger motifs, making the design challenging.	Easy. TALENs motifs with target specificities are well defined.	Easy. SgRNA design based on complementarity with the target DNA.
Cloning	Requires engineering linkages between zinc finger motifs.	TALENs do not require linkages. Cloning of separate TALEN motifs can be done using Golden Gate assemblies.	Expression vectors for Cas9 available. SgRNA can be delivered to cells as a DNA expression vector or directly as an RNA molecule or pre-loaded Cas9-RNA complex.

Table adapted from (12).

Although CRISPR holds many promising benefits, CRISPR and gene editing present new issues in society, one of which being hereditary off-target diseases.^{13–16} Hereditary off-target diseases, which are diseases that CRISPR accidentally creates on the human germline and can be passed on, present a serious risk to human society, especially when used in clinical applications. Because every country has different rules about genetic editing, CRISPR also presents a risk of being misused between countries for warfare. It reduces the technical barrier to the creation of biological weaponry, which is extremely dangerous in this turbulent world. As CRISPR technology advances, CRISPR may indulge human society into choosing “desirable” traits for

offspring, such as athleticism, extreme genius, or attractiveness. A notable example of the misuse of CRISPR is by the Chinese scientist He Jiankui, who edited two twin babies during their mother's pregnancy to remove the risk of HIV. At surface level, the scientist saved two girls from risking HIV, a serious infection in the white blood cells. However, this procedure presented significant risks to the girls and their mother, raising multiple ethical concerns. CRISPR advances rapidly and demands active efforts to regulate its usage so that it can be used responsibly for the benefit of this world.

This paper will cover the development and testing of CRISPR-Cas9, and the ethical implications of testing and editing animals, non-human primates, and humans. It goes over the effects of CRISPR on society and science.

APPLICATIONS AND LIMITATIONS OF CRISPR

The CRISPR-Cas9 system (Figure 1), founded in 1987, is naturally found in bacterial defense systems in archaea and bacteria;¹⁷⁻¹⁹ however, scientists have learned to use it as a method of editing the genes of any organism. CRISPR has many different varieties, and Class 2 is considered the simplest. Using an enzyme called Cas9, the nuclease makes a clean break on both strands of the DNA, which has a shape of a double helix. It utilizes an RNA tag and cuts any part of the DNA that matches it. Once that portion of the DNA is cut, the DNA's repair enzymes reseal the break. The whole process takes around 6 or 7 hours.⁶⁸

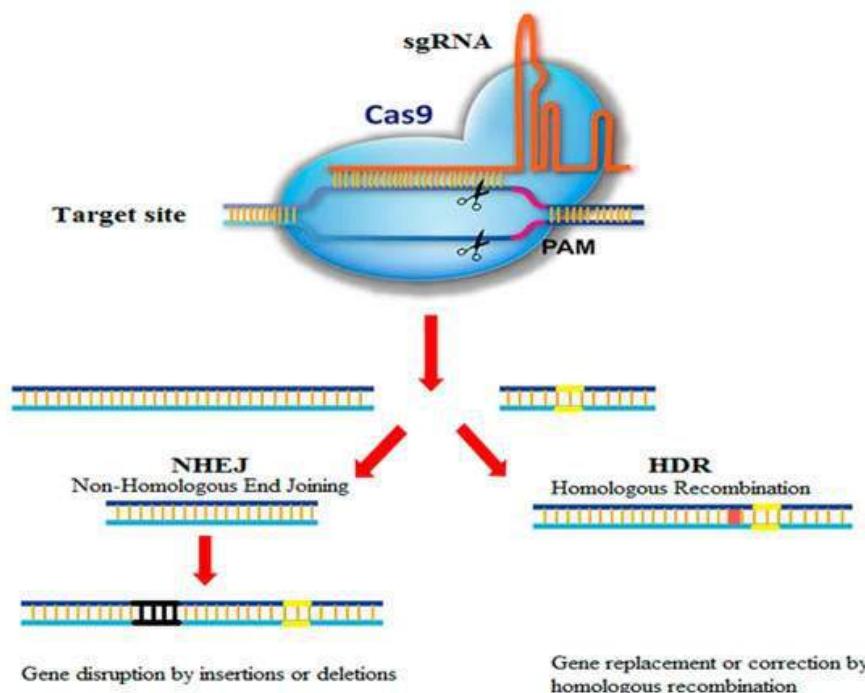


Figure 1: A basic level of how CRISPR works. The Cas9 enzyme causes a break in the target site, which CRISPR then edits.

In addition to its practicality, CRISPR has proven to be advantageous in the advances of science and research.²⁰⁻²⁴ Over 7000 monogenic diseases have the potential to be modified and cured by gene therapy and CRISPR. For instance, BCL11A, a gene that expresses hemoglobinopathies, a hereditary monogenic disorder where the hemoglobin is abnormally shaped, has been reduced to 54.6% in disease models using electroporation in a CRISPR trial. Additionally, CRISPR has increased scientific knowledge of cancer through tumor research modeling. CRISPR created rapid tumor models both in vitro and in vivo, which gives scientists a deeper understanding of the genetic determinants of the mechanisms underlying the creation and development of a tumor. CRISPR has also been commercially used within farm animals and crops. Genetically engineered farm animals enhance food quality. For example, pigs have been genetically engineered to express the Δ12 fatty acid desaturase gene derived from spinach to produce higher levels of Omega-3, producing more nutritional value²⁴. In addition, scientists have made efforts to clone endangered or threatened species to increase genetic diversity through CRISPR. Increasing the population of endangered species greatly boosts the ecosystem because it adds variation and decreases the risk of more animals going extinct.

CRISPR has revolutionized gene editing, but it still has safety risks and negative off-target effects.²⁵⁻²⁹ Off-target activity has been observed at a frequency greater than 50%, so current attempts addressing this concern include engineering newer Cas9 variants that exhibit reduced off-target effects and optimizing guide designs. Instead of “gently goading” cells into editing targeted genetic texts, CRISPR sometimes gouges irreparable gaps in cell DNA, causing disastrous effects by causing a substantial fraction of unwanted genome change, such as cells losing the ability to fight cancer. In addition, any off-target effects caused by CRISPR on germline genes have the potential to pass on to future generations. In the United States many scientists have called for a self-imposed moratorium on CRISPR until more is known, but other countries do not have such regulations on ethics and moral safeguards. Currently, in-utero treatment, where parents with heritable diseases can change the genes of a fetus, is undergoing preclinical research. This treatment is effective on the fetus because the fetus’s small size and immunological immaturity makes drug delivery simpler with less resistance. However, this could disrupt normal organ development, result in edits to germline cells, and risk the mother. CRISPR has ethical safeguards that closely regulate testing on humans, which makes testing more difficult.

ETHICAL IMPLICATIONS OF GENETICALLY EDITING ANIMALS

Wild animals:

As CRISPR and gene editing technologies advance, scientists have applied its usage to wild animals and insects such as mosquitos.³⁰⁻³³ Mosquitos are notoriously known for spreading malaria along with other diseases, so scientists aim to change the malaria holding genes in the insect through a process called gene drive. In gene drive, CRISPR changes the germline gene of an organism, so the new trait is hereditary. Unlike normal genes, which are passed on based on

gene dominance, the genes for mosquito offspring are self-propagating because the gene drive introduces bias (Figure 2). Back in the 1940s, mosquitoes were found to be the cause of malaria, and mosquitoes were eradicated using DDTs and insecticides. However, when scientists discovered the harms of DDT to the environment and the immunization of mosquitoes from DDTs, they developed a new method of sterilizing mosquitoes using X-rays. After the foundation of gene editing technologies like ZFNs and TALENs, major improvements followed; however, the expensive cost made it inefficient. CRISPR, on the other hand, popularized due to its relatively low cost and specific targeting abilities.

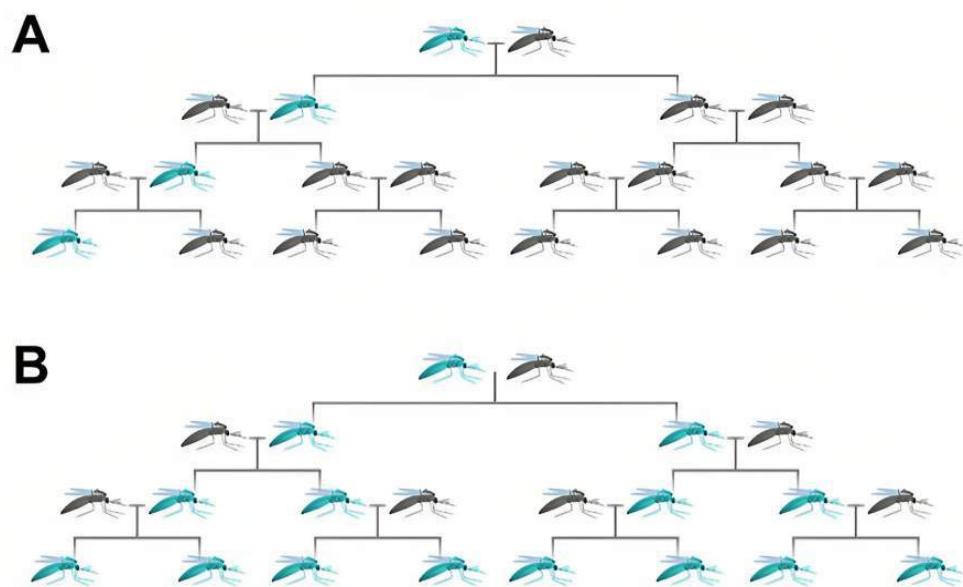


Figure 2: According to the figure, A is how normal inheritance would look like. Because this gene is recessive, it is eventually lost because very few mosquitoes inherit the gene. However, with the help of CRISPR the gene could take over the entire species with gene drive. This is illustrated through figure B.

Gene editing experiments performed entirely within a lab are easier to control instead of in the wild.²²⁻²⁴ Once a gene is released into the wild, it cannot be controlled and could lead to unpredictable outcomes. Any defects in the germline of a gene have the potential to be passed onto future generations, completely altering the species. In addition, by modifying genes and releasing them to the environment, the environment may suffer potential imbalances. Using CRISPR on wildlife requires much more research to assess the risks, benefits, and improvements of each situation using CRISPR. With such a powerful tool, awareness and ethics of the tool is needed by scientists and society.

When food is genetically engineered, their DNA is deliberately modified.³⁵⁻³⁶ For example, GABA (γ-aminobutyric acid) enriched tomatoes were one of the first genetically modified plants to enter the market, marketed as “health-promoting”. This technology is also used for parasite control, disease resistance, and agricultural pollution reduction.²⁴

The ongoing debate on genetically edited foods persists and meets strong resistance.³⁷⁻⁴¹ Controversies and public concerns include human and environmental safety, food security, and property rights. A common trend within consumers is their increased awareness towards genetically modified foods and their issues, and they tend to have higher concerns about GMOs than other food safety risks such as E. Coli (a bacteria that is spread through the consumption of polluted foods). Although awareness of genetically edited foods has increased, concerns about genetically edited foods have typically remained constant.

Aquaculture

Apart from land animals, scientists have further genetically enhanced aquatic animals, aiming to address crippling challenges from disease and fertility reduction to environmental pollution, coastal conflicts, or controversies over patenting research outputs.⁴²⁻⁴⁴ CRISPR gene editing battles the challenges faced in aquaculture, which is vital because aquaculture is the world's main provider of seafood. Species have also been edited to present a specific pigmentation or to prevent hybridization. Boosting aquaculture from traditional practices with modern applications of CRISPR will increase production and augment the quality of seafood. The application of genetics, selective breeding, and genome editing in aquaculture accelerates the genetic improvement of aquaculture species and introduces advantageous alleles.

While CRISPR has positive impacts in aquaculture, ethical concerns have been raised concerning the editing of aquatic animals⁴⁵. Genome editing of aquatic creatures, especially for human consumption raises ethical questions and questions about safety and legality. These seemingly trivial concerns tend to have a tremendous impact on analyzing the success of genome editing within aquaculture. For example, consumer acceptability of a fresh or frozen fillet depends on its origins, because they fear not knowing where their food comes from or how it has been edited.

In conclusion, non aquatic and aquatic animals are all undergoing changes in the DNA for human commercialization and safety. For example, mosquitoes are edited to reduce the spread of malaria through a process called gene drive, whereas GABA-enriched tomatoes enter the market to increase profit and provide added nutrition. CRISPR provides numerous opportunities for the increase in economic and technological boosts for society. However, it also threatens existing species of wildlife with off-target effects, and it does not have a positive public opinion. CRISPR needs to undergo many more tests and developments to understand this potent technology, what the impacts will be on the environment, and what impact it can potentially have on human health to be fully trusted by scientists and consumers.

ETHICAL IMPLICATIONS OF TESTING CRISPR ON NON-HUMAN PRIMATES

Non-human primates have been extremely beneficial to the progress of research regarding humans.⁴⁶⁻⁴⁹ Humans, like apes and monkeys, are primates, but binding laws closely regulate and restrict the use of humans in specific research, so NHPs are tested beforehand to protect human safety. NHPs are essential to human research because they have a similar physiology, behavioral tendency, and pathology. Scientists hope that genetic testing of human primates will improve the current understanding of neurological diseases and validate potential therapeutic interventions. Although NHPs account for only 0.5% of animals in medical research, they play major roles in finding cures for widespread ailments such as cancer, AIDS, Alzheimer's, or Parkinson's obesity. They are essential for the increase in scientific understanding of the human brain's role in cognitive, motor, and mental illnesses, while also aiding research on organ transplantation. Without NHP research, scientists would lose a resource that aids the understanding of ways to prevent miscarriage, stillbirth, and premature birth.

However, the use of non-human primates for testing has introduced numerous animal welfare concerns.⁴⁹⁻⁵¹ For example, NHPs have been subjected to rather cruel practices such as MRI scanning under anesthesia, pain threshold testing, and fear-inducing stimuli (high decibel level noise—120 dB). Testing methods tend to induce fear, discomfort, and distress within NHPs, especially due to their high intelligence. In addition, creating genetically modified NHPs induces stress among mothers (who die giving birth to genetically modified primates) and the genetically modified primates. Genetically engineered NHPs can develop severely debilitating diseases such as Huntington's disease or Parkinson's disease from testing. Technically, non-human primates have a right to bodily and mental integrity, but they are too valuable in research. They should not be tested on for arbitrary reasons, rather they should only be sacrificed for another good without options.

In conclusion, non-human primates (NHPs) play a crucial role in advancing human understanding of the neurological system through testing. However, it is important to address the ethical concerns associated with the treatment of NHPs, as they experience significant stress and discomfort. Fortunately, there are alternative research methods available, such as utilizing human embryonic stem cells (ESCs) which offer a more accurate representation of the human body compared to NHP models.⁵²⁻⁵⁴ Human-based models provide valuable insights as they closely resemble humans without species-specific differences found in NHPs. By prioritizing the use of human ESCs, scientists can enhance animal welfare conditions and allocate resources towards projects employing in vitro human models. Additionally, there are other testing approaches including voluntary human testing, as well as computational and mathematical models, which can provide greater accuracy, cost-effectiveness, and efficiency compared to traditional animal models.

ETHICAL IMPLICATIONS OF EDITING HUMANS

Gene Therapy

The very development of CRISPR-Cas9 and other gene therapies is to support the progression of humanity. CRISPR has the potential to remove around 7,000 monogenic diseases through gene therapy.¹⁷ Gene therapy is a process that changes the existing code of a site-specific gene and replaces it with a new code to remove a condition or disease.⁵⁵⁻⁵⁶ Although this process remains in a testing phase, scientists hope health practitioners will adopt CRISPR into treatment. Currently, the research approach is broad, aiming to repair many different recessive disorders such as cystic fibrosis, hemophilia, and sickle cell anemia. It also aims to repair acquired diseases such as cancer and certain viral infections like AIDS. However, despite evolving rapidly, gene therapy is risky and can trigger unwanted immune responses or edit the gene incorrectly, causing serious side effects like injury or death. Jesse Gelsinger, a patient who received gene therapy for a mild form of Ornithine transcarbamylase (OTC) deficiency, died from the immune response triggered by gene therapy. Testing on humans is strictly restricted, and although some patients choose to undergo gene therapy, they risk suffering from negative off-target effects.

Embryo Editing

Embryo editing and designer babies have increasingly become topics of interest and concern after Dr. He Jiankui's application of CRISPR in 2018.⁵⁸⁻⁵⁹ During this experiment, Chinese scientist He Jiankui illegally created the first gene-edited children, ignoring all restrictions. This brought upon a public outcry even from China, where regulations on CRISPR and gene editing were not fortified back then. Currently, public opinion about genome editing suggests that people support somatic genome editing for medical reasons, are somewhat supportive of editing hereditary traits, and are completely against genome editing for non-medical purposes.

Embryo editing is a tentative subject because of all it implies for the future of the human race. It could remove the chance of a child receiving a deadly disease, but it might also leave the child with even more problems due to off-target effects. In addition, it also brings forth questions regarding how it will be used after disease eradication. While embryo editing holds promise for disease prevention, it is necessary to approach this delicate subject with cautious consideration of the scientific and ethical implications, as demonstrated by the violation of established codes in Dr. Jiankui's experiment.

Blastocyst complementation

Clinical medicine faces an ever-constant problem: a shortage of human donor organs.⁶⁰⁻⁶⁵ Scientists fruitlessly attempted to grow organs themselves, so they instead now try to grow the organ within another host animal. By creating more organs within animals through CRISPR, organ shortage may no longer be a problem in clinical medicine and doctors can save more lives. This process is called interspecies blastocyst complementation (IBC) (Figure 3). In IBC, the recipient blastocyst carries a deficiency of a particular organ or tissue, and a new organ is generated through stem cells in another animal. CRISPR supports the process because it can be

co-expressed with a guide RNA to introduce double-stranded breaks at site-specific genetic loci. With the CRISPR–IBC technique, researchers perform IBC experiments at a larger scale and succeed in reproducing a rat pancreas, eye, and heart in a mouse. IBC is especially useful within non-human primates because of their closer resemblance to humans compared to other host animals.

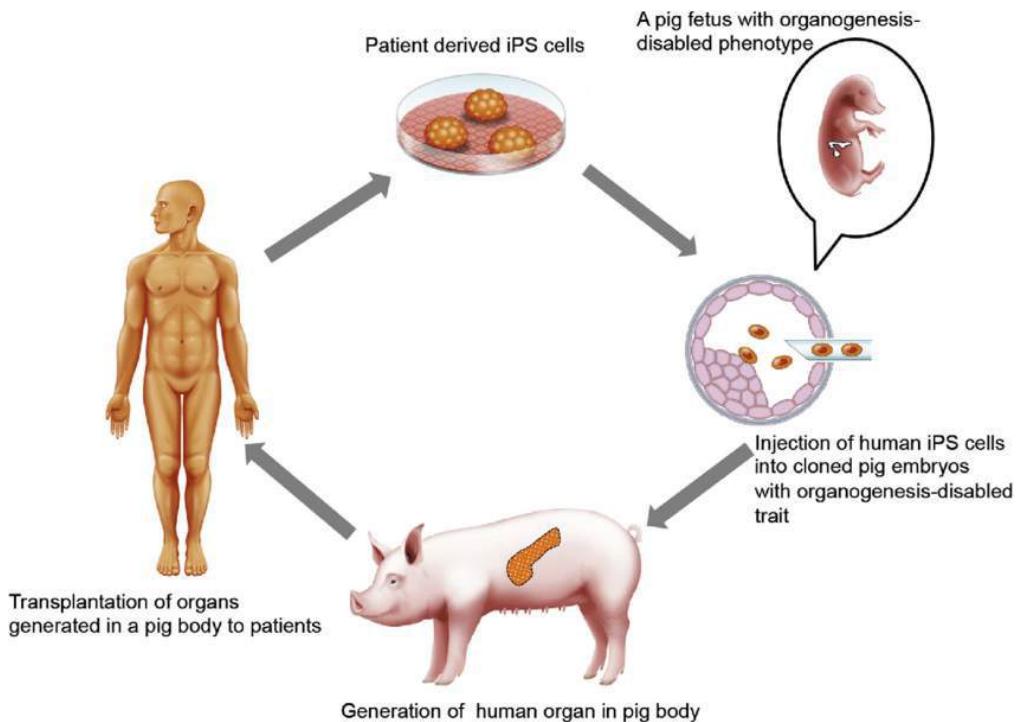


Figure 3: The figure above is a breakdown of blastocyst complementation. It shows the generation of human organs using organogenesis-disabled pigs as a platform. Induced pluripotent stem cells (iPS cells) are injected into the cloned pig embryos to generate a human organ into the pig body so it can eventually be planted back into the human

Even though blastocyst complementation has many potential benefits for generating organs for humans, a major concern about blastocyst complementation is the creation of human-animal beings with partial or substantial human brains.⁶¹ Animals possessing a human-like brain may possess human-like characteristics, and due to the lack of funding and understanding in the process, the ambiguity concerns many scientists.

Blastocyst complementation has the potential to increasingly benefit humans because of the increased availability of organs. Before IBC, transplant surgeons increasingly depended on human donors for organs, but there are not enough donors.⁶⁶⁻⁶⁷ However, even if there are more donors, the organ may be rejected or die early. With blastocyst complementation, organs will increase in availability and save many more lives. Humans increasingly benefit with the CRISPR genome editing technologies. Medical practitioners have the opportunity to edit embryos, changing the genome of humans before they are even born. Existing monogenic diseases can be wiped away with this powerful technology; organ availability can skyrocket. However, with all these benefits it becomes exceedingly important to remember setting ethical boundaries and learning more about CRISPR to safely progress humanity.

CONCLUSIONS

CRISPR is an ever developing and changing technology, but several measures can be taken to ensure it is used responsibly and ethically. Because no measure or guideline fits every instance for the usage of CRISPR, each situation needs to be assessed and evaluated to ensure that the proper steps are taken to properly handle such a powerful tool. In addition, differentiating curiosity research from medical research regarding CRISPR ensures that innocents are not sacrificed for trivial curiosities, rather they are only used after the proper background research is held.

CRISPR holds so much potential, and while it is extremely difficult to create a general set of guidelines to follow, minding the ethical implications of research and editing ensures a safer outcome. CRISPR holds many controversies, such as whether genetically engineered food should be eaten to whether humans should even be edited. However, if scientists and society understand the necessity of using this technology responsibly, it holds a bright future. As seen with the mosquitoes, CRISPR can remove malaria from the world, but misuse can also change the entire mosquito population. Ensuring that CRISPR is responsible fortifies the safety of animals, the environment, and humans themselves.

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The Body-Memory-Experience Paradigm of Self-Identity Maintenance Among Individuals with Dementia: Philosophical Inspirations from *The Father* Movie By Ziyuan Zhou

Abstract

This research paper explores the philosophy of self-identity maintenance in individuals with dementia, drawing inspirations from the 2020 film, *The Father*. By integrating insights from philosophy, clinical psychology and cultural studies, this multidisciplinary study seeks to supplement the predominant approach by examining how dementia impacts narrative identity—the evolving life story which connects the past, present, and future. The methodology involves a comparative analysis of philosophical theories on identity, real-world studies on dementia patients, and a narrative analysis of *The Father*. Findings reveal that individuals with dementia, despite cognitive decline, retain a dynamic but often confused sense of self through narrative reconstruction and social roles. Ultimately, these findings advocate for further research that prioritizes the perspectives of dementia patients to develop the best care strategies and understanding of the condition.

Introduction

In 2023, the World Health Organization (WHO) estimated that over fifty-five million people worldwide have dementia, a set of degenerative diseases affecting the central nervous system and resulting in cognitive impairment, with an additional ten million cases diagnosed each year.³² Dementia is a widespread condition, affecting millions globally, with symptoms ranging from memory loss and disorientation to impaired communication. With its rapid increase, dementia is considered one of the biggest health challenges of the 21st century, placing a significant burden on individuals, families, and society as a whole. In the medical field, the effects of anti-dementia treatment and medication have been found to be limited or even have adverse effects.³³ A comprehensive understanding of dementia requires input from various disciplines, as clinical psychology alone cannot fully explain the profound impact that the disease has on self-identity.

Despite advancements in clinical dementia studies, there remains a puzzle at the heart of the investigation: What happens to one's sense of self when one's memory and cognitive functions begin to fade? In addressing this question, it becomes clear that self-identity is not merely a medical or psychological issue but one deeply rooted in philosophical inquiry. Diagnosing dementia requires a comprehensive evaluation of cognitive decline and impairment in daily activities, "often corroborated by a close friend or family member, alongside a clinician's examination of memory, language, attention, visuospatial cognition, executive function, and

³² Dementia: World Health Organization. 2023. <https://www.who.int/news-room/fact-sheets/detail/dementia>.

³³ Tao P, Xu W, Gu S, Shi H, Wang Q, Xu Y. Traditional Chinese medicine promotes the control and treatment of dementia. *Front Pharmacol.* 2022;13:1015966. doi: 10.3389/fphar.2022.1015966.

mood.”³⁴ Additionally, the 2014 U.S. Preventive Services Task Force concluded that there is insufficient evidence to determine the balance of benefits and harms associated with universal screening for cognitive impairment, including clinical evaluations for diagnosis. This illustrates the challenges in current medical approaches to dementia, as they often lack the comprehensive evidence required for effective early detection. Yet, even with the present clinical rigor, the deeper question of self-identity extends beyond the reach of science.

Marya Schechtman writes in *The Self*, “Science will never be able to describe what it’s like to look out at a meadow on a warm summer’s day with a melancholy nostalgia for one’s youth,” nor can it “capture the vibrant green or the quality of light, let alone the nostalgic melancholy” (Pg. 3, Ch.1).³⁵ Similarly, while neuroscience explains the physical mechanisms underlying subjective experiences, it cannot fully encompass the emotions and complexities that shape consciousness. This highlights that self-identity in dementia is not merely a medical or psychological issue but one deeply rooted in philosophical inquiry. This concept of self-identity has long intrigued philosophers, including Christian theologian St. Augustine, British classical philosopher John Locke, and contemporary British philosopher Derek Parfit, who have explored its formation through different lenses, providing critical insights that clinicians might consider in their efforts to understand how dementia affects the self.

The most pressing concern at present is the lack of studies centered on the narrative identities of individuals living with dementia. The loss of communication abilities and prevalent symptoms of impaired memory contribute to this urgency.³⁶ On one hand, those living with dementia are often stigmatized as being unable to participate in research procedures and, thus, may face difficulties with traditional research methods. On the other hand, clinical researchers believe that the patients lose their sense of self as their abilities to narrate autobiographical memories are disturbed.³⁷ Therefore, researchers implemented discourse analysis to receive identity-related markers of individuals. Results show that, contrary to the prevailing belief that those living with dementia are destined to lose their sense of self, they can form meaningful, intricate narrative identities.

Building on these philosophical foundations, this paper will explore how these perspectives on self-identity relate to the portrayal of dementia in *The Father*.³⁸ The film offers a depiction of how dementia disrupts the traditional notions of self-identity, affecting memory, body, and personal experiences, through an insider’s point of view. By exploring these connections, this paper aims to bring attention to the complex and dynamic nature of self-identity, particularly in the context of cognitive decline. This paper conducts a

³⁴ Arvanitakis, Z., Shah, R. C., & Bennett, D. A. (2019a, October 22). *Diagnosis and management of dementia: Review*. JAMA. <https://pmc.ncbi.nlm.nih.gov/articles/PMC7462122/>

³⁵ Schechtman, M. (2024). *The self: A very short introduction*. Oxford University Press.

³⁶ Kłosińska, U., & Leszko, M. (2023, September 8). *Family relationships as a source of narrative identity of people with advanced dementia - BMC geriatrics*. BioMed Central.

³⁷ Kłosińska, U., & Leszko, M. (2023, September 8). *Family relationships as a source of narrative identity of people with advanced dementia - BMC geriatrics*. BioMed Central.

³⁸ Zeller , F. (2021, February 26). *The Father*. IMDb. <https://www.imdb.com/title/tt10272386/>

multidisciplinary literature review across philosophy, clinical psychology, and cultural studies to explore the concept of self-identity in dementia, drawing inspirations from the film, *The Father*.

One key takeaway from this analysis is that one crucial aspect of self-identity disrupted by dementia is narrative identity, which refers to a person's internalized and evolving life story, integrating the reconstructed past and imagined future to provide life with some degree of purpose. Narrative identity is a fundamental part of our identity and continues to evolve as we accumulate new experiences. In *The Father*, the breakdown of memory directly impacts the protagonist's ability to maintain a coherent life story, illustrating how dementia disrupts this sense of continuity.

Philosophical Foundations of Self-Identity: The Body, Memory, and Experience

The formation of personal identity is often viewed through the "body-memory-experience" paradigm. At the core of these philosophical inquiries about self-identity is the understanding that personal identity is a dynamic and evolving construct. It encompasses the ever-changing nature of our bodies, the development of our memories, and the accumulation of our life experiences. In everyday life, our access to the world happens through a first-person perspective. This perspective serves as the foundation of our experiences, an underlying construct that modulates one's apprehension of the world: the self. William James, in his *Philosophy of Mind*, describes this as "ontologically subjective," asserting that "feelings and thoughts only exist in relation to an experient of the experience."³⁹ This notion, which John Searle defines as "first-person ontology" underscores the fundamental property of consciousness in shaping identity.⁴⁰ In essence, self-identity is constructed from three components—body, memory, and experience—each factor shaping how we perceive ourselves over time.

For instance, our sense of the self is intricately tied to the continuity of our physical body, as bodily characteristics provide a sense of recognition of our past selves. John Locke emphasized the significance of the physical body in maintaining self-identity over time, stating, "[The] body as well as the soul, goes to the making of a man; and must be the same numerical body, as well as the same numerical soul."⁴¹ Thus, asserting that the body is not just a collection of separate parts but a cohesive whole that, along with the soul and consciousness, contributes to one's sense of self. Similarly, Rene Descartes' theory of Cartesian dualism puts forward that human beings are composed of both a material body and an immaterial mind or soul, with the latter remaining constant over time.⁴² Conversely, Hume's perspective challenges the emphasis

³⁹ James W. *The Principles of Psychology*. Oxford: Dover Publications (1950). p. 226.

⁴⁰ Searle J. Biological naturalism. In M. Velmans and S. Shneider (Eds.), *The Blackwell Companion to Consciousness*. Malden, MA: Blackwell Publishing (2007). p. 325-334. doi: 10.1002/9780470751466.ch26

⁴¹ John Locke (1689), *An Essay Concerning Human Understanding*, Book II, Chapter 27.

⁴² Rene Descartes (2006) *Philosophy of Mind: A Short Introduction*, part VII, pg. 168.

on physical continuity, directing attention instead to the fluidity of experiences and perceptions that shape identity.⁴³

Meanwhile, memories act as a bridge between who we are in the present and who we were in the past. These memories, along with our experiences, weave together to create a cohesive narrative of the self. So, rather than being a fixed entity, identity is constantly evolving, influenced by memories, emotions, preferences, and external labels. This fluidity brings memory into focus as an equally crucial element in the formation of self-identity. The brain's ability to process and retain information plays a central role in how individuals perceive themselves over time. A classical perspective on the relationship between memory and self-identity is offered by Saint Augustine, who in his *Confessions* underscores the importance of time in human memory. Augustine suggests that our experience of time—past, present, and future—is intricately tied to our sense of self, as our memories shape our understanding of who we are.⁴⁴

While both our physical presence and the memories we carry contribute to our sense of identity, it is through our lived experiences that these aspects come together. Our bodies—through physical appearance, body language, and speech—are expressions of individuality, but so too are our habits, emotions, and unique experiences we undergo, which distinguish us from others. This connection between identity and experience is explored by Hank Green. He suggests that our life can be represented as a mesh of separate chains that intersect at certain points.⁴⁵ As we progress through time, new links are formed and added to the chain, which reflects one's evolving interests and experiences. However, some links from our past may gradually drop off as they lose their psychological connection to our present selves. For instance, when one's interest in art diminishes, the corresponding link in the chainmail may drop down. But, a newfound love for a new subject adds a new link to the mesh. Our experiences, although ever-changing, are interconnected, creating a dynamic timeline of our identity.

The Fluidity of Self-Identity and Dementia: A Phenomenology

The fluidity of self-identity raises an ongoing debate about whether identity is fixed or constantly evolving. On one hand, the physical continuity of an individual's biological existence might lead one to perceive self-identity as stable and unchanging. Yet, philosophers like David Hume challenge this notion by proposing that personal identity is merely a collection of "ever-changing bundles of impressions," suggesting an evolving and fluid concept.⁴⁶ This fluidity becomes apparent in how individuals adapt to new experiences, relationships, and societal roles. As people grow, learn, and encounter diverse perspectives, their self-perceptions and worldviews can shift significantly. Ultimately, self-identity is a continuous process of self-discovery and redefinition.

Dementia, being the most prevalent among the aging population who have accumulated life-long memories and rich experiences, allows for a deeper understanding of how the

⁴³ David Hume (1739), *A Treatise of Human Nature*, Book I, part IV, sec.6.

⁴⁴ St. Augustine (AD 397-400) *The Confessions of Saint Augustine*, Book XI, lines, 17-41

⁴⁵ Hank Green (2018) *Arguments Against Personal Identity: Crash Course Philosophy #20*.

⁴⁶ David Hume (1739), *A Treatise of Human Nature*, Book I, part IV, sec.6.

body-memory-experience paradigm affects self-identity. While younger individuals often possess the cognitive and physical faculties necessary to maintain a coherent sense of self, those living with dementia experience a disintegration of these faculties. For instance, the body is a medium through which individuals experience the world. For children and young adults, the body operates relatively seamlessly, allowing them to perform routine tasks and interact with their environment. Their physical health reinforces a sense of continuity in their self-perception. In contrast, the aging population often faces a breakdown in their physical abilities. Dementia limits physical freedom, leading to difficulties in movement, coordination, and even basic self-care.

Memory, the second component of this paradigm, is arguably the most significantly affected by dementia. While younger individuals rely on memory to maintain a continuous sense of self—recalling past experiences and integrating them into their current identity—those with dementia often experience memory loss that disrupts this continuity. For aging individuals, whose identities have been shaped by a lifetime of experiences and accumulated knowledge, memories of past events, relationships, and life milestones serve as crucial markers of identity, helping them to reflect on who they are and how they've evolved. However, the loss of memory strips individuals of the ability to trust their recollections, leading to confusion and a weakened sense of self.

Personal experience is another crucial element of this paradigm. Younger individuals actively accumulate new experiences, which they can integrate into their evolving sense of self. In contrast, for the aging population living with dementia, their ability to process and store new experiences becomes impaired, despite their rich history of past experiences. This disconnection often results in an inconsistent reality where past and present experiences no longer align, complicating their sense of self-continuity.

Nevertheless, research teams studying final relationships have found that dementia patients can still form a sense of self through various means. For instance, their societal roles—whether as mothers, fathers, siblings, or children—serve as crucial anchors of their identity, allowing them to maintain connections to their past and their place within their families.⁴⁷ These connections are not static; rather, are reconstructed and reinforced through narratives shaped by family members and caregivers.

In a study conducted by the BMC Geriatrics Research Team⁴⁸, detailed interviews with family members and caregivers reveal how individuals with advanced dementia continue to find meaning and a sense of self. Participants emphasized their sense of belonging to a social group and their roles as family guardians. Some even contextualized their identity geographically, attributing a regional identity to their family. Additionally, many participants reconstructed their family stories, reflecting a sense of belonging even after the loss of loved ones. Through structured interviews, they described specific events and their consequences, creating a narrative

⁴⁷ Kłosińska, U., & Leszko, M. (2023, September 8). *Family relationships as a source of narrative identity of people with advanced dementia - BMC geriatrics*. BioMed Central.

⁴⁸ Kłosińska, U., & Leszko, M. (2023, September 8). *Family relationships as a source of narrative identity of people with advanced dementia - BMC geriatrics*. BioMed Central.

that connected family relationships with their sense of self. Furthermore, participants described themselves by reconstructing their family stories, expressing a sense of belonging to a social group, even after the passing of loved ones.

Through economic discourse, participants framed their contributions to society in terms that went beyond material wealth. While society often measures achievement by wealth accumulation, participants affirm their social value through roles that transcend economic success, suggesting that those living with dementia continue to see themselves in meaningful social roles. In contrast, through the autobiographical discourse, participants emphasized their sense of belonging within a social group and their role relative to their family. Together, these discourses illustrate how individuals with dementia construct their identities by affirming both personal and social values, challenging conventional views that reduce their worth to cognitive ability alone.

The Father Movie: A Window into People Living with Dementia

The Father, a 2020 psychological film directed by French playwright Florian Zeller, offers a distinctive portrayal of dementia by centering on the perspective of its protagonist, Anthony, an elderly man battling Alzheimer's. Drawing from personal experience, Zeller was inspired by his grandmother's battle with dementia. The film immerses viewers in Anthony's fragmented reality, allowing them to experience dementia from an insider's point of view. Anthony Hopkins stars as the protagonist, Anthony, while Olivia Colman plays Anne, his devoted daughter, who faces many challenges of caring for him as Anthony's condition worsens. The film captures the experience of those with disease, exploring themes such as memory decline and emotional disturbance. Additionally, *The Father* emphasizes how self-identity is related to the alignment of one's core memories.

Unlike many portrayals of such diseases, which position characters with dementia primarily as the object of observation, Zeller draws audiences directly into Anthony's disoriented world through specific narrative techniques and symbolism. Narrative approach is a common theme in popular cultural representation of dementia, and narrative structure plays a crucial role in *The Father*, as frequent shifts in time, space, and character identities mirror Anthony's experience. Unlike common cultural narratives that often emphasize the caregiver's journey, the film, instead, highlights the deeply personal impact of the disease on the individual. Through an analysis of these elements, this paper aims to uncover how the film achieves a nuanced and empathetic depiction that resonates both culturally and emotionally. Ultimately, contributions of philosophy, cultural studies, and narrative approaches are needed to paint a complete picture of how individuals navigate identity in the face of cognitive decline.

The body-memory-experience paradigm is also depicted in *The Father*—the first aspect, body, encompasses both the physical appearance and the environment, reflecting the toll of dementia on Anthony's sense of self. For example, at the beginning of the film, Anthony embodies dignity, dressed in a suit and tie that signify his strength, authority, and pride as the family's foundational figure. This aligns with the movie's title, which evokes the image of a

fatherly figure of stability and strength. However, later as his mental state deteriorates, so does his outward appearance. His attire shifts from cardigans to robes, then pajamas, and finally a plain T-shirt, as if regressing to a childlike state. This change in clothing mirrors the gradual erosion of dignity, once rooted in his position, respect given by himself and by others. Similarly, Anthony's living environment, a part of his "body" as it defines his physical context, begins to subtly change as well. Walls shift color, furniture moves, and spaces blend into one another, symbolizing his growing loss of control over his own reality.

Despite these changes, Anthony clings to his dignity, refusing to expose his vulnerability to others. Like many individuals, he tries to mask his fragility, acting as though he understands situations despite being completely lost. For instance, he reassures his daughter Anne and caregiver, Laura, with phrases such as "*I know, you've already told me a hundred times,*"⁴⁹ to project a sense of coherence. His mannerisms, such as using exaggerated gestures and jokes are all attempts to mask his confusion, marking his internal struggle to resist being dismissed and seen as inferior to others. Yet, as his perception of his surroundings becomes increasingly unreliable, he begins to realize that the others no longer regard his perception as valid or valuable. His disconnection from his physical environment and his attempts to maintain control of his identity illustrates the profound impact of dementia on one's body.

Anthony's persistent efforts to assert his dignity and autonomy, even as dementia erodes his sense of reality, reveal his struggle to retain his identity in the face of cognitive decline. Because of this disease that disrupts even the most basic abilities, he has a strong desire to maintain control over his life and environment, even as his mind betrays him. In his efforts to retain his identity, Anthony's sense of dignity transforms into feelings of resentment and defensiveness, fueling his harsh remarks. "*I'm going to outlive you. Both of you. In fact, I'm going to make a point about it. I'm going to inherit from her and not the other way around. And the day of her funeral, I shall give a little speech to remind everyone how heartless and manipulative she was,*"⁵⁰ he declares to his daughter Anne. These cutting words reveal his desperation to preserve a sense of control, even as his world and relationships crumble around him.

The second aspect of the paradigm, memory, plays a central role in the film, illustrating the distorted reality created by a fragmented mind. Memory is the pure essence in which one's identity is shaped, and when one's core memories are still intact, the earliest points of life, that is what builds a strong character that makes up one's identity. Thus, the erosion of memory leads not only to a fractured perception but also a profound loss of self, as Anthony struggles to hold onto the essence of who he was in an environment that is slipping from his grasp. As Anthony's perception of events and relationships become increasingly fragmented and even conflicting, it creates emotional and relational crises. For instance, he accuses his daughter Anne of stealing from him—a desperate attempt to rationalize his confusion.

⁴⁹ Zeller , F. (2021a, February 26). *The Father*. IMDb. <https://www.imdb.com/title/tt10272386/>

⁵⁰ Zeller , F. (2021a, February 26). *The Father*. IMDb. <https://www.imdb.com/title/tt10272386/>

Time plays a prominent role in shaping one's memory, as the ability to rationalize time and recall events in an orderly fashion maintains a foundational reference to reality. The film uses the symbol of a watch to show Anthony's declining sense of reality. His repeated misplacement of his watch and attachment to it reflects the deterioration of his mind as he struggles to keep track of his possessions and hold onto the linearity of time. This loss leads him to suspect there's a theft in his flat, even lashing out at those who are trying to help, proving his mistrust of those around him. This disrupted perception of "time" corresponds to the unstable nature of his own existence, which intensifies his fear and disconnection from the environment.

Though he yearns to present himself as being clear-minded and perfectly normal, he is ultimately perceived in a way that corresponds to his vulnerability. Anthony's resistance toward this infantilizing attitude is evident in his sharp response to his caregiver, Laura: "*Can I ask you a question? Are you a nun?*" When she answers "No," Anthony retorts, "*Then why are you speaking to me as if I'm retarded?*"⁵¹ This interaction demonstrates Anthony's awareness of his diminishing agency and his desperate attempt to hold onto his dignity. His defiance is further echoed in his bold declaration, "*I don't need help from anyone. And I'm not going to leave my flat. All I want is for everyone to move off. Having said that, it has been a great pleasure. Au revoir. Toodle-oo.*"⁵² This unwavering defiance towards his close ones, expressed through sharp wit and bold declarations, proves his desperate struggle to assert his authority over his life, even as his cognitive decline increasingly undermines his efforts.

Furthermore, the shifting appearance of Anthony's flat—visually represents his disorientation. Anthony's flat, the story's central setting, subtly changes, with the doctor's office blending into the entrance of his flat and furniture rearranged from scene to scene—representing his twisted perception of even the most familiar places. Changes that occur within seconds actually span years of forgotten memory. Yet, even in the midst of his disorientation, consistent elements which remain in each room provide a degree of stability, offering Anthony comfort and a loose grip on reality.

The third and final aspect of the paradigm is experience, and the experience of loss and disconnection is a central theme in the film, profoundly affecting the identity of the protagonist. The ability to connect past experiences with the present time is significant. When one's life flows with a sense of continuity, it establishes a connection to one's past selves. And reflecting one's experiences across different stages of life weaves a close-knit thread that forms the foundational framework of individuality. As Anthony gradually loses his possessions—his watch, his house, even his daughter, who appears to be scheming against him—he grapples with the distrust and fear of others. In Anthony's perspective, the location shifts, people asserting different names and histories, make it even more difficult to decipher the changes he encounters. Anthony's constant perceptions stem from a distorted reality rather than objective truth. The decline of his cognitive abilities, accelerated by dementia, erodes his understanding of the world around him, which are

⁵¹ Zeller , F. (2021a, February 26). *The Father*. IMDb. <https://www.imdb.com/title/tt10272386/>

⁵² Zeller , F. (2021a, February 26). *The Father*. IMDb. <https://www.imdb.com/title/tt10272386/>

the oldest and strongest part of him. The world, originally a reliable shelter, morphs into a shifting and dangerous entity, taking away the connection that one shares for another, as aspects of who they are will be in question.

Taking everything into account, the audience gradually realizes that Anthony, the protagonist, is an unreliable narrator. The constant changes in the film—identity shifts, characters becoming unrecognizable, events reimagined, and timelines collapsing into a chaotic, nonlinear narrative—are revealed to be distortions of his perceptions rather than reflections of reality. The shifting faces of caregivers and conflicting accounts of events immerse viewers in Anthony's fractured perspective, illustrating how the loss of memory, past experiences, and bodily symbols destabilizes not just the mind but the essence of one's selfhood. As this disease progresses, Anthony's understanding of the world—once the bedrock of his identity—crumbles. The once familiarity transforms into an unpredictable and threatening place, stripping him of power, control, dignity, and capacity to find joy. When the foundational aspects of an individual's identity erodes, one's connection with others and sense of self are profoundly questioned, dwelling in an fragmented and unrecognizable reality.

As the film draws to a close, the stripped branches of Anthony's self-identity reminds us that the threat of dementia is not merely just a loss of memory but a loss of every essence of the self. In a moment of extreme vulnerability, he pleads, expressing his suffocating despair: "I feel as if I'm losing all my leaves—the branches and the wind and the rain. I don't know what's happening anymore. Do you know what is happening?"⁵³ In the final moments of his life, Anthony equates the ravages of dementia to a tree stripped bare of its leaves, encapsulating the disease's devastating impact on identity. As the tree becomes vulnerable and exposed, so too does the individual, stripped of memories, relationships, and a sense of self. Losing this sense of self erodes the very foundation of who we are. When our identity is threatened, everything is threatened—our memories, our connections, and our place in the world. In the face of such profound loss, the need for compassion and understanding becomes ever more critical.

Conclusion

This paper proposes a narrative approach to understanding the world of people living with dementia. Although analyzing one movie has limitations for dementia-related self-identity research, it emphasizes the importance of bringing more attention to the lived experiences of dementia patients. Studies of shifting self-identity among individuals with dementia have not paid enough attention to an alternative dimension which is shaped by first-person narratives. In the field of dementia treatment, this is also referred to as "creative story therapy." Researchers show that by sharing self-defining stories, individuals reveal who they are, add meaning to their experiences, and maintain a sense of self-continuity.⁵⁴

⁵³ Zeller , F. (2021a, February 26). *The Father*. IMDb. <https://www.imdb.com/title/tt10272386/>

⁵⁴ Kłosińska, U., & Leszko, M. (2023, September 8). *Family relationships as a source of narrative identity of people with advanced dementia - BMC geriatrics*. BioMed Central.

However, neurological disorders like dementia challenges this process, complicating the ability to structure one's narrative. Yet, even within the disarray caused by cognitive decline, it creates new opportunities for meaning-making and reconstructing one's narrative. The way how individuals with dementia manage the integrations of disruptions into their evolving life story have significant impacts on their mental health and quality of life. Moreover, the manner in which traumatic experiences are integrated into one's narrative can also influence biological aging and stress coping mechanisms.⁵⁵ This emphasizes the importance in recognizing that narrative identities can be constructed differently for each individual struggling with dementia, revealing the variable nature of identity in the face of such illnesses.

More future research on how dementia impacts self-identity is needed. For example, one research area is family relationships and dynamics that are pivotal in shaping the identities of individuals struggling with dementia. This is evident in *The Father*, where Anthony's disoriented reality strains his relationship with his daughter, illustrating the emotional complexities that dementia can impose on familial bonds. Similarly, real-life interviews conducted by the BMC Research team reveal that dementia patients often maintain a rich inner world, whether it is through crafting a personal narrative that draws on their past, their role within the family, and other identity anchors like geographical history. Contrary to the perception of dementia as a complete cognitive decline, these findings suggest that individuals with dementia possess unique experiences and self-concepts.

Dementia remains a profound challenge, partly because, as outsiders, we cannot fully comprehend the confusion and loss of self-identity experienced by those affected. *The Father* is advocating in a direction of how to maintain a sense of self. All in all, future research should prioritize first-person perspectives to deepen our understanding of dementia from within. Creative approaches like this film demonstrate the importance of capturing the lived experience of dementia, which is difficult to convey through words alone. Thus, continued empirical research is essential to provide dementia patients with comprehensive support and a more profound validation of their internal realities.

⁵⁵ Kłosińska, U., & Leszko, M. (2023, September 8). *Family relationships as a source of narrative identity of people with advanced dementia - BMC geriatrics*. BioMed Central.

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AI's Role in Personalized Medicine By Sana Kandasamy

Abstract

Personalized medicine, the adaptation of medical treatment to a patient's unique genetic makeup, requires a complex series of procedures. These processes encompass genetic profiling, biomarker discovery, genomic analysis, patient-centered drug development, precise gene editing, treatment response monitoring, and therapeutic regimen modification. Because they are time-intensive, they face significant hurdles, leaving room for human-introduced error. The findings suggest that artificial intelligence has progressed in recent years and now dominates numerous steps while saving time and money. From documenting a patient's genetic information to influencing crucial treatment decisions, AI in healthcare is paving the way for a promising future for patients. Streamlining AI provides ongoing support and enhancement to conventional methodologies despite its limitations. This review highlights the potential of artificial intelligence in personalized medicine, demonstrating its significant impact on improving patient outcomes and addressing the limitations that must be considered.

Introduction

Personalized medicine is a medical approach that leverages a patient's genome to make medicine under particular regulations specific to the patient's health. In recent years, personalized medicine has been growing significantly, with advancements in technology - including the development of artificial intelligence (AI) - increasing the efficacy of these treatments (Sherani et al., 2024). It has been used to analyze genetic profiles, identify biomarkers and sequences, determine drugs for treatment, locate main target points in gene editing, and simultaneously monitor the patient while addressing critical adjustments (Figure 1). The first step is to create and analyze a patient's genetic profile. This profile contains biomarkers, genomes, mutations, and more. The next step is drug identification, which involves determining the most appropriate medication for a patient's condition and limitations. Artificial intelligence facilitates comprehensive investigation into drug mechanisms and which is best suitable for the patient (Collins et al., 2007).

Another medical approach, gene editing, uses precise tools to edit the DNA within a patient's diseased cell accurately. AI plays a significant role in identifying the target points that must be edited, reducing potential risks, and recognizing ethical considerations (Harrison & Hart, 2018). Despite the approach taken, the patient will always be monitored; therefore, AI-driven adjustments can be performed when there are any 'spikes' in data. This review will identify key challenges in personalized medicine and how AI is being improved to work around these challenges.

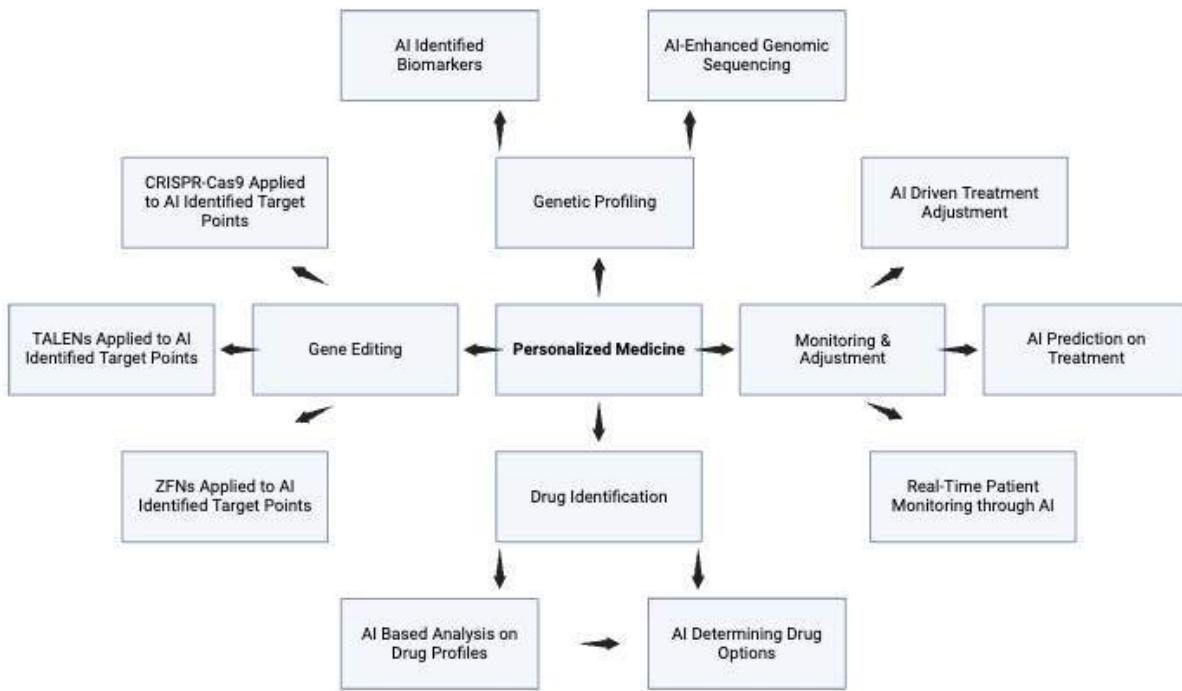


Figure 1. A flowchart depicting the holistic workflow of personalized medicine, focusing on areas where AI plays a significant role. Figure created using BioRender.

Methods

To gather a collection of information, Google Scholar was used to create a pool of relevant information and real-world examples. A strategy was to use keywords related to the prompt as search inputs, such as “AI in personalized medicine” or “AI’s role in [process name].” To maintain relevant options, articles that directly mentioned the application of artificial intelligence in healthcare were prioritized. When searching for theoretical and broad information, I limited my options to review and peer-reviewed articles. For more practical insights focused on specific examples, I used filters to seek research articles. I aimed to keep references recent, with all cited articles from the last three decades, 1998-2024.

Keywords Artificial intelligence, personalized medicine, data-driven healthcare, machine learning, AI in healthcare, AI-driven patient outcomes

Genetic Profiling

A genetic profile is a comprehensive record of a patient's genetic information, guiding treatment decisions. It outlines all potential obstacles, such as the patient's genome, genetic mutations, variations, biomarkers, and more (Rodríguez-Antona & Taron, 2015). The patient genome, discussed in section 3, is the most challenging component of a genetic profile to understand because of the vast patterns. Every patient's genetic profile presents barriers that must

be navigated for effective and targeted treatment, underscoring the significance of profiling in personalized medicine.

AI In Data Analysis (High Dimensional Processing)

Documenting genetic profiles using traditional methods is highly time-consuming. AI, however, analyzes such datasets quickly, reporting the most important facts when necessary (Capobianco, 2022). This information is too lengthy to understand; however, with the streamlining of AI, processing is easier (Abdallah et al., 2023). High dimensional processing allows a better understanding of the patient's health, leaving room for educated predictions, such as how a patient may react to certain drugs or selecting a treatment plan, as it involves thoroughly understanding what the profile presents (Quazi, 2022).

AI in Pattern Recognition

Continuous training allows AI to recognize specific genetic variants. Through training and long-term knowledge building, specific trends between multiple genetic profiles can be identified (Abiodun et al., 2019). Some patterns are linked to other diseases, and the sooner the relation is found, the easier it is to diagnose the patient. AI is fundamental when classifying specific parts of the genetic profile, such as associating biomarkers with certain diseases, shaping the future of treatment. Patterns, especially in the genome, are key to discovering solutions (Mo et al., 2013).

Genome Sequencing

An integral part of a patient's genetic profile is their genome sequence. Each patient's genome is unique and made up of the four nucleotides that comprise human DNA: adenine (A), thymine (T), cytosine (C), and guanine (G) (Amano et al. 2002). Because the human genome is complex, analyzing this data using traditional methods can be very difficult.

Application of AI in Genetic Sequencing

Once the genome is documented, interpreting it is another difficult part. Issues can be identified within nucleotide sequences, though traditional methods struggle to pinpoint these problematic parts. Analyzing is a lengthy process, especially given the genome's size—it's vast (Ahsun, n.d.). AI analyzes the genome and typical patterns that indicate disease can be found in less time than manual methods. (Dias & Torkamani, 2019). These modifications of the target points are made through a process called gene editing, which will be discussed in section 6.

Example: Sequencing COVID-19

During the COVID-19 pandemic, different variants of the virus were detected. Samples were taken from patients, and the nucleotide sequences within these samples were aligned and recorded in order (Ortiz-Gómez et al., 2024). From here, AI was used to interpret the data. The genomes were compared to find relationships between the known mutations and the

SARS-CoV-2 virus. This process raised awareness of different mutations of COVID-19, such as omicron, delta, alpha, and beta (Nawaz et al., 2021). The virus's rapid spread required a swift understanding of its nature to expedite vaccine development. With the assistance of AI, they found these mutations quicker than they would have with traditional methods. The genome sequencing and AI analysis followed by bioinformatic tools expanded the knowledge of COVID-19 and the SARS-CoV-2 genome, acknowledging the different mutations and providing enough information to start vaccine research.

Biomarker Identification

After establishing a genetic profile, the next step is identifying biomarkers. These molecular changes in patients indicate biological processes, including disease. Some treatments can negatively affect the therapy, potentially worsening the disease's progression (Strimbu & Tavel, 2010). Therefore, identifying and understanding these biomarkers is significant in guiding treatment decisions and their effects.

Application of AI in Biomarker Identification

AI's role in biomarker identification is fundamental. It significantly reduces the chances of crucial information, such as biomarkers, from being overlooked (Lancellotti et al., 2021). This functionality is particularly crucial for large-scale research, where conventional methods may overlook subtle indicators because of data volume. With AI, well-identified biomarkers remain on the radar, enabling healthcare professionals to work around them and avoid side effects. Furthermore, clinicians gain valuable data illuminating potential adjustments to therapeutic regimens, including dosage alterations, medication substitutions, and synergistic treatment strategies (Strimbu & Tavel, 2010).

Example: HER2 Biomarker for Breast Cancer

Patients who struggle with breast cancer require treatment to slow the progression of cells that worsen the spread of the disease. First, a biomarker known as HER2 overexpression is found in the patient's genetic profile. This biomarker indicates an excessive growth of HER2, which promotes the growth of cancer cells. A treatment for this, trastuzumab, targets these HER2 cells, preventing further growth (Leung & Chan, 2015). Trastuzumab is a monoclonal antibody that targets the causes of HER2 overpopulation, preventing its growth. Although trastuzumab cuts down the excessive growth of HER2, it is also recorded to cause cardiotoxicity in other patients with higher levels of cardiac biomarkers. Cardiotoxicity can cause heart problems and even failure in some patients (Grela-Wojewoda et al., 2022). With these elevated cardiac biomarkers present in the patient, a new concern arises as the patient is now prone to heart failure. Despite trastuzumab delaying the growth of cancer cells, it disturbs cardiac biomarkers, eventually being a potential risk for heart failure. In such cases, it is important to have possible alternative drugs other than trastuzumab.

Drug Identification

Once all challenges in a patient's profile are recognized, the medicine process can begin. Drug identification involves evaluating drugs that best fit the patient's needs (Huang et al., n.d.-a). Combining other drugs is necessary when preparing personalized medicine. There can be hundreds, if not thousands, of different drugs with similar characteristics.

Applications of AI in Drug Identification

Just like patients, drugs have their own profiles (Pauwels et al., 2011). These profiles contain background information on the drugs, including their applications, interactions, and limitations, which help determine if the selected drug is effective for a patient's disease. AI can analyze drug and patient profiles to recommend the most suitable treatment option for a particular patient (Huang et al., n.d.-b). With AI's assistance, less testing is required, saving time and money.

Example: Metoprolol and Atenolol

An example of two drugs with similar properties is metoprolol and atenolol, two types of beta-1 adrenergic receptor blockers (Heffernan et al., 2011). Both drugs lower blood pressure, regulate the heartbeat, and treat chest pain. With two drugs with similar causes, which one is the right one? Here, there may not be a 'right' drug. Instead, the patient's specific needs must be considered when deciding the best drug. After testing, slight differences were found between both medicines, such as the dosing frequency. AI used these test results to align even the slightest differences. These distinctions were used to work even better with the patient. Metoprolol must be taken multiple times daily, while atenolol is taken once daily. Nonadherent patients struggle with following their prescription dosage, which can delay the treatment process (Griva et al., 2014). This nonadherence would be described in the AI-analyzed patient profile. With a patient struggling with this issue, their needs would be better fulfilled with atenolol, where they will have fewer dosages to remember a day.

Gene Editing

Gene editing is a form of personalized medicine that allows scientists and doctors to modify mutated sections of a patient's genome with tools to correct defects that would otherwise cause disease (Doudna, 2020). The DNA is found within a cell, and most tools require cutting the corrupted DNA.

Applications of AI in Gene Editing

First, the patient's genetic profile is used to find mutated sections of DNA to target with precise gene editing tools. The diseased part can be identified by comparing diseased and healthy patients' profiles. (Gao et al., 2021). AI facilitates the identification of contrasting features between healthy and diseased patient data, which may reveal insights into the disease's origin

and where to perform the edit. Events like this build AI's background knowledge on the specific mutation, and they constantly learn more, easing the process little by little.

Gene Editing Tools

Once the target sequence has been identified, researchers can correct the patient's genome using one of several gene editing tools. These include ZFNs (zinc-finger nucleases), TALENs (transcription activator-like effector nucleases), and CRISPR-Cas9 (clustered regularly interspaced short palindromic repeat) (Dixit et al., 2024). Although all these tools serve the same purpose, they differ slightly in terms of use difficulty, efficiency, and room for human-influenced error.

ZFNs

While operating ZFNs, small proteins recognize the target points upon entering a cell, and a FokI enzyme performs the cut (Figure 2). The cell is where the target point is located. These specific proteins are known as zinc finger proteins. They attach themselves to the range containing the target point and proceed to cut the DNA (Lim et al., 2022). Since ZFNs cut a range of DNA, there is more space for mistargeting. Compared to newer tools, they are also less precise.

When DNA is cut, a natural repair system within the cell known as Homology-Directed Repair (HDR) comes into place (Liang et al., 1998a). This process allows precise DNA replacement and involves using a template of a healthy genome, often directly from a healthy patient. From here, bio-engineered data is designed to replicate healthy DNA to match the template. This healthy DNA replaces the diseased one that has been removed.

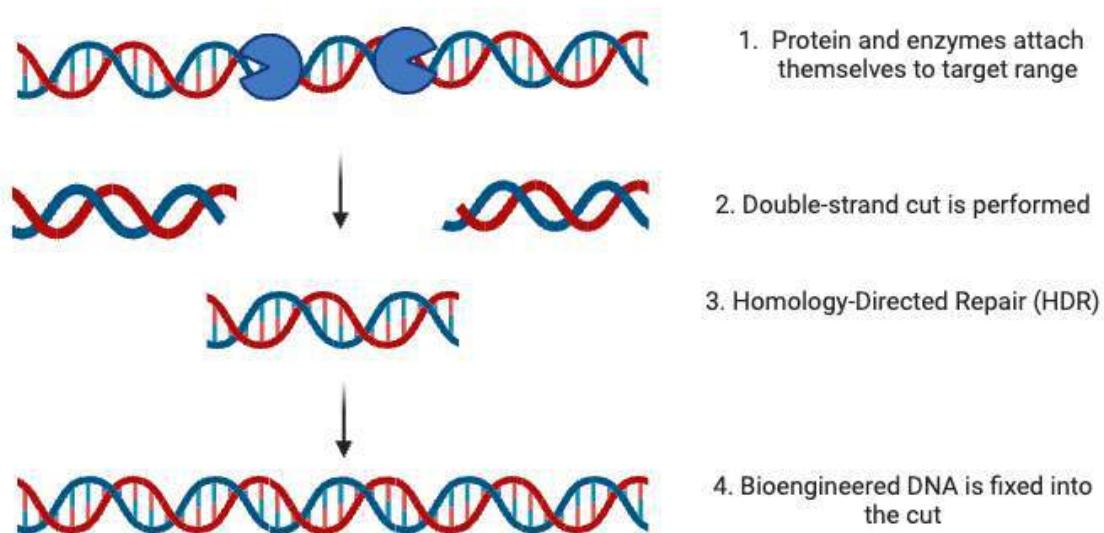


Figure 2. The process of ZFNs being applied to genetically modify DNA. Figure created using BioRender.
TALENs

Building upon the success of ZFNs with an enhanced approach, TALENs consist of two specific parts: the TALE proteins that target the mutation, and a restriction enzyme that cuts the mutation (Figure 3). These proteins are called TAL effector domains (Nemudryi et al., 2014). Similarly to ZFNs, it has engineered proteins that cut the DNA, yet are more efficient and easier to use. TALENs target precisely the point it is designed to target; therefore, compared to ZFNs, they have fewer mis-targets (Mayhew & Roth, 2018). The proteins guide the enzyme to the target point in the cell. The enzyme binds itself to the desired area and cuts it through a double-strand break. Again, here, HDR replaces the cut DNA and guides the following treatment with a template as a guide, and then the removed area is filled in with bio-engineered DNA (Liang et al., 1998b).

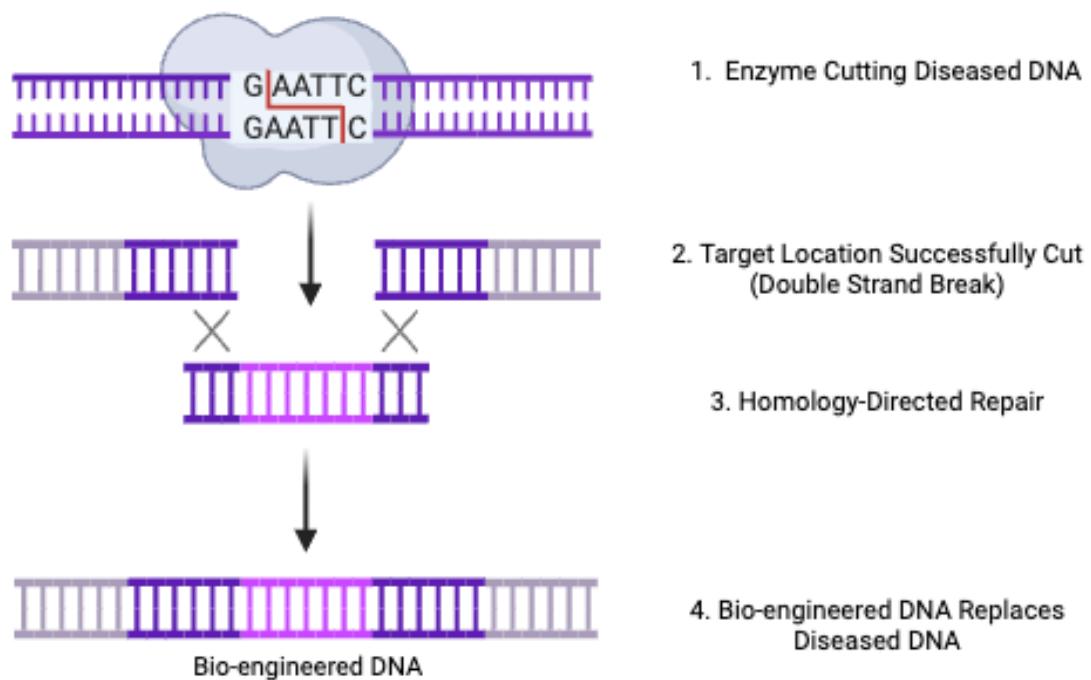


Figure 3. The process of TALENs being applied to genetically modify DNA. Figure created using BioRender.

CRISPR-Cas9

Among currently available gene editing technologies, CRISPR-Cas9 has gained widespread adoption because of its simplicity and effectiveness (Dixit et al., 2024). Although CRISPR-Cas9 exhibits similarities to ZFNs and TALENs in their DNA-cutting capacity, significant disparities exist. CRISPR-Cas9 has two major parts, a guide RNA and a Cas9 protein (Figure 4). Guide RNA is used to lead the Cas9 protein way to the targeted DNA (Zischewski et al., 2017). This Cas9 protein performs the cut in the target spot. CRISPR-Cas9 is more efficient and easier to use than alternative gene editing tools, as it can edit the DNA with guide RNA. This

tool can deactivate problematic DNA strands (Redman et al., 2016). When the diseased area of DNA is removed, HDR is performed to wrap up a process similar to ZFNs and TALENs.

In recent years, non-homologous end joining (NHEJ) has been more commonly used to wrap up the CRISPR-Cas9 process. This process directly binds the DNA using proteins without introducing any new sequence. Alternatively, the damaged section is excised, and the double-strand break is rejoined using these proteins.

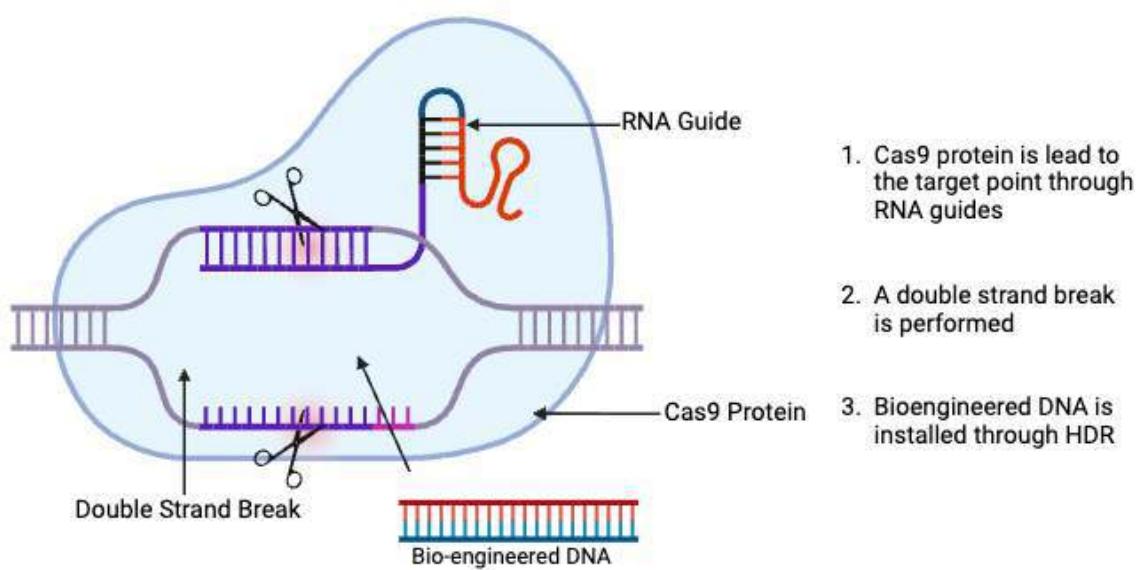


Figure 4. The process of CRISPR being applied to genetically modify DNA. Figure created using BioRender.

Example: AI and Gene Editing in Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is caused by a mutation in the dystrophin gene that results in severe weakness in certain muscles of males, leading to the progression of muscle weakness. DMD can make it hard for someone to perform everyday tasks, such as walking or being able to lift heavy objects (Strober, 2006). CRISPR-Cas9 has been used to edit the mutation. In cases of DMD, the dystrophin gene must be edited. This sequence of nucleotides is relatively large and can make it challenging to edit due to the diversity within the gene. Here, AI made it easier to edit such genes without human error through high-dimensional processing (Vera et al., 2022). This not only accelerated the process, but eliminated human error. When the target point was found, the rest of the CRISPR-Cas9 process continued. The exact location is found, and this spot is cut. A template that displays the correct version of the dystrophin gene is used to guide the actual editing. This template improves muscle function (Bengtsson et al., 2017). Although the process was robust, it was not strong enough to completely regain the muscle ability. For example, a person who is unable to walk because of DMD may still not be able to walk easily after CRISPR-Cas9 treatment. However, it leads to the slower progression of the disease. After all, the editing focuses on slowing the disease rather than excluding it entirely.

Monitoring & Adjustment

Patients are continuously monitored to ensure that any deviations in treatment can be identified and addressed promptly, preventing potential complications. By recognizing signs indicating an issue with a patient's treatment, the treatment can be modified to prevent problems.

Artificial intelligence can optimize treatment protocols by identifying areas for adjustment, generating dosage plans, and providing additional treatment details (Sheng et al., 2021). During the treatment, the patient's dosage amounts are likely to change, and when this happens, AI can make predictions, indicating potential outcomes based on treatment changes. This way, before drastic changes are made to the treatment process, researchers will know what could happen to the patient (Rajpurkar et al., 2022). With real-time data gathered through medical imaging, AI can detect specific patterns and unusual behaviors. Patient health being recorded live by AI reduces the chance of overlooking anything (Rahman et al., 2022). These machines learn from themselves, eliminating inaccuracies over time. Personalized medicine is progressing, and AI is used to guide decision-making in such cases.

Limitations

Despite AI's perks in personalized treatment, there are also certain limitations to using this tool. AI relies heavily on experience gained through training, and until training is perfected, it cannot be relied on entirely throughout treatment. It not only requires the convincing of researchers, but patients as well, who provide their personal data as input to AI technology.

Privacy

Providing data to any technology can raise privacy concerns about who can see it. Patient profiles are one of the most significant parts of personalized treatment, so there is also the risk of unauthorized access to this data (Li et al., 2024). Artificial intelligence has not reached the point where it doesn't make mistakes. One mistake could cost private information security; therefore, AI cannot be relied on entirely.

Input Data and AI Accuracy

For starters, AI needs a strong input to provide a strong output. Without enough information, responses will not be very accurate. After all, AI considers inputs such as genetic profiles, sequences, drug allergies, and family history when making a claim. In other cases, AI tries to compensate for missing information, resulting in biased information that cannot be relied on (Bolander, 2019). Another example of the significance of input is during training. When the data used to train AI is not of good quality, it can only be expected that every output given by that machine will lack some quality (Amri et al., n.d.).

Quality of Data

Biased information negatively impacts data quality. High-quality data is complete, unbiased, and reliable. Numerous mistakes can make this information less reliable, and when

unreliable data is used, every subsequent process becomes corrupted. For example, when a biased-trained AI claims to predict treatment, that prediction contains flaws (Amri et al., n.d.).

Conclusion

The role of artificial intelligence in personalized medicine is substantial, streamlining critical processes and leading to improved patient results. AI has been used to assist and improve the processes of personalized medicine that are prone to easy errors. AI's abilities to process large amounts of data and recall patterns from memory are used to their advantage while interpreting genetic profiles and sequencing the genome. While analyzing the genetic profile, AI can also interpret biomarkers and their reaction to certain drugs. These drugs are selected based on their likely reaction to the patient. Using the process of elimination and a strong memory, drug ranges are cut down, increasing the suitability of medicine for the patient. Another approach to personalized medicine is gene editing. AI can determine target spots because of the well-analyzed genome and pattern recognition. With the streamlining of AI, researchers can continue with this process smoothly. Despite the approaches taken, the patient is put under intense monitoring. AI identifies problems ahead of time so clinicians are prepared and know what to do when any turns are taken during treatment.

In summary, AI's abilities are remarkable compared to traditional methods. Traditional methods do not involve advanced abilities such as pattern recognition, high-dimensional analysis, or AI-based data analysis. Strategically placing AI in these processes enhances accuracy, eliminates many human mistakes, and optimizes treatment, leading to better overall outcomes. Despite all these positives, AI also has limitations that must be overcome to reach its maximum potential.

The continued evolution of AI will undoubtedly lead to better outcomes in medical processes. As AI continues to train, we move closer to a future where medical decisions are more precise and tailored to the unique needs of every patient. However, for this to happen, the limitations of AI must first be bypassed.

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Qualitative Analysis of How AI is Affecting Companies and Corporations in United States By Cheng Zhong

Abstract

This study's purpose is to explore the transformative effects of Artificial Intelligence (AI) on major businesses such as Nvidia, Meta, and Amazon in order to find the impacts on the work environment, revenue growth, and employee's job that are caused by AI. Including AI into businesses have caused improvements on productivity and decision-making with revenue growth while altering the traditional workspace structure. In this secondary research, this study will examine how adding AI into the HR department has impacted aspects around it like recruitment. I'll also be examining how AI tools and softwares are being implemented into big corporations and companies that boasted revenue growth, and finally how AI might replace jobs in the future. This research will be conducted by using both qualitative insights with quantitative data which will be used to highlight the importance of AI in the function of a company.

Key Word Artificial Intelligence, Work Environment, HR, Human Resources, Nvidia, earnings, Big Data, Revenue growth, Meta, Amazon, Softwares, Tools.

1. Introduction

Background

Artificial Intelligence(AI) is a technology that allows machines to simulate the process of thinking like a human being. It is currently a tool that is being used for data analytics, predictive analytics, risk management, fraud detections and much more; therefore, making them very beneficial for any businesses. Although AI has existed for some time, the technology has made leaps and bounds over the past few years, undertaking complex, high-skilled, and creative tasks that one might never have imagined possible. For example, from Quarter two of 2023 to quarter two of 2024, which was July 28th 2024, Nvidia's revenue has increased by 122% according to the earnings press release from Nvidia. Major tech companies like Nvidia, Tesla, Meta, and Microsoft in the last year or so have implemented AI applications into their service and products which is not only causing massive revenue growth, but also fundamentally altering the work environment for employees.

Purpose

The purpose for this research is to understand and find out the effects of implementing AI in companies.

Research question

What effects would the introduction of AI bring to corporations and businesses?

Thesis

AI has become a major monumental asset for major technology companies, since it has significantly altered or changed the work environment for employees and reassigned roles for everybody, while augmenting earnings and growth revenues.

2. Literature Review

2.1 AI's role in the HR Department

Previous studies related to this subject have been done before. For example, Alejandro Ramo's study called "The AI Revolution in Human Resources: Transforming Talent Management and Workplace Dynamics" digs in and investigates the effects of AI in work spaces like Human Resources (HR). In the study, he illustrates how machine learning AIs are able to rapidly analyse a big dataset, lead to a more accurate forecasting, enhance customer targeting, and streamline inventory management. By exploiting these skills, companies can make decisions based on previous data a lot more efficiently, while also reducing the costs previously needed. However, some issues are still to be kept in mind. For example, AI is using data accumulated from the past to make decisions; therefore, if the past data favoured let's say male over female, then the AI will make decisions based on that.

2.2 The McKinsey & Company report

The McKinsey & company report on "The State of AI in 2023: Generative AI's Breakout Year" illuminates the growth use of generative AI tools across all kinds of industries and how 60 percent of organizations with reported AI adoptions are using generative AI tools in their business function. Not only this, but also 40 percent of those organizations plan on investing more money in generative AI. This sudden growth can be explained by how generative AI has the ability to improve sales, products and service developments, and service operations. However, It's also worth noting that there are potential risks of AI that haven't been addressed properly. For example, according to this report, 32% of people say that risks of inaccuracy have been mitigated, and other risks like cybersecurity have also been mitigated. Not only this, but also because of the sudden growth and rise of AI in huge organizations and corporations, employees are needed to adapt to the sudden changes by learning how to be proficient in the use of AI.

3. Methodology

This paper will be researching how AI has transformed the work environment in employee roles, productivity, job satisfaction, and skill requirements. However, this paper will not include primary resources; therefore, I'll collect data from secondary sources in a qualitative way with quantitative insights by using both popular sources and scholarly sources.

3.1 Quantitative resources

For Quantitative resources we'll be using data already collected by McKinsey & Company's (2023) survey and report that highlight insights like productivity gains and cost reductions.

3.2 Qualitative resources

We'll be using sources like Davenport & Ronanki (2018) from Harvard Business review to understand how companies have incorporated collaborative Intelligence, where both human and AI work together side by side to enhance each other. We'll also be using scholarly sources such as The Neural Slate Journal (2024), which discusses how since the introduction of AI, work environment, and skill sets needed have all been changed; therefore, causing a massive amount of adaptations needed.

4. Results

4.1 AI's involvement with recruitment in HR

The introduction of AI has transformed HR immensely due to its abilities to perform repetitive tasks, analyse large data sets, and provide predictive insights. These basic abilities have enhanced all aspects of the HR compartment such as recruitment.

AI has been very beneficial on the subject of recruitment for the human resource department. The main AI tool that has been used for Recruitment is known as the applicant tracking system(ATS) and it has been able to reduce the amount of time required for the initial screening and time-to-hire phase by an immense amount, since it can scan through an abundance of resumes, online profiles, and other digital footprints to decide whether the candidate is competent or not.

ATS has been detected as in use by 98.4% of the Fortune 500 companies. This is tantamount to 492 companies out of 500 companies. However, it is also worth noting that the remaining 8 might have been using ATS as well but couldn't be detected; therefore, the system could've been built in-house according to the "2024 Applicant Tracking System (ATS) usage report: Key Shifts and Strategies for Job Seekers" written by Kelsey Purcell. In addition to all this, due to the abundant use of the ATS systems, the market cap for this service is worth 15.03 billion dollars in 2023; moreover, it is predicted to have a market growth of 8.3% from 2023-2030 expected to reach 26.24 billion dollars in 2030, ultimately creating more opportunities in new field.

4.2 Job Replacement Concerns

Generative AI has potential to alter the global economy as it enters the business world, capable of driving a 7% increase in global GDP while lifting productivity growth by 1.5 percent points over a 10 year period. However, the introduction of AI has raised a significant concern related to the displacement of jobs that involve doing repetitive tasks such as clerical or secretarial roles. According to a report conducted by Goldman Sachs, Jobs in agriculture,

mining, and other physical labours would be least dangerous to generative AI; however, jobs in information processing units like IT are most endangered, since generative AI can basically do the same thing they do. New waves of AI systems can have major very serious impacts all around the world, since they can be capable of replacing 300 million people's full time jobs into automations and that around two third of U.S. occupations are at risk of being replaced by AI.

It is also worth noting that although plenty of jobs are being endangered due to generative AI and other AI tools, new opportunities have also been created by the introduction of these AIs. For example, The World Economic Forum predicts that by 2027 the demand for machine learning specialists such as data analysts and scientists will rise by 30-35%, and another 31% rise for information security analysts. These would add up to be around 2.6 million jobs.

4.3 Effects on Revenue from AI

The emergence of AI has caused growth in revenues for major companies that implemented it. This section will be exploring how major businesses such as Nvidia, Meta, and Amazon have successfully implemented AI into their cooperation, which have caused earnings to almost double, while also exploring major businesses, such as Intel, which failed to implement AI and is also struggling its dominance in the market.

Nvidia is currently the world leader of AI, especially with the Graphics Processing Units(GPU) designed to optimise the use of AI softwares and applications. By including AI as a helpful tool inside the company, the role of many software engineers has been changing bit by bit. For example, employees are now expected to work side by side with AI so that the improvements on AI-driven GPUs can be maximised as well as the power of computing. It's also worth noting that Nvidia's revenue has increased by over 122% year-over-year in Q2 of 2024, which ended on July 28, because of its AI-powered data centre business according to Nvidia's Q2 financial report.

Meta on the other hand, by adapting AI to its platform, has caused a substantial amount of revenue growth. For instance, AI has been implemented in almost all aspects of meta, from Instagram's and Facebook's search tools to Generative AIs that are capable of generating images. As a result of this, Meta's revenue growth had a 22% increase in Q2 2024 which is also equivalent to a little over 39 billion dollars over the span of a year according to the second quarter 2024 financial highlight report that was published by meta.

In Q2 of 2024, Amazon also had a monumental revenue growth which was apparently achieved by implementing AI tools to a few aspects of Amazon. AI tools such as Rufus shopping assistant and Fire TV search are AI-driven personalization tools that have been implemented into Amazon which were designed to augment customer experience for improvements on sales. New AI-driven softwares such as Bedrock and SageMaker on the other hand was also implemented by Amazon used as cloud services. As a result of all this, Amazon's segment sale increased 19% year-over-year to 26.3 billion dollars in Q2 of 2024, while on the other hand net sale increased by 10% to 148 billion dollars also in Q2 of 2024 compared to just 134.4 billion dollars in Q2 of 2023.

5. Discussion

This secondary research highlights AI's role in transforming the work environment such as HR and revenues in major corporations. Tools like ATS have completely altered the recruitment system; therefore, making HR departments much more efficient in processing applications. However, there still remain potential ethical issues particularly for potential biases in decision-making processes. While on the other hand, companies like Nvidia, Meta, and Amazon are experiencing a rapid revenue growth in Q2 of 2024 due to incorporating AI in some aspects of the Company. For example Nvidia is making AI-driven chips with employees using AI to train the chips, Meta is implementing AI search bar and generative AI into their apps like Facebook and Instagram, and finally Amazon is implementing AI-driven personalizers and cloud that enhances and augments customer experience which was ultimately responsible for increasing net sales. Implementing AI into companies and organisations could be essential and good for time efficiency. However, issues like job displacement are still needed to be brought up since it can be detrimental to our society, but new job opportunities will also emerge; therefore, also benefiting our society.

6. Conclusion

This research highlights the transformation of the work environment that AI is causing while also driving up revenue; therefore, altering roles within companies. Gigantic companies on the fortune 500 list such as Nvidia, Meta, and Amazon have been optimising the use of AI by implementing it in numerous aspects of the business. However, these achievements and benefits also have a downside to it such as job displacement and the need to adapt to a new workforce that is centered around AI. In conclusion, AI is a very powerful tool that is capable of enhancing multiple aspects of the company; therefore, by implementing this monumental tool can help with productivity, and revenue growth while also creating new opportunities for new fields, but also replace jobs in some fields.

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Calculating Temperature of the Sun Using Phypho By Rakshith Ajay

Abstract

Calculating the temperature of the Star that keeps life alive on Earth through the means of ambient light sensors available on every smartphone in the world accessed through Phyphox. The paper deals with converting illuminance data collected from the ambient light sensor on the smartphone into spectral radiance to finally calculate the temperature of the sun. The paper entails conversion of units from lux to spectral radiance to calculate the temperature of the Sun. Through the use of paper filters of Red, Blue and Green colours, light was filtered into these 3 wavelengths. The temperature was calculated for each of these wavelengths and averaged to arrive at the final temperature. The accuracy was approximately 97%, this can be due to lack of consideration of all wavelengths, heat loss, and quantity of data points per wavelength.

Introduction

The Sun, the star that lights up the Earth, is the closest star to our planet and facilitates life on earth by providing the energy and heat . The Sun burns brightly at extreme temperatures, estimated to be around 5772 Kelvin (K) (Gray, 2008). However, is there a way to arrive at this value without relying on expensive, inaccessible equipment? This research paper aims to explore whether it is possible to calculate the temperature of the Sun using tools accessible to everyone across the globe. The motivation behind this problem is to democratize scientific knowledge by finding a way to observe a significant quantity, such as the Sun's temperature, with the available technology (Lindsey, 2020).

There are several methods scientists use to measure the Sun's temperature, including spectroscopy, space observatories, and pyrometers. Spectroscopy, for instance, involves studying the intensity and distribution of light at different wavelengths. A spectrograph splits the light intensity across different wavelengths, allowing the temperature to be calculated by relating intensity to the temperature of a black body (Andor, n.d.; Pasachoff, 2003). Pyrometers, the most accurate instruments, are commonly used to measure the Sun's temperature by focusing infrared radiation onto a detector, which then converts it into electrical signals. The temperature is then calculated through the intensity of the infrared radiation (Encyclopaedia Britannica, 2019; Hudson, 2017).

Phyphox is a mobile application created to use the array of sensors embedded in a smartphone. This ingenious tool transforms any device into a powerhouse for scientific exploration, leveraging sensors like sound, acceleration, and light to open a world of scientific discoveries (Staacks et al., 2018; Kuhn & Vogt, 2019). Through Phyphox, scientific discoveries have become accessible to the public. By experimenting with the wide range of sensors available in the Phyphox application, users can arrive at their own scientific conclusions. Phyphox uses existing hardware present in the phone; through background code, it extracts data from these sensors on demand from the user. All smartphones come with a treasure chest of sensors, and Phyphox can be treated as the key to unlocking and accessing this treasure (Lemay et al., 2021).

The aim of this research paper is to determine the temperature of the Sun using Phypyox to measure data on illuminance from the Sun. The data gathered is then converted from illuminance to spectral radiance, requiring a unit jump from photometric to radiometric quantities. The paper briefly discusses the conversion of quantities from photometric to radiometric. Following this, Stefan-Boltzmann's equation is utilized to calculate temperature values for each wavelength (Red, Green, and Blue). The final temperature provided in the results section is the average of these three temperatures (Walsh, 1926).

Methodology

The aim of this research paper is to calculate the surface temperature of the Sun using data on the light emitted from the Sun collected through Phypyox. The link between illuminance and temperature can be made using blackbody equations.

A black body is an object that is a perfect absorber and emitter of radiation, with an emissivity of 1. Emissivity is the ratio of energy radiated from an object to the energy emitted from a black body. Blackbody radiation is the energy radiated by any object that absorbs all the incident radiation. One of the main factors involved in blackbody radiation is the wavelength at which the energy is emitted. Black bodies emit some light at all wavelengths, but there is a peak wavelength that depends on the temperature of the object. The greater the temperature, the shorter the wavelength (Planck, 1901; Wien, 1893).

In the real world, there is no perfect black body except black holes. The Sun, however, is considered a near-perfect black body for the purposes of this study because it radiates continuously across all wavelengths due to the highly opaque inner layers that absorb all radiation. Nonetheless, a small fraction of light is reflected, preventing it from being a perfect black body (Stix, 2002; Adams, 1925).

The light sensors on a phone work by converting the detected light into electrical signals. These signals can then be interpreted and analyzed. Every phone contains an ambient light sensor, which detects light from the surroundings and adjusts the brightness of the phone screen accordingly. Phypyox accesses this sensor to collect light data (Staacks et al., 2018; Lemay et al., 2021). Phypyox contains programs capable of accessing sensors on every phone if the sensor has authorization to share data with third party apps.

The primary research method used in this study involves primary data collection using the Phypyox application. Through Phypyox, data was collected in the form of illuminance by detecting the light (illuminance) emitted by the Sun with the phone's light sensor. The data was collected by placing the phone outside in broad daylight. Furthermore, to collect data from different wavelengths, filter papers of various colors (Red, Green, and Blue) were used. The data was collected in 15-minute intervals for each wavelength. The objective of this study is to calculate the surface temperature of the Sun, which can be done using blackbody equations relating illuminance to temperature.

To calculate the temperature of the Sun using this data, the illuminance (the amount of visible light incident on a surface per unit area) needed to be converted to spectral radiance (the

radiant flux emitted as a function of wavelength). The conversion was done using the following formula:

$$\left(B(\lambda) = \frac{E(\lambda)}{\nu(\lambda) \times 683} \right). \text{ (Andor, n.d.)}$$

Quantity	Symbol	Unit
Illuminance	$E(\lambda)$	Lux
Luminous Efficiency	$V(\lambda)$	Lumens
Spectral Radiance	$B(\lambda)$	$\text{W} \cdot \text{sr}^{-1} \cdot \text{m}^{-2}$

Table 1

This relationship is used as the standard for converting photometric quantities to radiometric quantities (Andor, n.d.; Pope et al., 2018). Illuminance is a photometric quantity, meaning it refers to the quantity's perceived brightness to the human eye, while spectral radiance is a radiometric quantity, which concerns the power emitted by a light source over an area (Pope et al., 2018; Smith, 2020).

After converting illuminance to spectral radiance, Stefan-Boltzmann's equation was applied:

$$L = \sigma A T^4$$

Where T is the temperature, L is the spectral radiance, and sigma is the Stefan-Boltzmann constant. The area of the sensor, found to be approximately $8.09976 \times 10^{-6} \text{ m}^2$ (Texas Instruments, 2024), was used in the calculations. Upon substituting the values for each wavelength (Red, Blue, and Green), individual temperatures were calculated. The final temperature was then obtained by averaging these values, yielding a result close to the known temperature of the Sun.

We collected 3082 data points using phyphox. Through this data the average illuminance and other calculations cited in the methodology were performed as shown below.

Results

Wavelength Colour	Illuminance Mean (Lux)	Wavelength (nm)
Red	10041.6	650
Green	73049.41	550
Blue	105374	450

Table 2: Illuminance and Wavelength values

Wavelength Colour	Luminous Efficiency (Lm)	Spectral Radiance ($\text{W} \cdot \text{sr}^{-1} \cdot \text{m}^{-2}$)
Red	0.107	137.55621

Green	1	106.9538
Blue	0.038	4052.846

Table 3: Luminous Efficiency and Spectral Radiance Values

Wavelength Colour	Temperature (K)
Red	4160
Green	3906.6
Blue	9692

Table 4: Wavelength Colour and Temperature Values

Discussion

The study successfully accomplished the goal of calculating the approximate temperature of the Sun. The final value being within 150 Kelvin of the true temperature of the Sun. This calculation can be further refined through more accurate data collection, furthermore, instead of considering the mean value, median could be considered for a more accurate measure of central tendency which will not be influenced by outliers.

We find the temp extracted from this data to be 4160 K for red, 3906.6K for green, and 9692K for blue, The average comes out to be 5919.5K. The known value of sun temperature is 5772K, which is close to what we have obtained.

$$\text{Final Temperature} = \frac{4160+3906.6+9692}{3} = 5919.5 \text{ K}$$

$$\text{True Temperature of the Sun} = 5772 \text{ K}$$

Conclusion

We studied the solar temp using a hand held device and were able to measure it to a good accuracy. The variation can be attributed to losses in energy to come to the surface, climate, clouds, and other environmental factors. The quality of the sensors will have limitations as compared to a research grade apparatus. But we show that a mobile can still give a good approximation to solar temperature.

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How does Stigma Contribute to the Development of Mental Health Disorders Among Asian Immigrant Adolescents? By Sophia Baek

Abstract

Mental health discrepancies are prevalent among Asian immigrants in the United States, owing to stigma associated with traditional family values and a lack of education on mental health. Specifically, traditional Korean cultural values (*chaemyun* (체면) and *nunchi* (눈치)) may contribute to negative conceptions of psychological disorders. Consequences can be detrimental for mental health (e.g., suppressing one's feelings due to fear of being stigmatized against), especially during adolescence, which is a susceptible period for the development of mental health disorders. Anticipated stigma may prevent adolescents from seeking the mental health care they need, resulting in low self-esteem, social withdrawal, isolation, and avoidance. Self-stigma entails adverse feelings such as self-blame, which contribute to depression and other long-term problems. Furthermore, immigrants are more likely to suffer specific stressors, such as acculturation stress, which exacerbate mental health issues. Discrimination within their own cultural group worsens stress and reinforces maladaptive coping strategies, perpetuating mental health problems in the process of adjusting to a foreign environment. In this review paper, I explore how stigma contributes to mental health problems among Asian immigrant adolescents, focusing on Korean culture when possible. Importantly, I examine potential interventions like education initiatives, social media campaigns, and organization activism to address these challenges and improve mental health for future generations.

Introduction

Mental health disparities are prominent among Asian immigrant adolescents in the United States. Elevated depressive symptoms were higher among Asian American adolescents compared to their European American counterparts, with a difference of 17% (Kubik, Lytle, Birnbaum, Murray & Perry, 2003). Other estimates of prevalence find that depression and other mental health disorders are lower among Asian Americans compared to other ethnic and racial groups; however, these numbers may be inaccurate as Asian Americans tend to underreport feelings of sadness and depression (Kalibatseva & Leong, 2011). Underreporting likely occurs due to shame and stigma surrounding mental health problems and the cultural norms that shape the behavior of Asians in which they often suppress their unwanted characteristics (Wei, Su, Carrera, Lin & Yi, 2013).

In this review paper, I aim to explore the contributors to mental health disparities by examining the role of stigma as it relates to traditional Asian cultural values, focusing specifically on Korean adolescent immigrants. There is an important need to better understand this population. According to a meta-analysis, Korean-Americans have higher rates of depression (Kim et al., 2015) and more severe symptoms compared to other Asian American groups such as Chinese and Japanese-Americans (Lee et al., 2020). Furthermore, immigrants are prone to experience unique stressors, including acculturation stress, which exacerbates mental health

issues (Oppedal, Roysamb & Sam, 2004). Discrimination against those with mental health problems from within their own cultural group can further intensify stress and perpetuate maladaptive coping strategies, maintaining or worsening mental health problems. Additionally, emphasizing adolescence is essential since individuals within this developmental phase are particularly prone to mental health challenges within the process of identity formation (Uhlhaas et al., 2023). Lastly, I also examine possible interventions and education initiatives that may positively impact the outcomes of future Asian immigrants, with the ultimate goal of reducing mental health disparities among Asian immigrant adolescents in the United States.

Traditional Values and Social Constructivism Within Cultures

Social constructivism is the theory that groups of people within a culture interact to develop shared beliefs (Yang & Gergen, 2012). This concept is fundamental in establishing consentient norms and expectations within a community, where the individual's behavior is guided by the standards of the society (Lee, 1999). Cultural values can become deeply rooted through repeated interactions over generations to enforce adherence to the implicit norms in their respective cultures (Miyahara, Kim, Shin, & Yoon, 1998). These interactions can involve interpersonal conflict to dissuade transgressing a culture's values. Compliance to norms and values are therefore often driven by desires to avoid conflict and maintain harmonious relationships.

Korean culture is notably based upon traditional Confucian beliefs that emphasize maintaining harmony and values of collectivism (Han, Cha, & Lee, 2017). Collectivistic communities stress the significance of self-sacrifice and dependency rather than individualistic perspectives that prioritize one's personal desires (Wu, Yan, Zhou, Chen, Li, Zhu, Shen & Han, 2010). An altruistic devotion to their surrounding community exemplifies solidarity and promotes positive familism, or exhibiting loyalty with presumed responsibility for the members of one's family. Two critical concepts interrelated with these values are *chaemyun* (체면) and *nunchi* (눈치).

Chaemyun, which refers to the principle of saving face in public, is considered to be the backbone of many Confucian doctrines held by Korean individuals. The face-saving culture was originally based on a Taoistic shamanism viewpoint in which the sense of shame is theorized to emerge from consciousness of the failure to attain self-satisfaction (Lee, 1999). This feeling of discomfort is closely associated with an ontological sense of guilt, a common reaction to self-awareness and striving toward self-realization. Thus, by saving face, an individual is protecting their reputation by doing what is socially acceptable in order to compensate for their remorse. For individuals with mental illness, this compelling need for societal prestige and preserving one's own sense of dignity can create undue pressure. In particular, those with mental illness may fear losing status due to being considered an outgroup from the rest (i.e., discrimination and shame).

Nunchi (literally translated, “eye-measure”) is often described as an aspect of emotional intelligence (EQ) that signifies the ability to gauge and evaluate social situations through subtle

cues ([Yim, 2017](#)). Its correlation to interpersonal awareness allows individuals with a more developed sense of nunchi to display higher levels of self-esteem. Consequently, the collectivistic mindset of Korean culture encourages the practice of nunchi as a way to mediate one's emotional wellbeing, as well as behaving in a way that forestalls conflict between relationships. The behavioral aspect of nunchi can impact both the stigmatized and the stigmatizing group ([Yim, 2017](#)). High levels of nunchi may shape an individual's belief towards mental health disorders in order to accommodate for the united values of their surroundings (i.e., peers who have stigmatizing beliefs). In other words, being surrounded by people who take part in discriminatory behaviors can significantly impact the perspectives of others by causing them to hold similar beliefs.

These two cultural values (chaemyun and nunchi) play an important role in stigma outcomes, with both beneficial and harmful effects for individuals. Consequences for people with mental health problems in cultures with traditional Korean values are discussed below.

Stigma

Social stigma can be defined as the discrediting of one's status based on a quality or characteristic that distinguishes them from others in the society. Stigmatizing beliefs related to psychiatric disorders, known as mental health stigma (MHS), are commonly reinforced by social cognitive processes where prejudicial attitudes may lead to discrimination ([Sickel, Seacat & Nabors, 2014](#)).

Mental health stigma (MHS) can be categorized into three mechanisms most relevant to the stigmatized group of individuals: 1) internalized stigma, 2) anticipated stigma, and 3) experienced stigma ([Fox, Earnshaw, Taverna & Vogt, 2019](#)). The stigmatized group consists of people with a history of mental illness and therefore susceptible to MHS manifestations such as prejudice and discrimination.

Experienced stigma is the firsthand act of MHS where individuals directly encounter stigmatizing attitudes within interpersonal relationships ([Cechnicki & Bielańska, 2009](#)). Examples of experienced stigma can range from momentary biases to major prejudice in which the stigmatized are devalued through discriminatory beliefs (e.g., that those with mental health problems are dangerous, unpredictable, and out of control) ([Fox, Earnshaw, Taverna & Vogt, 2019](#); [Han et al., 2020](#)). Repeated encounters of experienced stigma can provoke dissonance in one's self-evaluation, thus contributing to behaviors like disengagement and isolation ([Kondrat, Sullivan, Wilkins, Barrett & Beerbower, 2018](#)). Additionally, these moral judgments against those with a mental disorder can lead to other detrimental consequences such as label avoidance (refraining from receiving treatment to avoid being assigned a stigmatized label) and treatment non-adherence (choosing to deviate from treatment) ([Fox, Earnshaw, Taverna & Vogt, 2017](#)) that may prevent the fulfillment of human needs (i.e., love and belonging, esteem, and self-actualization) ([James, 2016](#)). Anticipated stigma, often referred to as felt stigma, involves one's expectations regarding how they may be perceived by others ([Quinn, Williams & Weisz, 2015](#)). Anticipated stigma can arise via vicarious learning whereby witnessing negative episodes

of MHS discrimination can result in the acquisition of fear ([Askew, Hagel & Morgan, 2015](#)) and lead to expectations that others will discriminate against them in the future. Consequently, people with mental illness may anticipate being stigmatized or discriminated against outside of an actual occurrence of stigmatizing behavior ([Fox, Earnshaw, Taverna & Vogt, 2019](#)). Lastly, internalized stigma occurs when a person internalizes the negative stereotypes of public stigma ([Mittal, Sullivan, Chekuri, Allee & Corrigan, 2012](#)). High levels of self-stigma are associated with decreased self-efficacy and self-esteem ([Fung, Tsam, Corrigan, Lam & Cheung, 2007](#)), as well as low quality of life ([Yen, Chen, Lee, Tang, Ko & Yen, 2009](#)). Most people with a psychiatric disorder are aware of the stereotypes formed against their group and often concur with these thoughts to form a sense of demoralization ([Corrigan & Watson, 2002](#)). Notably, these categories of stigma can interact with each other. For example, studies indicate that increased levels of anticipated stigma correspond to intensified feelings of internalized stigma ([Quinn, et al., 2015](#)).

Traditionally stigmatizing values held by Korean and other Asian communities can have detrimental consequences for those with mental illness. Despite Asia's rapid growth rate, their mental health service utilization was reported to be one of the lowest in the world ([Devitre & Pan, 2020](#)). Values such as chaemyun and nunchi create culture-specific barriers that prevent mentally ill patients from seeking necessary treatment ([Goel, Thomas, Boutte, Kaur & Mazzeo, 2021](#)). Additionally, the prevalence of stigma within these cultures creates cognitive conflict where the individual must choose between treatment for their disorder or maintaining in-group harmony.

Acculturation and Mental Health

In addition to grappling with stigma related to traditional Korean values, Korean immigrants to the United States or other countries also experience unique added stressors related to acculturation and the contrast between the two cultures they are straddling. Therefore, the concept of acculturation stress can aid in our understanding of Korean immigrant mental health specifically. Immigrants often struggle with adapting to their surroundings when exposed to a new culture ([Kosic, 2004](#)). The cognitive stress imposed on immigrants often induces a process called acculturation, where the individual navigates cross-cultural differences that may lead to increased mental problems ([Rudmin, 2008](#)).

This phenomenon can be split into two categories: (1) features of the original society, and (2) personal insights and characteristics ([Kosic, 2004](#)). The societal aspect of acculturation mainly stems from balancing traditional standards of one's host community and the foreign elements of their new environment. Individuals face confusion in their identity in the process of accepting an unfamiliar culture. Similarly, individual personality characteristics such as self-esteem, locus of control ([Ward & Kennedy, 1993](#)), and internal conflict are factors that can contribute to depressive symptoms when met with challenges during immigration ([Park & Rubin, 2012](#)). For instance, the feeling of being obliged to fit into new groups of people can create psychological distress that may interfere with critical periods in adolescent development (i.e., role confusion and identity formation) ([Streeck-Fischer, 2015](#)).

There are stark cultural differences between Korean and American societies. Indeed, studies suggest that among Korean immigrants in the United States, structural confusion during the process of immigration relates to elevated levels of stress ([Oh, Koeske & Sales, 2010](#)). The mediating influence of acculturation also derives from facing different norms as the individual must maintain their traditional roots while embracing the standards of their surrounding culture ([Kim, 2013](#)). Additionally, elements like limited social support within Korean communities can extend the struggles of such immigrants as the lack of facilitated resources prompts helplessness and alienation ([Moon & Pearl, 1991](#)).

Overall, Korean adolescents who have immigrated to the United States represent a population who is particularly deserving of attention when it comes to their mental health needs due to 1) acculturation stress, 2) mental health stigma related to traditional cultural values that may stand in contrast to American values, and 3) their developmental stage of adolescence, which is a sensitive period for the onset of mental health disorders as well as a time period when individuals attempt to establish their identities ([Uhlhaas et al., 2023](#)).

Interventions

South Korea, despite its rapid growth rate, is severely lacking regarding the psychiatric treatment provided for those with mental illness ([Seo, Song, Ku, Park, Myung, Kim, Baek, Lee, Sohn, Yoo & Park, 2022](#)). Mental health stigma in Korea has negative effects on help-seeking, with emphasis on several structural barriers related to mental health literacy. Additionally, previous studies show that Korean immigrants in the United States tend to dismiss available mental health services, causing treatment delay and exacerbating their symptoms ([Han, Cha & Lee, 2017](#)). This chronic cycle perpetuates discrepancies between the number of people in need of treatment and those who actually receive it ([Seo, Song, Ku, Park, Myung, Kim, Baek, Lee, Sohn, Yoo & Park, 2022](#)).

Regardless of the ubiquity in treatment avoidance, Koreans who are willing to seek help are often unable to do so (e.g., due to not knowing if their mental health problems are treatable, or how to access treatment). The lack of education on mental health, or mental health literacy (MHL), is significant in South Korea ([Choi, 2022](#)). MHL is an essential preventative measure that should be implemented into educational institutions as it may allow children and adolescents to access and utilize mental health-related resources with ease. The impact of these circumstances is evident in the varying help-seeking behaviors among Korean adolescents. For example, those who are unaware of what mental illness they possess and therefore do not recognize a problem can be educated through MHL to familiarize themselves with treatment availability. Furthermore, adolescence is an important period in the onset of mental disorders ([Uhlhaas et al., 2023](#)), making it vital for these individuals to acquire appropriate knowledge on one's mental health during this time. Possible interventions and MHL strategies are discussed below.

Educational Initiatives

The most reasonable intervention would be to implement MHL education curriculums in more schools across the United States. Several U.S. K-12 schools have already adopted health programs into their educational track and provide counseling services for those suffering with mental illness (Teich, Robinson & Weist, 2008). School-based mental health education can teach individuals about various MHL factors including knowledge on mental health, MHS components, and help-seeking management (Nguyen, Dang, Bui, Phoeun & Weiss, 2020). Underrepresented countries in Asia often struggle to provide mental health resources for children, causing treatment inadequacy (Malhotra & Patra, 2014). Unfortunately, no studies to date have tested the effectiveness of implementing school-based MHL programs in South Korea. However, a small body of research has examined school-based programs in other countries in Asia and Europe, with mixed findings. In a multi-site study conducted in schools in Vietnam and Cambodia, teachers and students were educated on the topic of mental health (Nguyen, et al., 2020). Teachers are integrated as the ‘trainer’, in which they are initially trained to teach their students on MHL, thus being positioned as a knowledgeable educator within the institution. Effectiveness of this method has been assessed via systematic reviews where variables (i.e., mental health knowledge, stigma, and help seeking) were analyzed before and after the implementation of MHL at schools from various regions. Results from this study show that MHL curriculums increased the students’ level of knowledge and willingness to interact with those with mental illness post-intervention, but did not result in significant differences in stigma or help-seeking. This finding was surprising as researchers predicted that changes in knowledge and attitudes (in this case, willingness to interact with people with mental illness) would result in an impact for stigma-related constructs.

In contrast, a study outside of Asia assessed the impact of MHL using a different approach. To evaluate the extent to which MHL curriculums may impact students' knowledge and attitudes towards mental illness, a school-based intervention was implemented to five-hundred and forty-three adolescents aged between 12-14 in northern Portugal (Campos, Dias, Duarte, Veiga & Palha, 2018). The participants were split into two groups, the control group (CG) and the experimental group (EG), where a trained psychologist delivered 90 minute sessions that educated students on MHL factors following an interactive methodology to the EG (i.e., group dynamics, music and videos). The effects of this intervention were measured with a Mental Health Literacy questionnaire (MHLq), which was assessed one week pre-intervention and one week post-intervention. It was found that the EG had significantly higher values in all sections of the MHLq (Knowledge/Stereotypes, First Aid Skills and Help Seeking, and Self-Help Strategies) than the CG, which suggests effectiveness of the intervention. The intervention also improved other dimensions like level of knowledge on mental health and self-help strategies (e.g., more likely to seek help when needed). Taken together, this program resulted in better results compared to Nguyen, et al., 2020, especially in terms of increasing help-seeking, which may be due to using assessment tools that were more sensitive to change, or due to using an

intervention that was engaging (i.e., music, dynamics, videos), delivered by a mental health professional, and was adapted to the specific population.

Regarding the positive results of this study, future initiatives should address the lack of MHL programs in underrepresented regions of the United States tailored for Asian or Korean immigrants. Immigrants with limited access to mental health education can benefit from in-school resources to enhance their understanding of the subject. The promotion of mental health advocacy and knowledge can be greatly impacted by education initiatives, as observed in this study. It is crucial that more schools participate in implementing an educational curriculum for youth and adolescent groups in order to yield positive results for future generations.

Organizational Activism

In order to increase adolescents' help-seeking behaviors and knowledge on mental health, many high-schools and universities have developed and/or promoted voluntary groups that spread mental health awareness ([Gallagher & Taylor, 2014](#)). Specifically, non-profit organizations like Active Minds work to educate students on MHS and other variables related to mental health struggles (i.e., help seeking, self-care, and crisis information) ([Active Minds](#)). Once adopted by schools, Active Minds is peer-led by students within the institution to provide free and accessible resources for those in need.

Previous research has shown that exposure to narratives regarding mental health from those experiencing it can significantly reduce stigmatizing attitudes within individuals ([Corrigan, Morris, Michaels, Rafacz & Rusch, 2012](#)). Given this consideration, Active Minds provides a variety of organizational activities that work towards their main goal: to "change the conversation on mental health." These activities include K-12 initiatives, public presentations, and fundraising events which educate the students that were previously unknowledgeable on MHS.

To assess Active Minds' impact on students' behaviors and beliefs indicative of mental health (i.e., rates of depression, stigma, knowledge on services, and help-seeking), comparative data from the Healthy Minds Study and Active Minds were collected and compared ([Kridel, 2016](#)). The Healthy Minds Study is an online survey conducted by the Healthy Minds Network at the University of Michigan, where American universities are surveyed on a variety of mental health variables including mental health screenings, beliefs, help-seeking, and more ([Eisenberg, Hunt & Speer, 2013](#)). Data from the Healthy Minds Study was assessed to measure potential differences in the variables between students attending a school with and without an Active Minds chapter. Ultimately, the study's findings revealed that institutions with an Active Minds chapter have better overall mental health among their students than those without (Einsberg, et al., 2013). Students were found to have lower levels of direct and indirect stigma, better attitudes towards psychological disorders, and had improved knowledge on mental health. These results suggest the capability of Active Minds and other voluntary organizations to have a beneficial influence on adolescent mental health.

Social Media

Another strategy to combat stigma and improve mental health outcomes is focusing on social media interventions, specifically targeted towards adolescents. Social media has increasing potential to promote awareness for the adolescent group as it provides a unique space for individuals to connect with their community ([Kruzan, Williams, Meyerhoff, Yoo, O'Dwyer, Choudhury & Mohr, 2022](#)). Such media-based interventions allow flexibility and create an influential platform that can deliver psychoeducational content. This can consist of informational blogs on the types of psychiatric disorders and their correlational symptoms, motivational discussion feeds, and visual content related to/about mental health awareness.

In a study that tested the impact of a brief online campaign on mental health awareness in Canada (called *In One Voice*), adolescents reported an improved personal stigma and social distance one year later ([Livingston, Cianfrone, Korf-Uzan & Coniglio, 2014](#)). This intervention included a 2-minute public service announcement from a popular hockey player in Canada who spoke about mental health, which was publicized on several different social media platforms such as Facebook and Twitter. Additionally, they promoted a youth-focused website that educated adolescents on the topic of mental health. The original evaluation occurred 2 months after the intervention but showed no significant results, which led to an increase in the post-intervention follow-up period for more accurate outcomes. The longest follow-up assessment, recorded 1-year post-intervention, yielded greater statistical differences. A brief questionnaire that was given 1-year post-intervention showed that categories like exposure to the website, shifts in attitude, and levels of personal stigma had improved significantly. Such examples of the correlation between social media interventions and increased awareness on mental health show the feasibility of these campaigns to deliver widespread interventions to the public.

Limitations and Conclusion

The purpose of this literature review was to gain insight into the experiences of Asian immigrant adolescents, specifically the Korean-American community, by exploring the traditional aspects of Korea's culture that influence mental health and stigma. The role of discriminatory prejudice within Korean culture can be emphasized when discussing MHS. Cultural norms, such as the emphasis on saving face (chaemyun) and the practice of nunchi (EQ), further complicate the mental health landscape by reinforcing stigma and discouraging open discussions about mental health. Furthermore, systemic factors, such as inadequate mental health education and lack of culturally competent care, significantly contribute to these disparities (see Figure 1). Figure 1 depicts contributors and interventions.

The integration of social constructivism reveals that cultural values and norms deeply influence individual behaviors within interpersonal relationships. In Korean culture, the pressure to conform and the fear of losing social status due to mental illness exacerbate the stigma associated with psychiatric disorders. These cultural values contribute to internalized stigma, anticipated stigma, and experienced stigma, which in turn affect mental health outcomes and

treatment-seeking behaviors. Each type of stigma was correlated with each other, whereby experiencing one category of stigma may lead to the onset of another (e.g., encountering experienced stigma can develop thoughts related to internalized stigma). For Korean specific experiences on stigma, it was found that the values stressed by Korean culture often created culture-specific barriers which may relate to harmful consequences like treatment avoidance and lack of treatment utilization.

Acculturation stress, coupled with the cultural stigma of mental health issues, presents unique challenges for Korean immigrants. The process of balancing traditional values with new cultural norms often results in heightened psychological stress and difficulties in identity formation, particularly during adolescence. The lack of mental health resources and support within immigrant communities further compounds these challenges, leading to delays in seeking treatment and exacerbation of mental health conditions.

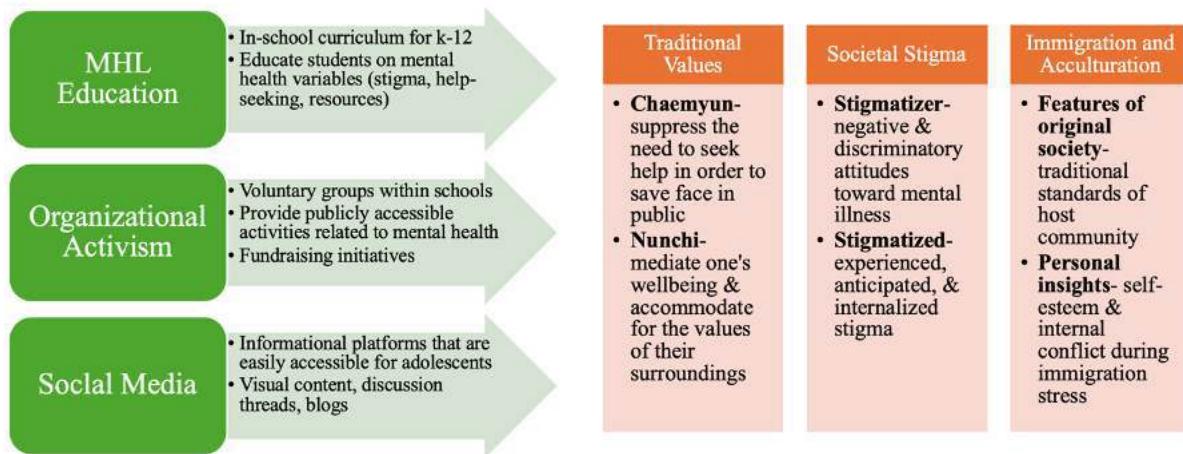
To address these issues, I recommend targeted interventions and educational initiatives. Implementing MHL curriculums in schools, similar to those adopted in other regions, could significantly enhance understanding and reduce stigma related to mental health among Korean adolescents. Interactive methods such as group activities may also be used to create a comfortable environment for those undergoing MHL in schools. Additionally, leveraging social media as a platform for mental health awareness and education (i.e., discussion threads and visual campaigns) offers a promising approach to reaching a wider audience and promoting positive change. With social media being easily accessible to adolescents, this initiative has significant potential in reaching a variety of individuals from around the world. It should be emphasized that these interventions may vary in outcomes but are influential actions that can be taken in available regions. Thirdly, organizational activism has great potential to promote mental health education in a low-cost, easily accessible manner. Voluntary groups can be designed both in-person and online to conveniently expose the public to mental health awareness. Specifically, schools that engage with the activities of a non-profit organization can integrate this activism into their student body, extending its influence across the entire institution.

These intervention strategies can be especially effective for immigrant adolescents from underrepresented regions like Southeast Asia. Due to their lack of resources in education, many schools in these countries do not prioritize the need for subjects other than traditional core classes, developing a cycle of uneducated populations. The implementation of these interventions in regions predominantly populated by immigrants will result in significant impact to their knowledge on mental health.

Despite the insights gained, this study acknowledges significant limitations. The grouping of Asian countries in existing research often obscures specific findings related to Korean adolescents, highlighting the need for more studies that focus on distinct cultural groups. Future research should aim to disaggregate data to better understand the unique mental health experiences of Korean immigrants and develop more effective, culturally tailored interventions. In summary, addressing mental health disparities among Korean adolescent immigrants requires a comprehensive approach that considers cultural values, acculturation stress, and systemic

barriers. By enhancing mental health education and utilizing innovative intervention strategies, there will be distinct progress in reducing stigma and improving mental health outcomes for future populations.

Figure 1



Contributors to and Interventions for Mental Health Disparities

Note. MHL = Mental Health Literacy

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Divergent Paths of Asian Communist States: A Comparative Analysis of China and North Korea By Yayi Zhang

Abstract

In contemporary East Asia, the political landscapes of China and North Korea represent two of the most captivating and complex authoritarian systems. They are intriguing examples of communist nations with similar revolutionary beginnings but radically different political paths in the context of modern authoritarian rule. Even though both countries were the products of communist revolutions in the 20th century, their political systems have developed through essentially different processes of 1) institutional adaptation, 2) economic reform, and 3) international engagement.

This essay will employ three pairs of comparative cases to illustrate the profound differences between these systems. Through these representative cases, I demonstrate how China has evolved toward pragmatic, institutionalized authoritarianism that enables economic dynamism and global engagement. At the same time, North Korea has developed an exceptionally rigid, personalistic system that prioritizes regime survival through isolation and extreme social control. More interestingly, while China and North Korea share a common starting point from the communist regime, their distinct paths highlight a paradox about the survival of nationalism: China's apparent 'loosening' through market reforms and bureaucratic institutionalization has strengthened state control by creating carefully managed pressure valves; whereas North Korea's increasingly 'tight' personalistic rule and isolationism have made its system more fragile and dependent on external crisis-manufacturing.

Comparative Analysis

Case Study 1

The first pair of representative cases comparing the divergence between Chinese and North Korean governance focuses on the contrasting approaches to leadership transition and political structure. The transition of power in China from Hu Jintao to Xi Jinping in 2012, contrasted with North Korea's succession from Kim Jong-il to Kim Jong-un in 2011, reveals key differences in the mechanisms of institutional development and political stability.

Although the leadership transitions seemed to share some similarities initially, their institutional structures and methods of execution eventually showed clear distinctions. During Hu Jintao's presidency (2002-2012), China adopted a model that was built on Deng Xiaoping's reforms that emphasized collective leadership and age-based retirement rules (Vogel 678). Decision-making processes were distributed among the Politburo Standing Committee, implying a power balance within the Communist Party of China (CPC). This structure was intended to avoid excessive centralization and foster internal checks inside the leadership framework. In 2012-2013, the transition from Hu to Xi followed this pattern of institutional succession in the CPC. This demonstrates that the CPC strongly valued institutional stability and smooth power

transfers, as seen by Xi's careful grooming through progressive leadership responsibilities, including his role as Vice President and his membership in the Politburo Standing Committee (Li 45-47).

These institutional adaptations in China under Xi revealed a complex interplay between established party mechanisms and personal power consolidation. While Xi inherited a system of collective leadership, he successfully leveraged existing party structures toward a more centralized model. This shift was institutionalized through constitutional amendments removing presidential term limits and establishing personal control over key decision-making bodies, such as the Central Military Commission (CMC) and newly formed central committees overseeing economic and security matters (Economy).

While both transitions in North Korea and China occurred in single-party systems, the North Korean case showed less institutional adaptation but a strong reliance on the legitimacy that came from the military backing and personality cult of the Kim Family. Kim Jong-un's succession was notably rushed compared to the methodical decades-long preparation of Xi in China (Haggard and Noland 89). After Kim Jong-il's death in December 2011, Kim Jong-un came to power with extraordinary speed, exemplifying a hereditary succession model deeply rooted in the personalistic dictatorship of the Kim family (Cha 156).

North Korea's transition, however, focused primarily on rapidly establishing Kim Jong-un's authority through a combination of family legacy, military support, and selective eliminations of potential rivals. Within weeks of his presidency, he was declared the "Supreme Leader" and assumed the role of Supreme Commander of the Korean People's Army (KPA). By April 2012, he had solidified his position by taking on the roles of First Secretary of the Workers' Party of Korea (WPK) and "First Chairman" of the National Defense Commission (Isozaki 58). The speed of transition and grip of power underscored the personalistic nature of North Korean politics.

In terms of the institutional adaptation of the two countries, Xi's China saw the enhancement of party institutions even as power became more centralized, while Kim's North Korea maintained its distinctive blend of family rule and military-party support structures.

Case Study 2

Besides the political structure that shapes high-level decision-making, economic policies play an instrumental role in determining the material foundations of regime legitimacy and national power. The economic paths of China and North Korea are particularly divergent when it comes to market reforms and economic modernization.

The second pair of case studies employ the iconic economic transitions from Mao Zedong to Deng Xiaoping in China and from Kim Jong-il to Kim Jong-un in North Korea to compare economic development and reform. Both China under Mao and North Korea under Kim Jong-il had centrally planned economies with limited private economic activity, state-owned businesses, and collective agriculture (Vogel 234). Within the centralized command economy system, the single central authority directs and controls the whole economy and renders all

economic decisions, including policy planning and resource allocation (Jo 77). Over time, this framework began to show its limitations and led to consequent economic problems in both countries: China's economy was disrupted by the Cultural Revolution, leaving widespread famine and significant industrial stagnation by 1976; North Korea was confronted with severe economic difficulties, including hyperinflation, mass fleeing labor, and extensive food shortages.

In China, following the death of Mao Zedong in 1976, the country experienced a substantial economic transformation under the leadership of Deng Xiaoping. The symbol of Deng's reform's start began with the household responsibility system in agriculture, which represented a radical break from Maoist policies. It allowed farmers to sell the surplus in free markets after fulfilling state quotas, thus laying the foundation for broader market mechanisms and higher productivity. Later, he established Special Economic Zones (SEZs) in coastal areas, such as Shenzhen. By providing tax incentives and reduced regulatory burdens, the zones attracted foreign investment and successfully integrated China into world trade networks.

As Vogel points out, "Deng did not have a clear blueprint about how to bring wealth to the people and power to the country; instead...he 'groped for the stepping stones as he crossed the river'" (Economy 2). Deng's pragmatic approach led to the gradual expansion of market reforms across industries. The subsequent "Reform and Opening Up" policy systematically incorporated market mechanisms while maintaining party control. It not only ensured market liberalization but also preserved the CPC's monopoly on power. Such a dual strategy of political solidity and economic flexibility became a feature of China's development model, which ensured both rapid growth and social stability (Vogel 340-342). Deng's reform is historic throughout China and even the world. It moved China's economy away from planned production measures toward market-driven growth. Today, under Xi Jinping's leadership, China still maintains its market-oriented system and has become the world's second-largest economy.

North Korea's economic policies were characterized by the Songun (military-first) principle during Kim Jong-il's time, which greatly prioritized military spending at the expense of civilian needs. This strategy made economic challenges worse, especially during the 1990s' Arduous March when hundreds of thousands of people died from starvation. Although Kim Jong-il implemented some limited market mechanisms during that famine period, these were mostly seen as temporary measures rather than systematic changes. This shows that Kim Jong-il's reliance on centralized control and secret trade networks failed to reduce systemic poverty despite the maintenance of the regime (Zook 134-135). When it comes to Kim Jong-un, while he has shown slightly more openness to reform than his father, his economic initiatives remain constrained as compared to Deng's. Just as Isozaki observes, Kim Jong-un exhibits a "tendency toward pragmatism" but mostly in his criticism of "formalism" in industrial management instead of supporting systemic market reforms (54).

To be noticed, Juche, the general government policy of self-reliance, has always been associated with North Korea's economic goals, even all aspects of this country. Under Kim Jong-un's leadership, the Juche ideology was conservatively separated while maintaining its core values. He did make progress on the way of decentralization, reforms allowed for limited market

activities, such as the growth of farmers' markets, where individuals could trade goods outside state control. As a practical response to ongoing food shortages, Kim Jong-un's agricultural reforms allowed farmers to keep a portion of their harvests for private sale. These actions demonstrated his recognition of the limitations of the command economy while upholding the Juche ideology (Isozaki 56–57).

In addition, Kim Jong-un has also tried out Special Economic Zones (SEZs) similar to the ones that were successful in China. However, these areas have struggled due to international sanctions and inadequate infrastructure, implying the constraints of reform within North Korea's isolationist and authoritarian framework. Unlike Deng's broad modernization, Kim's efforts have been gradual and more concerned with regime survival rather than economic transformation.

Case Study 3

Beyond the economic level, China and North Korea also present distinctive approaches to international engagement. This case study shows, via a close analysis of their strategies, how North Korea has turned to crisis diplomacy and retreated into isolation, while China has strengthened state control and established sophisticated mechanisms for world participation.

China's approach to international engagement reflects considered pragmatism and institutional sophistication. "The Belt and Road Initiative has positioned China at the center of the international system, with its physical, financial, cultural, technological, and political influence flowing to the rest of the world," according to Economy, is an example of this approach (58). Beijing carefully manages different narratives for audiences both at home and abroad. Internally, Xi promotes an ambitious vision of Chinese leadership, while externally, China emphasizes "win-win cooperation" and development partnerships.

North Korea, on the other hand, mainly relies on confrontational diplomacy and crisis manufacturing in its foreign policy. "CCTV's history lesson... portrays the archetypal beneficiary of OBOR as a young person in a developing country who aspires to connect with the globalized world and access economic opportunity," Shaw explains, illustrating how North Korean state literature primarily uses a conflict-focused lens to depict interactions with the outside world. However, Lily, an American child who is in awe of China, is the protagonist for Western audiences (217). This reflects the regime's deficiency in detaching diplomatic engagement from its crisis-dependent legitimacy narrative.

Furthermore, the divergence becomes particularly apparent in their handling of international sanctions. China has developed extensive defenses against external pressure while maintaining engagement. "Xi ably uses China's economic power to induce and coerce compliance with his vision," according to Economy (53). "Sanctions are portrayed as 'frantic' and 'crazed' attempts by the United States to prevent North Korea's inevitable and imminent victory" (214), Shaw reveals, referring to North Korea's reaction to sanctions, which involves strengthening isolation.

These divergent strategies illustrate an essential contradiction: North Korea's extreme isolation makes its system more vulnerable and crisis-dependent, while China's managed

engagement helps reinforce its centralized control by constructing institutional pressure valves and leverage points. This paradox could help explain their distinctive trajectories from similar starting points.

Through the three pairs of comparative cases examining institutional adaptation, economic reform, and international engagement, the essay demonstrates China's more resilient system developed from its pragmatic institutionalization, while North Korea's increased fragility and isolation due to the rigid personalistic rule.

However, recent events imply that these paths are not always fixed. North Korea's growing military alliance with Russia in 2023-2024, especially the arms transfers and diplomatic coordination, indicates that even the most isolated regime can find new avenues for limited international engagement when conditions suit its strategic interests. As a result, the question of whether North Korea could progressively modify its foreign policy strategy while preserving its fundamental control structure is intriguingly brought up by this development.

Looking into the future, as East Asia's geopolitical landscape continues to evolve, both countries will face new challenges, thus, how they handle these difficulties might have an impact on our understanding of how political systems adjust and survive in such a globalized society.

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Women Entrepreneurs: Ruth Handler, Martha Stewart, Vera Wang and Estee Lauder

By Siyan Guo

Introduction

Ruth Handler, Martha Stewart, Vera Wang and Estee Lauder are four of the most successful female entrepreneurs in American history. Each came from a modest background and went on to build a huge business empire; along the way each introduced many innovations to the way products are produced and marketed. These women became extremely wealthy based on their ability to sell their brand name to the public.

Ruth Handler

Ruth Handler (1916 – 2002) is one of the best-known female entrepreneurs in the United States; she and her husband Elliot were the founders of the toy company Mattel in the 1940's. In 1959 Ruth invented one of the most successful toys in history: the Barbie doll. To date, Barbie dolls have sold over one billion units, making it Mattel's most successful product. The Barbie name has since been extended to new products, including video games, films and television series. In 2023 the latest Barbie movie was released, "Barbie." It grossed over \$1 billion worldwide at the box office, making it one of the most successful movies of all time. This in turn increased sales of Barbies by over 25%. Ruth and Elliot Handler ran Mattel until they were forced to resign from the company in 1975 after being charged with the SEC for the filing of false financial statements.

Mattel was founded in 1945 by Ruth and Elliot Handler. Currently, Mattel is the country's second largest toy company by sales, with Lego being the largest. Two of Mattel's most important products, Barbies and Hot Wheels, have been named the top global toys by the marketing research company NPD Group.

Mattel initially sold picture frames and were able to produce and sell furniture for dolls produced out of these frames. In addition, they produced toy pianos, music boxes and ukuleles. The success of these products inspired Ruth and Elliot to focus their attention on designing and producing toys. The company went on to become a sponsor of the Mickey Mouse Club, which in 1955 became the first television show to show commercials specifically aimed at children.

The Barbie Doll

On March 9, 1959, the Barbie doll was first offered for sale to the public. Ruth's inspiration for the Barbie doll came from her own daughter, Barbara. Ruth noticed that Barbara liked to play with adult paper dolls and realized that all available dolls in the market were intended for much younger girls and decided to fill the gap with an adult doll. Although it was never made clear exactly how old Barbie is, the earliest versions show her as a young adult, approximately 19 years old. In 1960 the company revolutionized the doll industry with the release of Chatty Cathy, which was the first doll that could talk by pulling a string. In 1961 Mattel introduced the Ken doll, Barbie's boyfriend. Ken was named after Ruth's son. In 1962

Barbie's Dreamhouse was released, providing Barbie with a dollhouse. In May 1968 Mattel released another of its most successful products, Hot Wheels. These were intended to compete directly with Matchbox cars with the additional feature that they were very fast and could be used by children for racing. The success of Hot Wheels eventually enabled Mattel to acquire Matchbox in 1997. Earlier in 1993 Mattel had bought out another of its major rivals, Fisher Price.

In 1975 disaster struck Mattel as founders Ruth and Elliot Handler were forced to resign from the company due to the issuance of false and misleading financial statements. Ruth sold her stock in 1980 and thereby cut all ties with the company.

The Barbie doll is currently one of the most recognized dolls in the world, along with her boyfriend Ken. The Barbie doll has been Mattel's most successful creation. Among the many innovations by Ruth Handler was the introduction of a wide variety of accessories for Barbie as well as new friends. Ken was introduced in 1961, followed by best friend Midge in 1963 and younger sister Skipper in 1964. Over the years clothes were introduced to enable Barbie to work in different professions, including airline pilot, astronaut, doctor and many other roles that were not typically filled by women during this period. In other words, Barbie was an independent path-breaking woman who was not bound by traditional female roles.

In 1986 pop artist Andy Warhol painted a portrait of Barbie, which led to the creation of a special version of the doll. This demonstrates how important the Barbie doll had become an integral part of American culture. At least two writers have used Barbie in their works, including A.M. Homes and Barbara Kingsolver. Barbie has also appeared in dozens of movies, most recently "Barbie" in 2023.

Ruth Handler's Influence on Advertising

Mattel was one of the first companies to take advantage of the power of advertising on television, becoming a sponsor of the Mickey Mouse Club show in 1955. Since this was a children's show, advertising Mattel products was a perfect match, reaching an enormous audience of potential buyers. This venture was a tremendous gamble, as it required the investment of \$500,000 (nearly all of Mattel's net worth.) Fortunately, the gamble paid off as sales of the "BurpGun" set new records. This experience also changed the way that toys are marketed, with the emphasis switching from parents to children. The result was that toy sales were no longer as dependent on the seasons, creating a year-round demand for them. Among other successful products, Mattel promoted its "Mouse Guitar", which was actually a ukulele. Another of Mattel's earliest successes was the "Magic 8 Ball." By the time Barbie was introduced in 1959, Mattel was already a household name due to its advertising efforts. Television advertising was instrumental in marketing Barbie to young girls, showing her to be a successful young woman with different interests and hobbies with many available accessories as well as different clothes. Previously only baby dolls were available; this was the first time an adult doll was accessible to American consumers. Barbie dolls were an instant hit, selling 20,000 per week within a few months of their introduction. During the first year 350,000

Barbies were sold. The success of Barbies led to an expansion of new accessories, such as the Dream House, a car, airplane, yacht and many others along with a wide variety of clothes. Some of these clothes were designed by well-known fashion designers, such as Christian Dior and Oscar de la Renta.

Ruth Handler later admitted that she never expected Barbie to have this type of success or longevity.

Breast Cancer Survivor

In 1970 Ruth Handler was diagnosed with breast cancer, forcing her to spend less time at Mattel. She underwent a mastectomy to fight the disease. She soon discovered that there was a need for a breast prosthesis, which was not readily available at the time. She decided to produce her own, forming a new company to manufacture the new prosthesis. Joining with business partner Peyton Massey, she founded Ruthon Corp., producing a prosthesis called "Nearly Me." The product was so successful that First Lady Betty Ford became a customer. Ruth also received many awards for her charitable activities. She was named Outstanding Business Woman by the National Association of Accountants in 1961, Woman of the Year by the Los Angeles Times in 1968, a member of the seventy-five Outstanding Women in America by the Ladies' Home Journal in 1971. Ruth and her husband Elliott were also inducted into the Toy Industry Hall of Fame in 1988 and Ruth also became the first woman to be named Woman of Distinction by the United Jewish Association in 1992.

Martha Stewart

Martha Stewart is one of the most instantly recognizable female entrepreneurs in the United States. Her media empire, Martha Stewart Living Omnimedia, consists of four basic divisions: publishing, Internet content, broadcasting media and merchandise. The company owns several magazines, television and radio shows and e-commerce websites. Her net worth is estimated to be approximately \$400 million, although at one time she was the first self-made female billionaire.

Early Years

Martha Stewart (born Martha Kostrya) graduated from Barnard College in 1962 with a double major in history and architectural history, one year after marrying Andrew Stewart. Martha started out as a stockbroker in 1967, but in 1976 she founded a catering business. Her first cookbook, "Entertaining", was published in 1982. This quickly led to several more publications, including "Martha Stewart's Quick Cook" (1983), "Martha Stewart's Hors D'Oeuvres" (1984), "Martha Stewart's Pies and Tarts" (1985) "Weddings" (1987), "Martha Stewart's Secrets for Entertaining" (1988) and "Martha Stewart's Christmas" (1989). She also wrote extensively about cooking and home entertainment for newspapers and magazines while making appearances on TV shows such as "The Oprah Winfrey Show" and "Larry King Live."

In 1990, Martha Stewart started her magazine “Martha Stewart Living”, with its annual circulation reaching two million copies by 2002. In 1993, Martha Stewart started up her own television show, “Martha Stewart Living.” She also continued to make appearances on numerous other television shows such as “The Today Show.” In 1997 Martha Stewart was able to buy up all the properties associated with her brand name, forming the company Martha Stewart Living Omnimedia. She also set up an internet business and mail order catalog business at the same time. The new company went public on the New York Stock Exchange in 1999. Shares of the stock sold for \$38, making Martha Stewart the first self-made female billionaire in the United States.

Scandal

Things went sour for Martha Stewart when she sold shares of ImClone stock in December 2001 based on inside information, which led to her spending several months in jail. After being released from prison in March 2005, she returned to running Martha Stewart Living. She made deals to sell home furnishings through Sears and K-Mart. She also returned to television with a new show called “The Martha Stewart Show” in September 2005. She continued to write new books, while her company began offering home building services and entered a deal to sell home furnishings through Macy’s. She also started a radio show on Sirius in November 2005. In September 2007 Martha Stewart Living Omnimedia entered into an agreement with the E.J. Gallo Winery to produce a line of wines under the name “Martha Stewart Vintage.” The company also entered into an agreement with Costco to sell food through the Kirkland brand name. In July 2008 Martha Stewart Living Omnimedia entered into an agreement to sell home furnishings through Walmart; at the same time Martha Stewart began a new cooking show on the Hallmark channel, “Martha Bakes.”

Recent Years

In recent years Martha Stewart has continued to make regular television appearances, including as a guest judge on “Chopped”. She has also become involved in selling legal cannabis and has started up a podcast on iHeart Radio. She also introduced three new television shows on the Roku Channel in 2022.

In 2023, Martha Stewart appeared on the cover of the “Sports Illustrated Swimsuit Issue” at the age of 81, making her the oldest model to ever appear on the cover.

Cooking Shows

Martha Stewart follows a long line of female cooking show hosts dating back to the debut of Julia Child in February 1963. Julia Child worked hard to convince the public broadcasting station WGBH in Boston that a cooking show on television could be successful, based on her recently released book “Mastering the Art of French Cooking.” She was able to showcase her talents to the network with a live demo of how to cook an omelette. The show, entitled “The

French Chef”, was immediately successful and earned several key rewards during its ten-year run.

The success “The French Chef” led to the introduction of other cooking shows. One of these was “Joyce Chen Cooks” in 1966. Joyce Chen was a pioneer of bringing Chinese cuisine to the United States. She opened the first Mandarin restaurant in New England and introduced many innovations that are now taken for granted, such as buffet-style service and menus written in both English and Chinese. While Joyce Chen’s television show was not as successful as Julia Child’s she did introduce Chinese cuisine to a wider audience, including Peking Duck, scallion pancakes and hot and sour soup.

Martha Stewart’s first cooking show, “The Martha Stewart Show”, began in September 2005. Previously she had appeared on “Martha Stewart Living” from 1993 – 2004. “Martha Stewart Living” was focused more on lifestyle, interior design and arts and crafts than on cooking. Martha Stewart began her involvement in food after reading Julia Child’s “Mastering the Art of French Cooking” and decided to get involved with catering. As her reputation grew, she began to publish cookbooks, such as “Martha Stewart’s Quick Cook” (1983), “Martha Stewart’s Hors d’Oeuvres” (1984), Martha Stewart’s “Pies and Tarts” (1985) up to her 100th book, “Martha – The Cookbook” (2024). These books established her reputation in the culinary world, enabling her to start her cooking show in 2005. The show lasted for seven years. Martha Stewart was able to turn these TV shows and her books into a media empire based on her entrepreneurial and marketing talents, eventually becoming a billionaire.

Martha Stewart Living Magazine

The “Martha Stewart Living Magazine” was oriented toward home decoration, entertaining, party planning, wedding planning and other lifestyle issues, including cooking. The magazine began as a quarterly publication in 1990 and became a monthly publication in 1994. The magazine was last published in April 2022; now the content is available at the website MarthaStewart.com.

Marketing the Martha Stewart Brand Name

Martha Stewart began her lifestyles advice and cooking career by starting up a catering business in 1972. She quickly developed a reputation for innovative menus and the presentation of her food. This was followed by the publication of several cookbooks, along with lifestyle books, which further enhanced her reputation. Her first book “Entertaining” (1982), sold 625,000 copies which cemented her reputation as a lifestyles expert. This led to appearances on television and she eventually starred in her own shows, such as “Martha Stewart Living” and “The Martha Stewart Show.” She also founded her own magazines, such as “Living”, “Everyday Food”, “Martha Stewart Weddings”, “Whole Living” and “Martha Stewart Babies.” Her best sellers were “Martha Stewart Living” and “Everyday Food.” Martha Stewart also writes four newspaper columns: “Ask Martha”, “Living”, “Weddings” and “Everyday Food.”

Martha Stewart was able to secure a lucrative deal to sell her housewares through Macy's, sold under the name "Martha Stewart Home Goods." She also sells merchandise through Walmart as well as Amazon.com; this includes cookware, towels, curtains, bedsheets, etc.

Martha Stewart founded the company "Martha Stewart Living Omnimedia" (MSLO) in 1997 as a conglomerate that could promote all her various enterprises. The company acquired all her franchises to operate them under one roof. The Initial Public Offering (IPO) raised over \$1 billion. The four divisions of the company are: publishing, internet publishing, broadcasting media and merchandising.

Vera Wang

Vera Wang is a well-known fashion designer and entrepreneur who has built an international fashion brand, making her a celebrity and a multi-millionaire. Vera Wang started out as a figure skater but shifted her focus to fashion and design after attending Sarah Lawrence College. She became an editor of Vogue magazine after graduating from college and held that position for 17 years, eventually reaching the role of senior fashion editor. She then moved to Ralph Lauren as a design director in 1987 after being turned down for the job of editor-in-chief at Vogue. During her two years at Ralph Lauren, Vera Wang developed 18 lines of accessories for the company and learned a great deal about the business side of the fashion industry.

In 1990 Vera Wang selling bridal clothes, opening a store in the Carlyle Hotel in New York City. She was inspired to design her own wedding dress when she was dissatisfied with the available choices for a 40-year-old bride. Opening the store required her to leave her position at Ralph Lauren and required a \$4 million loan from her father. Fortunately, Vera received the support of her former colleagues at Vogue who published an article about the store that helped put her on the map. Vera's designs proved to be extremely popular, leading her to expand her stores to London, Tokyo and Sydney while adding ready-to-wear clothes, evening clothes and accessories.

In 2001 Vera Wang released her book "Vera Wang on Weddings." In 2002 Vera Wang introduced a line of perfumes, followed by a line of home accessories; this was known as "The Vera Wang China and Crystal Collection." In 2007 she began offering a line of less expensive clothes, known as "Simply Vera", through the retailer Kohl's. By 2012 Vera Wang entered a partnership with Men's Wearhouse to offer a line of tuxedos.

Vera Wang has produced wedding dresses for many celebrities over the years, including Chelsea Clinton, Ivanka Trump, Mariah Carey and Kim Kardashian. In addition, many figure skaters have worn costumes designed by Vera Wang, including Nancy Kerrigan, Michelle Kwan and Nathan Chen. She also designed costumes worn by the cheerleaders for the Philadelphia Eagles football team. In 1992 and 1994, Vera produced costumes for the U.S. Winter Olympics Figure Skating Team. The resulting publicity further enhanced her reputation and strengthened her sales.

Vera Wang has won numerous awards over the years, including the Chinese American Planning Council's Honoree of the Year Award in 1993. She also won many fashion awards, such as the CFDA (Council of Fashion Designers of America) Womenswear Designer of the Year in 2005. In 2006 Vera Wang was awarded the Andrea Leon Talley Lifetime Achievement Award. She was inducted into the U.S. Figure Skating Hall of Fame in 2009. In 2013 she received the CFDA (Council of Fashion Designers of America) Lifetime Achievement Award.

Estee Lauder

Estee Lauder was born in Queens, NY in 1908; her parents were Hungarian immigrants. Estee grew up working in her father's hardware store but soon found that she preferred working for her uncle's business. Her uncle, Dr. John Schotz, was a chemist who produced and sold beauty products such as facial creams, lotions and fragrances. After graduating from high school, Estee became involved in promoting and selling her uncle's products in New York City. Estee Lauder then founded her own company with her husband Joseph in 1946. Estee was an extremely aggressive promoter of her products. Estee visited hair salons to give out free samples of her products. She also was one of the first to offer the promotion of giving away a gift with each purchase.

Initially the Estee Lauder company focused on skin cremes and lotions. In 1948, the company formed a partnership with Saks Fifth Avenue in New York City to sell Estee Lauder products. The company then developed its own line of cosmetics. In 1953 Estee introduced her own bath oil and perfume, "Youth-Dew". By 1960, Estee Lauder products were available at Harrod's in London. This was followed a year later by the opening of a store in Hong Kong. In 1964 Estee Lauder introduced Aramis, a high-end fragrance for men, which was the first time that a men's fragrance was available in department stores. In 1968 Estee Lauder introduced Clinique, which was developed by a dermatologist to avoid allergies and provide scent-free cosmetics. This was followed up by a men's version called "Skin Supplies for Men." In 1981, Estee Lauder cosmetics became one of the first American brands to be available in the Soviet Union. In the 1990's the company rapidly expanded through the acquisition of other brands, such as MAC Cosmetics, Bobbi Brown Cosmetics and La Mer. The company also entered into licensing agreements with companies such as Tommy Hilfiger and Donna Karan. By 1995 the company went public on the New York Stock Exchange. In the 2000's Estee Lauder continued to acquire more brands, including AERIN Beauty, RODIN and Le Labo. Other acquisitions include a minority stake in Forest Essentials, GLAMGOW and Becca Cosmetics. Estee Lauder has also used well-known "spokesmodels" to promote its brand, including the actresses Elizabeth Hurley and Gwyneth Paltrow. By 2024 the Lauder family's net worth reached \$25.9 billion, with the descendants of Estee Lauder running the company.

Conclusion

These four women are perfect examples of how business empires can be formed with innovative ideas, marketing savvy and risk-taking. All four rose from humble beginnings to

change the way products are marketed in the areas of toys and games, multimedia, fashion and cosmetics. Their names became synonymous with their companies and they all earned great wealth as a result. Their life stories can serve as an inspiration for anyone who has entrepreneurial ambitions. In recent years there have been many successful female entrepreneurs following in the footsteps of Ruth Handler, Martha Stewart, Vera Wang and Estee Lauder; as of 2024, there were 31 self-made female billionaires in the United States.

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Social Proof in Digital Marketing By Zhenyu Tan

Introduction

In recent years as the volume of internet commerce has exploded, new marketing strategies have been developed to respond to the unique challenges of doing business online. One of the most successful marketing methods for online business is known as “social proof marketing”, where customers are persuaded to buy products based on the experiences of other customers. Social proof is especially important with online marketing as customers can’t see or touch the merchandise as they would in a “bricks and mortar” store. Amazon.com was one of the earliest and most successful pioneers of the use of social proof marketing online; it has offered customer reviews and product recommendations since it began doing business in the mid-1990’s. Since then, many others have followed, finding unique ways to provide customers with information about which products were being purchased by other customers. Social proof marketing has proven itself to be highly successful for online companies for the past thirty years; newer and more sophisticated forms of social proof marketing are likely to be developed for the foreseeable future as technology continues to improve.

What is Social Proof?

Social proof is a psychological phenomenon in which consumer behavior is influenced by the choices made by other consumers. The concept of social proof was introduced by the psychologist Robert Cialdini in his book “Influence: The Psychology of Persuasion.” The concept of social proof has been used as an effective marketing tool for many decades; it consists of recommendations and testimonials by actual customers of a product. Consumers are much more likely to buy a product if they see positive reviews from other people, as this gives them more confidence in the product. Positive reviews by celebrities can have a huge impact on brand awareness and generate enormous revenues for the seller. Since the advent of internet commerce, social proof marketing has proven to be an extremely effective method for attracting new and repeat customers.

How Social Proof is Used in Online (Digital) Marketing

Traditionally, marketing has taken place through radio, newspaper and television ads; with the rise of the internet, marketing now includes internet advertising and the use of various forms of social media, such as Facebook, Instagram, TikTok and YouTube. Social proof marketing has proven to be especially effective in social media where it is possible to quickly find a great deal of information about any product. In addition, the use of technology such as videos can increase the effectiveness of online marketing compared with the more traditional forms of marketing.

Social proof marketing can take many forms. For example, the following classification scheme has been proposed by the marketer Alfred Lua⁵⁶:

- expert: people can be heavily influenced by the opinions of “experts” in any field. A recommendation by an expert can lead to substantial sales of a product. For example, the Michelin-starred chef Gordon Ramsay has endorsed a new line of cookware produced by the Hexclad company. As a result, the company is expected to have sales of \$600 million in 2024, just eight years after the company was formed.⁵⁷
- celebrity: celebrity endorsements can dramatically increase the sales of a product, as people may want to emulate celebrities in their daily lives. The effectiveness of celebrity endorsements can be seen by noting that celebrities are often paid enormous sums to endorse a product. One of the best examples of a celebrity endorsement is Nike’s partnership with former NBA star Michael Jordan, whose name has helped the company sell over \$3 billion worth of his sneakers since 1984.⁵⁸ Michael Jordan is estimated to have earned over \$1 billion from this deal.
- user: positive experiences with a product by actual customers can help influence consumers to buy a product as they can have more confidence in it. As an example, according to the marketing website Quietlight, a drop in average customer rating from 4.5 to 4.0 can reduce sales by 20-30%.⁵⁹
- the “wisdom of the crowd”: many people will buy a product simply because many others have done so; these people will be influenced by sales data, thinking that a product must be good if many people have bought it. As an example, people are more likely to visit a restaurant if it has long lines waiting to get in, based on the logic that the food must be good!

⁵⁶ “13 Stunning Examples of Social Proof That Elevate Trust”, Ted, Vrountas, Instapage. <https://instapage.com/blog/social-proof-examples/#:~:text=Wisdom%20of%20your%20friends%3A%20This,authoritative%20figure%20in%20your%20industry>.

⁵⁷ “Would You Risk It All for a Shot at Building a Billion-Dollar Brand with Gordon Ramsay?”, Bryan Elliott. August 25, 2024. Inc.com. <https://www.inc.com/bryan-elliott/would-you-risk-it-all-for-a-shot-at-building-a-billion-dollar-brand-with-gordon-ramsay.html>

⁵⁸ “How Much Has Nike Made From Jordan?”, Federico Lopez, January 16, 2023. Shoeffect.com. [https://shoeeffect.com/how-much-has-nike-made-from-jordan/](https://shoeffect.com/how-much-has-nike-made-from-jordan/)

⁵⁹ “The Impact of Reviews and Ratings on Amazon Business Value”. Quietlight.com. <https://quietlight.com/the-impact-of-reviews-and-ratings-on-amazon-business-value/>

- the wisdom of friends: many people will buy products because they have confidence in the judgement of their friends who have bought a product.
- certification: people will often assume that the status provided by certification enhances the credibility of a recommendation. For example, the “Blue Check” given to some Twitter users can provide confidence in the opinions of the recipient of the Blue Check.

The “wisdom of the crowd” form of social proof is extremely useful in internet marketing. This is based on the idea that consumers will accept the choices made by many other people based on the assumption that their knowledge and experience can be relied on. This is why customer reviews and testimonials are so successful in persuading customers to buy unfamiliar products and services.

Research has shown that for many businesses, social proof marketing is essential for success in 2024. According to Smbguide.com⁶⁰:

- 97% of consumers look at reviews before buying a new product
- 77% of small businesses use social media to promote their products
- 82% of marketing professionals agree that the use of social media influencers to promote products is a highly successful approach
- 88% of Generation Z (born between 1997 and 2012) and Millennials (born between 1981 and 1996) place value in the recommendations of social media influencers

As proof of the effectiveness of internet and social media marketing, total spending on marketing through social media influencers is estimated to have reached \$24 billion in 2024, up from \$1.7 billion in 2016.⁶¹ Research has shown that businesses generate an average of \$6.50 in sales for every dollar spent on social influencer marketing⁶², making this a far more effective

⁶⁰ “20+ Social Proof Statistics and Trends in 2024”, Beatrice Manuel, July 12, 2024. Smbguide.com.

<https://www.smbguide.com/social-proof-statistics/#:~:text=Social%20proof%20has%20evolved%20beyond,trend%20that's%20here%20to%20stay>.

⁶¹ “20+ Social Proof Statistics and Trends in 2024”, Beatrice Manuel, July 12, 2024. Smbguide.com.

<https://www.smbguide.com/social-proof-statistics/#:~:text=Social%20proof%20has%20evolved%20beyond,trend%20that's%20here%20to%20stay>.

⁶² “On Average, Businesses Generate \$6.50 for Every \$1 Invested in Influencer Marketing”, Saleslion.io.

<https://saleslion.io/sales-statistics/on-an-average-businesses-generate-6-50-for-every-1-invested-in-influencer-marketing/#:~:text=Influencer%20Marketing%20Delivers%20a%20Strong,failing%20to%20generate%20any%20revenue>.

form of advertising than more traditional approaches such as television ads. This type of advertising also has the potential to reach a much larger audience than traditional forms of advertising.

Studies have shown that the youngest generations of consumers are heavily influenced by social media, especially Facebook, and their buying decisions can depend on social proof marketing. Studies have shown that 72% of Generation Z and Millennials regularly follow at least one social media influencer⁶³; these influencers can heavily affect sales with their recommendations. For example, the actor Ben Affleck is the official “ambassador” for the donut chain Dunkin. Ben Affleck appears in a series of commercials for the company; these have been tremendously successful in raising the company’s name recognition and sales.

In the recent past several companies have dramatically increased their brand name recognition through the use of social proof; four of these are:

- Five Guys
- Red Bull
- Chipotle
- In-N-Out

After its founding in 1986, the fast-food chain Five Guys was able to expand to over 1,000 restaurants in the United States by 2024. The rapid growth of the company was helped by posting product reviews, customer reviews, newspaper articles, etc. on the walls of its stores. This information made prospective customers far more likely to try their food; the company’s focus on quality ingredients ensured a great deal of repeat business.

Red Bull advertises a great deal on television; its slogan “Red Bull Gives You Wings” is one of the most successful in marketing history. As a result, Red Bull is now the third largest soft drink brand after Coca-Cola and Pepsi. One of Red Bull’s most innovative attempts at social proof marketing took place in London in the early 1990’s, when the brand was virtually unknown. The company placed empty cans of Red Bull throughout the city in garbage cans near clubs and college campuses. This was done to give the illusion that many people were drinking Red Bull. This strategy was designed to encourage people to try the product, thinking that it must be extremely popular for a reason. The efforts were highly successful, making this one of the most original approaches to social proof marketing in history.

Chipotle is a fast-food chain that specializes in Mexican foods such as tacos, quesadillas and burritos. One key feature of Chipotle’s strategy for success in the fast-food industry is that its restaurants are all owned by the company to ensure consistent standards. Chipotle’s strategy is to keep the number of offerings on its menu very small but to ensure that the quality of these

⁶³ “The Influencer Report”, October 2019, MorningConsult.
<https://pro.morningconsult.com/analyst-reports/influencer-report>

menu items is very high. The company emphasizes its commitment to fresh ingredients and avoids the use of artificial flavors, colors and preservatives. It also uses beef that is raised in a humane way. Thirty years after its founding, the company accounts for 10% of the fast-food industry sales in the United States. Chipotle's social proof strategy is to impress customers with the quality of its food and its commitment to sustainability, which have resulted in many repeat customers.

In-N-Out Burger is a fast-food company, mainly located on the west coast and southwestern U.S., specializing in burgers and fries. In-N-Out was founded in 1948 and has rapidly grown due to its unique approach to fast food. The company emphasizes the quality of its ingredients and food preparation methods; they advertise the fact that they don't use microwaves, they don't freeze anything and the fact that nothing is pre-packaged. To show the strength of their commitment to quality food, the lettuce is "hand-leafed" and the shakes are made out of real ice cream, even though this significantly increases costs of production. In-N-Out owns all of its restaurants and is privately owned in order to ensure quality control of its offerings. In-N-Out also has several unusual offerings under the title "Not So Secret Menu" with items such as "4X4", which is a quadruple burger; grilled cheese sandwiches and bun-free burgers. These items are not actively promoted; they are identified by customers through word-of-mouth advertising.

According to Datareportal.com, 56.1% of internet users buy something online at least once each week, and 52.1% of internet users research products on the internet before buying.⁶⁴ Another study by Hubspot.com showed that the average internet user reads ten reviews before making a purchasing decision, showing the influence of the "wisdom of the crowds" on buying decisions. The power of internet reviews to influence customers is shown by a study in which it was shown that 71% of internet customers would not do business with a company with an average rating of less than 3 stars.⁶⁵ In addition, the percentage of online customers who are willing to buy from low-rated companies is steadily declining over time. Online customers expect businesses to have a substantial number of reviews, showing that they lose confidence in a company with a small number of reviews. As an example of the importance of reviews, Amazon.com always displays the average ratings for each of its third-party suppliers on its website.

More evidence of the power of social media marketing comes from a study showing that 44% of people prefer to learn about new products or services from short videos, while reading a

⁶⁴ "Digital 2024: Global Overview Report", January 31, 2024, DataReportal.com.
<https://datareportal.com/reports/digital-2024-global-overview-report>

⁶⁵ "20+ Social Proof Statistics and Trends in 2024", Beatrice Manuel, July 12, 2024. Smbguide.com.
<https://www.smbguide.com/social-proof-statistics/#:~:text=Social%20proof%20has%20evolved%20beyond,trend%20that's%20here%20to%20stay.>

manual finished a distant second with 16%.⁶⁶ The ability to show videos is one the unique strengths of internet marketing and would be impossible with more traditional forms of advertising. This provides a huge opportunity for marketers to reach customers through informative, entertaining videos. As technology advances, producing high-quality videos has become progressively easier and cheaper in recent years so that any business can produce these videos.

There are many benefits of using social proof for internet marketing:

- social proof increases the confidence of potential customers in buying a product for the first time
- research has shown that internet shoppers are more persuaded by reviews from other customers (user-generated content or UGC) than brand names
- a large percentage of consumers rely on reviews before buying a product
- videos are an effective tool for promoting products to customers
- online reviews help customers find a company's website by improving search engine optimization
- social proof marketing enhances a company's credibility as it is based on positive customer experiences

There are several methods available for using social proof for internet marketing, including:

- testimonials and reviews
- case studies
- other user-generated content (UGC)
- influencer endorsements
- celebrity endorsements
- names of awards won by a company
- contests and other promotions

Case Study: Amazon.com

As an example of the early success of social proof marketing on the internet, Amazon.com was a pioneer in the use of internet sales and marketing. In 1995 Amazon began offering customer reviews on their website, which enabled consumers to evaluate different products and provide ratings. This information proved to be invaluable to other customers who were then able to make more informed decisions about which products to buy. Amazon also added their own recommendations to customers based on their shopping history, providing even

⁶⁶ “20+ Social Proof Statistics and Trends in 2024”, Beatrice Manuel, July 12, 2024. Smbguide.com.

<https://www.smbguide.com/social-proof-statistics/#:~:text=Social%20proof%20has%20evolved%20beyond,trend%20that's%20here%20to%20stay>.

more useful information to these customers. Amazon also was one of the earliest users of Artificial Intelligence to determine which titles customers would buy based on their shopping and browsing history. In the past 30 years, Amazon.com has evolved into one of the largest online retailers in the world, with an average of 2.3 billion visits each month. Their share of online commerce in the United States is 37.8%; Walmart is a distant second at 6.3% and Apple even further behind at 3.9%.⁶⁷ The company's market capitalization is over 2.3 trillion dollars, making its owner, Jeff Bezos, one of the richest people in the world.

Case Study: eBay.com

eBay is an online auction site through which buyers and sellers get together to find items that might be difficult to obtain locally. The company was founded in 1995 at a time when consumers began to have access to computers and the internet in their homes. eBay has grown rapidly since its introduction and currently has a market capitalization of about \$30 billion. It has over 130 million active users and the annual volume of transactions is over \$70 billion. Customers can obtain information about the other participants through a “reputation” system. After each transaction users are invited to provide a rating, so that each buyer and seller develops a “reputation” that strongly influences that amount of business that he or she receives. Reputation is especially important for internet sales since the customer can't physically inspect the merchandise of interest. Developing a strong reputation is the best way for a seller to drive repeat business; this can be viewed as a form of social proof marketing as customers can have confidence in a seller with many positive reviews.

Case Study: Facebook

Facebook is one of the most successful social media platforms in history. As of 2023, Facebook had over 3 billion users, with revenues of about \$135 billion and a market capitalization of approximately \$1.3 billion.⁶⁸ Studies have shown that the average user spends about an hour on Facebook each day. As a result, Facebook provides a potentially massive audience for any company that can take advantage of Facebook's unique setup through the use of social proof marketing.

Facebook derives its revenues from advertising, and companies can take advantage of social proof media by including several key elements in their ads:

- testimonials from current customers

⁶⁷ “21 Top Amazon Statistics for 2024”, Lyn Wildwood, December 9, 2024. Bloggingwizard.com. <https://bloggingwizard.com/amazon-statistics/>

⁶⁸ “Facebook Statistics (2024)” David Ch, Sendshort. <https://sendshort.ai/statistics/facebook/#:~:text=User%20base%3A%20Facebook%20has%203.03.%241.27%20trillion%20in%20Q3%202024.>

- celebrity/expert endorsements
- videos showing the key features of a product
- using clips from podcasts

Among the many companies that successfully advertise on Facebook are:

GoPro – GoPro produces hand-held video cameras that can produce content for social media such as Facebook, Instagram and TikTok.

Nike – Nike produces athletic footwear and is famously associated with Michael Jordan. Their ads on Facebook are designed to show some of the different areas in which they are involved, such as research and development.

Tasty – Tasty produces pizza, pasta and Asian dishes. It has taken a unique approach to advertising by producing videos showing its offerings that do not contain any audio.

National Geographic – The National Geographic Society is one of the most famous names in the fields of natural science and education. Their publication “National Geographic” has been one of the most iconic scientific publications since its first issue appeared in 1915. National Geographic promotes itself online through the use of articles, photos and videos about science that attract the attention of online consumers. The company is extremely active on social media, posting an average of 7 times per day on Facebook and 12 times per day on Instagram. National Geographic also promotes itself through the use of campaigns such as “Heros of the Ocean” which promotes conservation efforts for the world’s seven oceans.

Conclusion

Research has consistently shown that online social proof marketing is an extremely effective marketing tool and has enabled many companies to grow rapidly due to their effective use of this type of marketing. There are many examples of the unique ways in which successful online companies have been able to use social proof marketing.

For example, the company Intercom offers a customer service platform to online sellers that is based on Artificial Intelligence methods. The company shows pictures of testimonials from its customers which include a quote along with the name, title and picture of the individual who recommended Intercom. By placing all the testimonials together in one location, it is clear that there are many satisfied customers of Intercom.

The online company Zoom, which provides access to a platform for online meetings, earns the bulk of its revenues from subscriptions. In their online advertising, they show testimonials from satisfied business owners who regularly use Zoom meetings.

The telecommunications giant Cisco offers its customers information about how to create their own online case studies to persuade customers to try their services.

Fitbit produces fitness tracking watches; it shows articles, reviews, testimonials, etc. about its products on its website to show potential customers how well-regarded their products are.

The common feature among companies that have successfully used social proof marketing is that they were able to combine the important features of their products with their own unique approach to online marketing to keep their brand name in front of the public while developing a loyal following.

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A Framework for Inclusivity: Applying Universal Design for Learning and Self-Determination Theory to Support English Language Acquisition in Neurodiverse Classrooms in South Korea By Eunsoo Lee

Abstract

In South Korea, neurodiversity is an emerging concept, meaning there is a lack of accommodations for neurodivergent students in the education system. In addition, there is a gap in the literature regarding the specific context of neurodiverse South Korean classrooms. This research was conducted to increase the level of inclusivity in neurodiverse South Korean classrooms and to address the gap in the literature. This research hypothesizes that students who experience increased belonging and competence in a classroom will improve their confidence in learning a second language. To test the hypothesis, the principles of Universal Design for Learning (UDL) and Self-Determination Theory (SDT) were applied in an art class composed of six male elementary school students between grades 2 and 6 designed to teach students English. The qualitative research method of field notes was used to document the results of the application of SDT and UDL frameworks. Based on the field notes, a ten-session scope and sequence was developed to outline inclusive English learning lessons in a neurodiverse South Korean context. Although the study's impact was limited, students demonstrated retention of English vocabulary and responded positively to the inclusive approach. The results indicate that neurodiverse South Korean classrooms can make learning more effective and accessible by adopting inclusive frameworks such as the UDL and SDT. Further research can be conducted in this specific context to address the gap in the literature and to advance the quality of learning in the context.

Keywords Neurodiversity, Universal Design for Learning, English Language Learners, South Korea, Self-Determination Theory

Introduction

Neurodiversity is a term that refers to neurological differences, including but not restricted to autism, ADHD, and dyslexia (Azuka et al. 57). According to neurodiversity, neurological differences are a natural part of biodiversity and thus must be embraced (Azuka et al. 57). However, many neurodivergent students face barriers to learning (Azuka et al. 57). Especially in public school systems, where teaching is often aimed at “typical” learners, many neurodivergent students struggle to adapt to their learning environments (Griffiths and Leach 3).

Furthermore, in South Korea, neurodiversity is an emerging concept, which means there are few to no accommodations available to neurodivergent students attending public schools. For instance, until 1978, only private residential special schools offered special education (Kim et al. 797). Even after two federal education laws were passed to foster an inclusive learning environment for students with special needs at public schools, they were ineffective (Kim et al. 801). Given such circumstances in South Korea, there are not yet enough programs that identify,

accept, and plan instructions catered individually to each neurodivergent student, especially in the public education system.

To accommodate such students and facilitate meaningful learning, Universal Design for Learning (UDL) has emerged (Meyer et al.). UDL is a framework encompassing three principles that intend to make education accessible to all types of students by increasing engagement, varying representation of information, and offering multiple means of action and expression. UDL is an approach to teaching and learning that aims to create and foster inclusive environments.

When combined with Self-Determination Theory (SDT), the potential for learning with neurodivergent students increases (Guay 87). According to SDT, students can learn more effectively when they feel competent, autonomous, and related in a classroom. Therefore, to increase the efficiency and the enjoyment students receive from learning in a neurodiverse classroom, the principles of UDL and SDT can serve as useful tools.

In addition to UDL and SDT, Differentiated Instruction Tools can be utilized to increase the accessibility of the lessons to a wider range of students (Azuka et al. 61-62). Differentiated Instruction Tools include the variation of content, process, grouping, and learning space (Azuka et al. 61-62).

The context for the current study is an orphanage in Anyang, a region in South Korea. The art classroom where this study was carried out has six elementary school boys aged between second and sixth grade. Half of the students are diagnosed with ADHD. They seek to learn English but face barriers in a traditional public school classroom in which the principles of UDL and the basic psychological needs of SDT are not fully considered.

The current study was conducted to apply the principles of UDL and SDT to make learning English a more effective experience for the six students during a weekend art class at the orphanage. The art class instructors observed a need to increase engagement with the six students. Therefore, field notes documenting observations were used to develop a ten-cycle scope and sequence that can be replicated in similar contexts in South Korea. The scope and sequence highlight the importance of the application of the UDL guidelines to increase competence, autonomy, and relatedness. It was hypothesized that students who experience increased belonging and competence in a classroom will improve their confidence in learning a second language. The primary motivation behind this research was to make the experience of learning a second language more engaging and fun and reduce the barriers each faces in a given learning environment. This study also aims to add to the current, but limited literature that applies directly to the context of South Korean public school settings applying the UDL guidelines.

Literature Review

The literature review first covers the SDT framework, which was a primary tool this research utilized to foster a more inclusive learning environment. The following section discusses the inception of Universal Design and the adaptation of this concept in education as

UDL. Since UDL is another framework that is central to this research, its history and use in education are explained. The third section focuses on neurodivergent students and the impacts of SDT and UDL on their educational experiences. Past research was reviewed to observe the impact of these frameworks on neurodivergent students. Next, the literature review addresses previous research on English language learners, specifically in a South Korean context to connect more directly to this specific research. Lastly, the section ends with the introduction of the qualitative research method and how it was utilized in this research.

Self-Determination Theory Framework

In SDT, three basic requirements must be fulfilled in a classroom to keep the students motivated (Ryan and Deci 57). Students must feel competent, autonomous, and related. Further, these three psychological needs work interdependently to inspire a student (Guay 80-81). Therefore, when planning a lesson, teachers and educators must consider how these psychological needs will intertwine within the lesson. Once these three conditions are fulfilled, students gain motivation—both intrinsic and extrinsic types (Guay 79).

Intrinsic motivation, regarded with more importance, refers to a person's innate interest or affection for a particular activity or field of knowledge (Ryan and Deci 55). For instance, a student with an intrinsic motivation for English would study the subject for the sake of pure pleasure and enjoyment. Extrinsic motivation, on the other hand, refers to external sources of motivation (Ryan and Deci 55). Whether studying English to avoid punishment from parents or to utilize the knowledge gained through the subject in other fields of study, a student is motivated by external factors in both cases and is thus experiencing extrinsic motivation. While extrinsic motivation has been regarded as less important in comparison to intrinsic motivation, both types of motivation are powerful and effective in empowering students in a classroom setting (Guay 76-77).

Universal Design for Learning

In addition to SDT, UDL is a tool through which instructors can effectively and efficiently teach their classes. UDL originates from the concept of Universal Design. A paper by Story et al. outlines how Universal Design came into existence. In doing so, it separates the history of Universal Design into three large parts: demographics, legislation, and economy (Story et al. 6).

The idea of Universal Design came to be popularized as the old and disabled population increased with time (Story et al. 7). Particularly, as the disabled population increased with the return of veterans from WWII, the need for universal and accessible tools and environments became important (Story et al. 7). For instance, in the 1950s, rehabilitation engineers developed assistive technology that aided disabled people in environments where their needs were not satisfied (Story et al. 7).

The principles of Universal Design grew in importance with the federal government passing legislation that protected the rights of the disabled population (Story et al. 7-8). With the

government requiring institutions to provide an accessible environment for everyone, buildings, tools, and everyday objects began to adopt qualities that made them widely available (Story et al. 8). As product designers and engineers realized that these accommodative devices were useful for everyone, the demand for such devices increased (Story et al. 10). Kitchen utensils with broader bases, for example, were popularized once people realized how they are useful and comfortable (Story et al. 11).

Universal Design has existed and evolved through time. According to the Centre for Excellence in Universal Design, environments built with the principles of universal design in mind are more accessible and available to everyone. With applications in a range of different fields, Universal Design has been applied to the field of education as well (Chita-Tegmark et al.). This application has been named Universal Design for Learning (CAST).

According to the guidelines set forth by CAST, UDL must be engaging (motivating students in the learning material), representative (allowing for various ways of presenting information), and diverse in terms of action and expression (providing diverse ways of engagement) (CAST). Each category has three subcategories, further defining the components of engagement, representation, and diversity. These subcategories clarify what each of the three categories means and precisely how they can be applied in general settings.

A documented example of the successful application of the UDL framework to the students is a year 3 geography class (Griffiths and Leach 5). To help students learn about earthquakes, the geography class placed students in a ‘disaster zone’ (Griffiths and Leach 5). This zone was a simulation of a post-earthquake environment. Students were allowed to observe the scene both close up and from afar. They were allowed to choose how they interacted with the lesson. Essentially, they were allowed a wide range of action and expression (Griffiths and Leach 5). Information was also presented in a wide range of ways. Instead of presenting information in a single way, the ‘disaster zone’ provided information in multiple ways: posters with words of varying fonts and colors, audio, and videos (Griffiths and Leach 5-6). Students could choose the medium through which they could absorb information most effectively. Finally, the students were allowed to choose through which medium they would show their learning outcome. Choices included but were not limited to videos, presentations, mind maps, and comic strips (Griffiths and Leach 6).

Students could choose the medium they felt the most confident about and were able to effectively demonstrate their learning. The case study of this geography class is evidence that classrooms do have the ability to provide effective personalized learning for students. Instructors must not be limited to the traditional “one size fits all” method. Instead, they should gradually incorporate the UDL framework into their lessons to make learning more effective for unique individuals, each with a different learning style, including neurodivergent students (Griffiths and Leach 6-7).

These guidelines are the foundation for the application of UDL for teachers seeking to implement those principles. The guidelines are constantly updated to reflect the changing needs of inclusivity in educational contexts. (CAST). One context in which UDL is shown to be

effective is in a classroom that serves neurodiverse students. UDL aims to help teachers create and maintain a fully inclusive learning environment for all students.

Neurodivergent Learners

Of the three factors in UDL, neurodivergent students found the “engagement” aspect to be the most influential on their learning outcomes (Cole 18). This shows that neurodivergent students can learn more effectively when they understand the reason behind their studying and can truly engage in the material (Cole 19).

In addition to UDL, Differentiated Instruction Techniques can also be implemented to improve the learning qualities of students. Differentiated Instruction Techniques concern content, process, grouping, and creating a supportive learning space (Azuka et al. 61-62). This includes varying difficulty levels (content), providing a wide range of activities through which students can complete their learning process (process), putting students in flexible groups (grouping), and fostering an inclusive learning environment (creating a supportive learning space). Teachers can also incorporate the use of assistive technologies to accommodate students in their learning processes; for instance, the use of text-to-speech applications can make learning more accessible for certain students (Azuka et al. 62). Such techniques can also be used to teach students who are learning English as a second language, and who are also in need of effective learning strategies.

English Language Learners

This study’s main focus, in addition to neurodiversity, is teaching English to South Korean students. English as a Foreign Language (EFL) teachers in South Korea use various methods to motivate their students to learn English, and the ARCS (Attention, Relevance, Confidence, and Satisfaction) model was used as a criterion to evaluate the teachers’ motivational strategies (Maeng and Lee 26).

The ARCS model has many overlapping areas with SDT, which proposes that competence, autonomy, and relatedness must be fulfilled within a student for effective learning to take place (Guay 79). For instance, the confidence factor in ARCS is highly related to the competence and autonomy factors in SDT; a student feels confident when they are given learning requirements, success opportunities, and personal control (Maeng and Lee 27). When these three conditions are fulfilled, a student feels both competent and autonomous in their learning environments.

A factor of the ARCS model that the SDT does not cover, however, is satisfaction, which is akin to a determination to persevere that arises upon reflection at the end of the lesson. Satisfaction is important because this is what allows a student to feel more determined and positive about the next lesson and what encourages that student to continue their learning journey (Maeng and Lee 27).

Evaluation of South Korean EFL teachers using the ARCS model yielded that, while teachers frequently incorporated motivational strategies to increase the students’ attention, the other three categories were substantially less stimulated (Maeng and Lee 33). In addition to the

teaching strategies of teachers, how students learn in particular contexts is also important in designing lessons.

According to Chita-Tegmark et al., culture impacts how students learn. Therefore, it is important to explore how culture affects learning and how UDL can be applied to better educate learners of all cultural backgrounds (Chita-Tegmark et al.). Because current literature specific to the context of South Korea is limited, challenges may arise for teachers when attempting to apply UDL and SDT outside of Western cultures.

Methodology

This study used the qualitative research method to achieve its purpose of teaching English more efficiently and enjoyably to a South Korean neurodiverse classroom. According to Mack (13), in qualitative research, researchers seeking to conduct participant observation must enter the environment that possibly holds the answer to their question. Researchers must act discreetly and naturally to avoid disrupting their study results (Mack 21). This way, they can obtain important information, which they will record in their field notes (Mack 21).

Additionally, in qualitative research involving humans, taking into consideration ethical concerns is of utmost importance (Mack 16-17). In particular, confidentiality must be ensured; participants must remain anonymous and any information that may reveal the identity of the person must not be disclosed (Mack 17). This is why the field notes will center around the experiences and revelations of the instructor rather than the actions and dialogues of the human participants.

Qualitative methods implemented included observation of a neurodiverse classroom and documentation using field notes based on the observations. These research methods were used to evaluate the qualitative results of the application of the principles of UDL and SDT in the learning environment. In addition, this research also includes a literature review, in which there will be a discussion about how UDL and SDT have been studied and applied previously to enhance learning environments. Finally, based on the two previously mentioned research methods, a scope of sequence was developed. The essence of this research lies in devising an effective scope and sequence for the students, not primarily in observing and taking notes of the students' behaviors as would be done in a typical case study.

After every session at the orphanage, the field notes were organized to discern the pros and cons of each session. Based on such takeaways, the next session will be planned carefully to bring out more of the advantages and reduce the disadvantages that have been discovered through the previous sessions. The scope and sequence therefore can be seen as a result of the trials and errors in attempting to apply the principles of UDL and SDT in a neurodiverse South Korean classroom, as well as an application of the literature review.

Results

The researcher instructed a class of six male students whose grade levels ranged from second to sixth grade. Depending on their prior experience in speaking English (whether they

learned English in school or received tutoring previously), each student's English proficiency varied. The researcher instructed the class with at least one other instructor at all times. The number of instructors present in the classroom varied from two to five, including the researcher.

The researcher applied the UDL framework to all of the lessons. Based on previous classes, the researcher controlled the difficulty and pace of the lessons. The researcher addressed the UDL principles in the following ways: Information was represented in a variety of ways using visual elements, multiple languages, and spoken presentation; students were allowed to engage in lessons by being provided with a wide range of materials and choices; and an environment in which a wide range of action and expression were allowed by giving students choices in all activities. The most significant way in which students were allowed flexibility in action and expression was by giving the students a choice to opt out of certain activities if they did not feel comfortable doing them (e.g. overstimulation or sensory issues).

The scope and sequence were developed in order to foster the coexistence of meaningful learning of English and the joy of creating art. The scope and sequence aimed to address and satisfy all three principles of the UDL framework.

Discussion

To teach English to a neurodiverse classroom in South Korea, the principles of SDT were applied in designing lesson plans and instructing the class. The lessons revolved around each aspect of SDT and were revised upon students' feedback and attitudes toward each of them.

Firstly, the students gained a sense of competence through words of affirmation and encouragement when they spoke English. The lessons having been designed to increase the English proficiency of the students, it was crucial that the students felt enough confidence and competence when speaking a language that was foreign to them. Because they were unfamiliar with English, the students were reluctant to speak English at first, possibly due to vulnerability or unfamiliarity. However, the more time they spent listening to English, the more they felt comfortable with it. Finally, when they spoke English, they were praised for their efforts and knowledge. Further, they were encouraged to repeat the phrases they felt the most confident and comfortable speaking out loud.

Secondly, to fulfill their sense of autonomy, the students were given freedom to speak English instead of being forced to speak it. At the beginning of every lesson, the students had a chance to read the lesson plans, which were written in both English and Korean. This way, they could understand the contents of the lesson. Therefore, they were made aware of each step and specific vocabulary terms used in every lesson. Instead of being forced into reading and speaking English, they were given freedom in their choices, increasing their sense of autonomy in their classroom.

Lastly, to foster a sense of belonging, the sessions incorporated familiar elements. Particular attention was directed toward this aspect of SDT, regarding the fact that English is a major unfamiliar aspect for the students. Throughout the lessons, students encountered their favorite items, including characters and animals. Some lesson plans were designed based on the

knowledge of each student's interests. The lesson plans aimed to increase students' sense of belonging in the classroom by formulating an environment that was familiar and hospitable to them.

Despite attempts to cover all aspects of SDT in the lessons, there were barriers during much of the research. One of the most significant barriers was that the students were reluctant to speak a new language. Presumably, because they were unfamiliar with English, they withdrew from speaking English and adhered mostly to speaking Korean. As a result, when instructors spoke in English, students showed little to no signs of interest and their concentration level on the class material decreased. This was presumably due to their need for more confidence in speaking English, as it was their second language. According to SDT, students must feel competent in a learning environment to learn the material efficiently (Guay 79-80). Therefore, to adapt to this barrier, the following lessons were primarily done in Korean. However, this posed another barrier. Because the students were comfortable with Korean, their first language, they only spoke Korean and further retreated from speaking English. Therefore, finding a balance point between the two languages was a primary challenge in designing each lesson plan. While this barrier could not be completely overcome, efforts were made to minimize their negative impacts on the lesson. The lesson plans became more and more individualized to give each student competence, autonomy, and belonging. To achieve this goal, the common, unified lesson plan was simplified as much as possible, taking the form of a backbone. Later, in the actual learning environment, further details of the lessons were improvised to cater to each student's needs and to tap into each individual's interests.

Limitations

This research was limited due to difficulty in finding sources specific to this exact context. Literature concerning UDL, SDT, neurodiverse classrooms, and EFL individually was accessible. However, most of the available literature centered around a more general context of each concept, and there was a lack of literature available regarding this particular context. Further, the majority of the available literature was specific to the US and mostly focused on cultural differences. However, this research was set in a South Korean orphanage, where all six students grew up in a similar sociocultural context. This lack of context-specific literature made it difficult to discern between what would and would not be effective in the context of this research. This served as a motivation for developing a scope and sequence that is specific to its context.

The limitations of the study were not confined to the literature but consisted of the aspects of the lessons themselves. The first aspect of the lessons was the infrequency of interventions. Sessions were held roughly once a month. Because the students would not practice English intensively outside the sessions, they would forget a large portion of the English words spoken during the previous lesson. Essentially, their English skills would be "reset" every class. To address this barrier, the vocabulary words learned in the previous lessons were reviewed and

reiterated every lesson to remind the students of and improve their retrieval of the English vocabulary words.

The second aspect was that each student had different levels of English proficiency. Because the age gap between the six students was 4 years, a relatively large gap, especially during elementary school, each student had different proficiency in the language. This called for a personalized lesson for each student based on their knowledge and proficiency in English. While the lesson plans were initially designed with the entire class in mind, later lesson plans began to take the form of a personalized lesson. The earlier versions of the lesson plan aimed to satisfy the needs of all six students simultaneously as a unified class; however, since that was not possible, the lesson plans became differentiated based on each student's needs and interests. An example of this is the slides that were presented to the students before the start of every lesson. While the slides previously only had single words on them, it was later discovered that some students were more proficient in English than others, and full sentences were added to the slides to stimulate the interest of more proficient students.

The third aspect was that the researcher was the instructor. This meant that the researcher took part in the lesson. Due to the need for active participation in the lessons, the researcher was not able to observe the lessons from a third-person perspective, implying that the researcher may not have been able to collect as much meaningful data.

Despite such aspects of the study, the UDL and SDT frameworks were actively incorporated in both designing and carrying out the lesson plans to maximize the benefits of both of these frameworks to the six South Korean students.

Conclusion

This research was conducted to increase the efficiency of English learning for a neurodiverse classroom in South Korea composed of six South Korean male elementary students by applying the concepts of UDL and SDT. The researcher hypothesized that students who experience belonging and competence in a classroom will be confident in learning a second language. By designing accessible and personalized lesson plans, the researcher found that the students experienced increased belonging and competence. The students improved their English skills every session, building upon their knowledge from previous lessons. Such effects reflect the importance of accessible and personalized teaching techniques in neurodiverse classroom settings.

By applying the three principles of UDL (representation, engagement, and action and expression), lesson plans were formulated to stimulate each student's personal interests and English proficiency levels. The trial and error method was used to control the level of difficulty for the entire class and later for each student. As a result, lesson plans shifted from focusing on the entire class to a more personalized learning interaction catered to each student. The students were able to feel more comfortable in the learning environment and felt a stronger sense of belonging and competence. This was not only limited to neurodivergent students who were diagnosed with ADHD but applied to all six of the students. This implies that the effectiveness of

the UDL and SDT frameworks is not limited to neurodivergent students but to every student in a classroom.

It must be acknowledged that the findings of this research are limited due to multiple barriers, including the lack of available literature in this specific context with these particular keywords and the infrequency with which the lessons were held. The first barrier implies a greater need for study in the South Korean context focusing on neurodiversity, UDL, and SDT. The second barrier suggests a need for more comprehensive and frequently held lessons that study the impacts and benefits of applying UDL and SDT to South Korean neurodiverse classrooms.

Special attention and efforts must be directed toward research regarding education in neurodiverse classrooms in South Korea through the application of UDL and SDT. Through such studies, a greater understanding of the impacts of UDL and SDT on neurodiverse South Korean classrooms can be achieved, thereby creating pathways to more efficient and enjoyable learning for a wider range of South Korean students.

The researcher hopes this study will inspire further research on neurodiverse classrooms in South Korea, addressing a significant gap in the literature. Specifically, a trial of the scope and sequence is recommended to increase the understanding of how the principles of SDT and UDL can apply in the South Korean context. This way, more accessible and personalized learning experiences can be extended to South Korean students. This, in turn, may foster a stronger sense of belonging and competence, making the learning process more enjoyable and efficient.

In conclusion, this research was aimed at understanding the impacts of SDT and UDL in a neurodiverse classroom in South Korea. The results of this study point to a greater need for attention directed at neurodiverse South Korean classrooms and the application of inclusive learning strategies in these contexts. This way, education can be made more effective, enjoyable, and accessible to neurodivergent South Korean students.

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BMP Signaling: Unveiling the Role of Ligands in the Dynamic Process of Fracture Healing

By Spencer Kojima

Abstract

The regulation of the bone morphogenetic protein (BMP) pathway is crucial for the proper maintenance and post-injury repair of bone tissue. This paper covers the mechanisms by which BMPs can differentiate stem cells into cartilage and bone-forming cells, including chondrocytes, osteoblasts, and osteoclasts. Furthermore, it aims to show how each BMP ligand seems to have a unique role in the bone forming process. Through this literature review, it is demonstrated that BMP-2, in particular, is critical for proper bone healing, while others seem to be dispensable. However, it also proposes that the necessity of BMP-2 means not that it is the most osteogenic, nor that it has the most potential in clinical settings. While BMP-2 is the most studied BMP, others show more promise. It is argued that BMP-6 and -9 should be explored because of their unique resistance to antagonists of the pathway. This, in turn, leads to high osteogenic capabilities.

Introduction

Since the first discovery of a bone morphogenetic protein (BMP) in 1965 by Dr. Marshall Urist, BMPs are now understood to be vital components in the formation of bones. During skeletogenesis and fracture repair proper BMP signaling plays crucial roles in differentiating the body's stem cells into cartilage-forming chondrocytes and bone-forming osteoblasts. Accordingly, there have been numerous attempts in recent years to introduce BMPs into the clinical setting, when natural human bone healing has malfunctioned.

While most bone injuries respond to traditional therapies such as immobilization, rest, and fixation, bone injuries can sometimes be difficult to heal. Up to 10% of patients who sustain bone fractures experience complications. (Thomas et al., 2023) Every year, approximately 100,000 fractures in the United States progress to non-union, which are generally defined as fractures that persist for 9 months or more. (Thomas et al., 2023) Some emerging treatments for these fractures include autologous bone grafts and injection of platelet-rich plasma (PRP). (Lissenberg-Thunissen et al., 2011) And now, as a result of recent studies showing the osteogenic effects of BMP signaling, the use of BMPs is a promising alternative as well.

Recombinant human BMP (rhBMP) treatment through injection at fracture sites offers a relatively new and alternative approach to traditional methods of fracture treatments. They could potentially help provide faster recovery times. This paper aims to give an overview of the BMP signaling pathway and to show how in the case of non-union and other difficult fractures, BMP expression is essential to bone healing. Furthermore, the use of BMPs could potentially hasten the process of fracture repair because of their ability to induce osteogenesis.

Fracture Repair

When a bone gets fractured, it can repair itself in two ways. The first way, called intramembranous ossification, involves the bone directly healing itself across a fracture. There is no noticeable callus with this process as blood vessels help bridge the fracture gap through Haversian systems. (Dean et al., 2009; Einhorn et al., 1998)

Conversely, the bone can heal through an indirect mechanism, beginning with an inflammatory stage. Cytokines like Interleukins 1 (*IL-1*) and Interleukin 6 (*IL-6*), as well as tumor necrosis factor-alpha (*TNF- α*), are secreted from macrophages and mesenchymal cells to begin the repair. (Dean et al., 2009; Kon et al., 2001) After inflammation, the “fibrovascular phase” begins. (Bahney et al., 2019) This phase is characterized by vascular remodeling, with processes such as angiogenesis and neovascularization taking place. When a bone gets fractured, oxygen supply drastically decreases as a result of lack of vascularization, so new blood vessels need to be formed so that the callus can be supplied with oxygen and nutrients, and get rid of waste. (Bahney et al., 2019) The vascular endothelial growth factor (*VEGF*) helps initiate and drive the two processes responsible for revascularization: angiogenesis and vasculogenesis. (Bahney et al., 2019) Angiogenesis is the process by which blood vessels are formed from pre-existing vasculature; vasculogenesis is the process by which new endothelial cells form within the callus, helping to create new blood vessel connections.

An important component of the fracture callus is mesenchymal stem cells (MSCs). These cells are recruited from the periosteum and bone marrow. (Bahney et al., 2019) Prompted by signals from growth factors like stromal-derived growth factors (SDFs) and BMPs, the next stage in healing is the differentiation of MSCs into osteoblasts and chondrocytes, which commences the bone-forming stage. Cartilage is formed first, through the differentiation of chondrocytes. Then, osteoblasts help ossify this cartilage into mature bone. (Dean et al., 2009) Endochondral bone formation, as the bone formation process is known, takes place specifically in the fracture gap. The proteins collagen II and aggrecan are essential to this cartilage as they make up over 90% percent of the weight of the tissue. Collagen X is also a protein that is often expressed with chondrocytes and is critical to mineralization. (Bahney et al., 2019) Finally, the fracture repair ends with osteoclasts, which are responsible for breaking down and remodeling bone, and replacing it with newer bone. (Bahney et al., 2019)

The BMP signaling pathway

The BMP signaling pathway consists of three main components: ligands, receptors, and intracellular signal transducers. The BMP ligands are essential because they are the first proteins that activate this complex signaling pathway that leads to repair. BMP ligands are a part of the transforming growth factor β (TGF- β) superfamily, which, along with BMPs, includes growth differentiation factors (GDFs), transforming growth factors (TGFs), and activins. (Salazar et al., 2016) The BMP peptide ligands differ from each other in structure and function. These functions range from the development of bone and cartilage to the development of the liver and kidney. (Lissenberg-Thunnissen et al., 2011) Further, some BMPs, like BMP-2, -4, -5, -6, -7, and -9 have shown particularly high osteogenic potency; they differentiate pluripotent MSCs and

pre-osteoblastic cells at higher levels than their counterparts. (Cheng et al., 2003) Thus, while the BMP family is alike and has its own subfamily as a result of its sequence similarity, the specific ligands vary in structure and function.

The BMP ligands bind to type I and/or type II receptors—which have serine/threonine kinase activity—to initiate the signaling cascade. There are seven type I receptors to which the TGF- β family binds, but BMPs mostly use activin receptor-like kinases 1, 2, 3, and 6 (ALK-1, -2, -3, -6). (Katagiri et al., 2016) There are also three types of type II receptors that BMPs use in mammals: BMP type II receptor (BMPRII), activin type II receptor (ActRII), and activin type IIB receptor (ActRIIB). (Katagiri et al., 2016) BMPRII responds specifically to BMPs, while ActRII and ActRIIB respond to BMPs, as well as activins and myostatin. (Katagiri et al., 2016) BMP ligands have a higher affinity for type I BMP receptors and a lower affinity for type II receptors. (Shi et al., 2003) However, these receptors normally work in conjunction with each other. BMPs usually bind to complexes of type I and type II receptors, which together have a stronger affinity than individual ones. (Sanchez-Duffhues, et al., 2020; Gomez-Puerto et al., 2019)

After the BMP ligands bind to receptors, they recruit Smad proteins. There are currently nine Smads that are split into three groups. The first group is the receptor regulatory Smads—Smad1, 2, 3, 5, and 8—these Smads bind to the aforementioned receptors and are activated by their kinase activity. The second group consists of just Smad 4. The final group consists of Smad 6 and 7, which are inhibitory Smads. (Zou et al., 2021) BMP-receptor interaction leads to the activation of Smads 1, 5, and 8. (Katagiri et al., 2016) After one of these Smads has been activated, they form cofactors with Smad 4. (Katagiri et al., 2016) From there, the Smad complex regulates the expression of transcription factors responsible for osteoblast differentiation (e.g. *osterix* and *Runx2*) and chondrocyte differentiation (e.g. *Sox9*). (Nishimura et al., 2012) Interestingly, the BMP signaling pathway also regulates *VEGFR2*, which encodes for the receptor crucial for angiogenesis and vasculogenesis. (Katagiri et al., 2016)

BMPs also have several proteins that antagonize the pathway. The aforementioned Smads 6 and 7 are inhibitory and interfere with the phosphorylation of Smad 1, 5, and 8, which as a result prevents heterodimers with Smad 4. Some receptors, too, like BMP and activin bound protein (BAMBI) interfere with BMPs' natural affinity to BMP-specific receptors. Some BMPs, like BMP-3, are themselves inhibitory. Many other proteins regulate BMPs themselves. Noggin, for example, directly binds to BMPs in the extracellular matrix and has the highest affinity for the subgroups of BMP2 and 4. Noggin expression prevents overgrowth of bone which can lead to complications. Gremlin is another regulator of the BMP signaling pathway. Like noggin, its effects are seen in the extracellular matrix, binding to BMPs. Chordin is also a prominent antagonist, and like gremlin and noggin, it binds to BMP-2, -4, and -7 in the extracellular matrix. (Dean et al., 2009)

Disrupting Expression of BMPs in Fracture Healing:

BMPs are produced by mesenchymal stem cells, osteoprogenitor cells, chondrocytes, as well as osteoblasts. (Dean et al., 2009) It is a cyclical process. BMPs help to differentiate stem cells into bone-forming cells, and then they are formed from the same bone-forming cells that they produced before. This means that if BMP signaling is disrupted, both the ability of BMPs to induce osteogenesis and the future production of BMPs is disrupted. However, BMP ligands differ from each other in structure, function, and expression localization. (Lissenberg-Thunnissen et al., 2011; Zhu et al., 2022) Because of these varying capabilities, disrupting the expression of different BMPs has varying effects on living species.

A study conducted by Tsuji et. al. found that BMP-2 is essential for the initiation of fracture repair. (Tsuji et al., 2006) Mice with a conditional *Bmp2* expression knockout in the limb, who had sustained femoral fractures, were not able to form a bridging callus and initiate chondrogenesis. This was shown by low levels of type II collagen, which is necessary for fracture repair. (Tsuji et al., 2006) The presence of undifferentiated mesenchymal progenitor stem cells at the site of the fracture site further implies that BMP-2 is essential in initiating their differentiation into osteoblasts and chondrocytes. (Tsuji et al., 2006) Later studies support Tsuji's findings. Wang et. al also showed the presence of undifferentiated mesenchymal cells at femur fracture sites in mice who were given a BMP-2 deletion at the initiation stage of fracture healing. (Wang et al., 2010) There was between an 80-90% decrease in bone formation and a 75-85% decrease in cartilage formation. (Wang et al., 2010)

The work of Cho et al., which analyzed quantities of BMPs in fracture sites in Balb/c mice, supports these findings; they found that the highest levels of BMP-2 were expressed 1 day after the fracture time, implying its unique role in fracture initiation. (Cho et al., 2002) It was also found that BMP-2 regulates two important genes needed for bone formation. BMP-2 was seen to increase the transcript of Runx2, (Zhu et al., 2022; Shu et al., 2011) which is known to be responsible for the production of both osteoblasts (Komori, 2010) and chondrocytes. (Shu et al., 2011) Sox9 expression was another, which regulates the expression of proteins like collagen type II, a protein that is heavily expressed in cartilage. (Zhu et al., 2022; Zhao et al., 2017)

However, it is important to note that BMP being essential may only be true in the initiation of fracture healing and the differentiation of MSCs. Once osteoblasts have already formed or osteoprogenitors are already committed to differentiation, mice experience normal fracture healing without BMP-2. (Salazar et al., 2016; McBride-Gagyi et al., 2015; Mi et al., 2013) Thus, while BMP-2 is necessary for skeletogenesis and fracture healing, its role only seems to be necessary for the initiation of this process and the differentiation of stem cells.

While it would be expected that BMP-7 could have a significant effect on fracture healing because of its high expression around the fracture site, this does not seem to be the case. Fajardo et al. compared quantities of BMPs in both human nonunion tissue and healing fracture tissue. (Fajardo et al., 2009) It was found that in healing bone, along with a (slight) increase in BMP-2 in the fracture callus, BMP-7 was highly present. It was absent in the contrasting nonunion tissue. (Fajardo et al., 2009) However, despite the high quantities of BMP-7 in fracture calluses, BMP-7 has not shown to be as necessary as BMP-2. Tsuji et al. found that, unlike

BMP-2 in their earlier study, other BMPs were able to compensate for the lack of BMP-7 and help form a bridging callus. (Tsuij et al., 2010) Thus, further research is needed to clarify whether BMP-7 has a unique role—like BMP-2 seems to have—on fracture healing. Current studies seem to suggest that BMP-7's removal does not have adverse effects.

Other BMPs have special roles in bone formation but are significantly less important in fracture repair. While female littermate *BMP-6*-null mice have impaired skeletogenesis as a result of impaired growth plate function, skeletogenesis is not the same as fracture healing. In terms of bone mass itself, these same mice do not experience a change in cancellous bone mass in tibiae, which would imply that MSCs are still able to differentiate an adequate amount of osteoblasts and chondrocytes. (Perry et al., 2008) Solloway et al. noted that both BMP-2 and BMP-6 are coexpressed in hypertrophic cartilage, which could mean that BMP-2 can compensate for the lack of BMP-6 (Solloway et al., 1998). Furthermore, when mice were made with a global deletion of *BMP-9*, aside from some defects in tooth development, there were almost no skeletal abnormalities, again implying compensation from BMP-2 and other BMPs. (Mostafa et al., 2019; Huang et al., 2019) BMP-4, too, was shown to be dispensable in terms of fracture healing and skeletogenesis. (Tsuij et al., 2008) When mice with a limb-specific knockout were given femoral fractures, callus formation, and fracture healing occurred normally. (Tsuij et al., 2008)

In conclusion, different studies show differing functions of BMP ligands. Analysis of the concentration of BMPs at fracture sites and in vitro MSCs shows high quantities of BMP-2 and BMP-7. More experiments, however, are needed to be done in mice with fractures to show the effects of the specific BMP ligands in different aspects of fracture healing like callus formation, chondrogenesis, and ossification. Currently, it seems that in terms of the initiation of fracture healing, even osteogenic BMPs like BMP-4, -6, -7, and -9 are dispensable because other BMPs can compensate. On the contrary, BMP-2 is the one BMP that is necessary for the initiation of fracture healing.

Overexpressing BMPs in Fracture Healing.

It was shown that, when disrupting BMP expression, BMP-2 was most necessary in the process of fracture healing. Here, the specific results of what happens when certain BMPs are overexpressed, whether it be by genetic modification, recombinant BMPs, or removal of antagonists, will be displayed.

As deleting BMP-2 from mice disrupts the process of bone healing, overexpressing through genetic modification or the addition of a recombinant human BMP-2 (rhBMP2) speeds up the process. A study conducted by Murnaghan et al. found that in mice with femur fractures, exogenous activation of the BMP pathway promoted fracture healing. Specifically, the study found that mice that were injected with rhBMP-2 at day 0 or 4 after the fracture would heal significantly better than a saline control group and quicker than mice injected with rhBMP2 after 8 days. (Murnaghan et al., 2005) Other studies would later support Murnaghan's conclusion of BMP2 as a potent primer of osteogenesis. Pensak et al. showed how, compared to a control

group, the delivery of BMP-2 either by transduced bone marrow cells or a collagen sponge led to healing in mice with femoral defects. (Pensak et al., 2015) Geng et al. showed recently that the co-delivery of BMP2 and VEGFA led to, in bone marrow stem cells (BMSCs), increased alkaline phosphatase activity, which is an important indication that osteogenic differentiation is taking place. (Geng et al., 2021)

BMP-7 is a notable ligand because of its high expression at the site of fracture. In vitro studies have shown the positive effect of the overexpression of BMP-7. In one study using BMP-7 over expressing adipose-derived (ad-) MSCs, there were significantly larger increases in gene expressions such as *RUNX2* and *ALP* compared to the Ad-MSC group alone without BMP-7 overexpression. (Kim et al., 2018) These genes indicate high transcript levels of osteogenic differentiation. (Kim et al., 2018) Another in vitro study tested mRNA levels in BMP-7- overexpressing BMSCs. It also found higher levels of ALP compared to a control, a result of the BMP-7 expression; the ALP activity also increased osteoblastic differentiation. (Yan et al., 2018) In vivo studies in animals showed similar positive effects of BMP7. In a sheep model, even a low dose (1.75mg) of BMP-7 had comparable healing capabilities to the conventionally used bone autograft. (Cipitria et al., 2013) Overexpressed BMP-7 in MSCs also prompted healing in canine radial defects compared to a control. (Kim et al., 2018).

Individualizing other osteogenic BMPs and using other methods of overexpressing BMPs have shown promise and help bone formation in different ways. Although it was not as potent as BMP-2, BMP-5 has been shown to enhance osteoclastogenesis. (Wutzl et al., 2006) BMP-4 also helped to accelerate bone formation in rats with injured calvaria. (Shen et al., 2009) Removing antagonists also helps to augment the expression of the BMP pathway and helps to initiate bone repair. When inhibitor Smad6 was genetically removed with microRNA in C57/BL mice, there was increased callus formation because of the increased activity of the BMP pathway. (Wang et al., 2019) Suppressing noggin in a pre-osteoblastic cell line increased the transcript of both Smad1 and Smad5, implying increased osteogenic potential. (Wan et al., 2007) Furthermore, these cells would reach peak levels of differentiation markers *OP* and *RUNX2* days earlier than cells without noggin suppression. (Wan et al., 2007)

Interestingly, although BMP2 secretion is critical for proper fracture healing, BMP6 and BMP9 demonstrate high osteogenic potential that is resistant to canonical BMP pathway antagonists. In C3H10T1/2 MSCs, the adenoviral-mediated overexpression of BMP-9 led to significant increases in ALP activity. (Lamplot et al., 2013; Xu et al., 2012) adipose-derived mesenchymal stem cells (ASCs) placed into a medium containing BMP-6 experienced increases in ALP activity. Cheng et al. showed that in C3H10T1/2 and C2C12 cell lines, BMP-2, BMP-6, and BMP-9 showed similar ALP-inducing effects. (Cheng et al., 2003) Some explanations for this include these BMPs' resistance to antagonists. Although BMP-6 has many similarities to its highly osteogenic family member, BMP-7, it differs in amino acid 60; BMP-6 has lysine at this position. (Lissenberg-Thunissen et al., 2011; Rosen, 2006; Song et al., 2010) This small change allows BMP-6 to disassociate from Noggin and not bind to it, making BMP-6 even more osteogenic. BMP-9 also has unique resistance to antagonists. Like BMP-6, BMP-9 is resistant to

noggin. It is further unpenetrated by antagonists in its resistance to BMP-3; it is the only BMP that is resistant to this antagonist. (Lissenberg Thunissen et al., 2011; Kang et al., 2004)

In vivo studies convey the results of these molecular differences. Pigs with vertebral defects who received BMP-6 overexpressing MSCs experienced quicker bone regeneration. (Pelled et al., 2016) Combined with angiopoietin 1, BMP-9 helped to accelerate tibial fracture healing in albino rats. (Fadhil et al., 2024) BMP-6 and -9 are also more osteogenic than BMP-2 in some models. BMP-6 was more effective than BMP-2 at differentiating MSCs in vitro. (Mizrahi et al., 2013) When compared to BMP-2, BMP-9 was also more potent in a white rat model by increasing the connectivity density of the bone. (Khorsand et al., 2017)

Current Clinical Applications and Future Directions

Because of the successes of BMP-2 in animal studies, clinical trials involving recombinant human BMP-2 began in the early 2000s. Early studies such as Govender et al. showed in 2002 that when giving quantities of either 0.75 mg/mL of rhBMP-2 or 1.50 mg/mL of rhBMP-2, patients healed quicker than a controlled sample. (Govender et al., 2002) RhBMP-2 was also shown to help people in achieving spinal fusions. (Lykissas et al., 2017) BMP-7 has also shown promise in clinical applications. In one study involving patients with tibial, femoral, and humeral nonunions, rhBMP-7 delivered by an autologous bone graft led to union in 100% of cases. (Giannoudis et al., 2009) In long bone non-unions, 52/60 patients who received BMP-7 were healed, compared to 41/60 in patients who used platelet-rich plasma (PRP), another emerging treatment for bone non-unions. (Calori et al., 2008) Ultimately, both of these treatments showed promise.

Both BMP-2 and BMP-7 have been approved by the FDA for clinical use in certain cases. BMP-2 is approved for open tibial fractures and anterior lumbar interbody fusions, and BMP-7 is approved for long bone nonunions and posterior lumbar interbody fusions. (Rodham et al., 2023) However, there are also some major drawbacks as well. The production of BMPs has extremely high costs because of the processing challenges. (Rodham et al., 2023) There are also risks involved. There are conflicting results concerning cancer risk with BMP-2 usage in spine surgery. (Devine et al., 2012) In addition, when BMPs are prescribed in high doses, it can lead to ectopic bone formation. (Lissenberg-Thunissen et al., 2011)

While BMP-2 and BMP-7 are the only BMP treatments approved currently, it would be beneficial to explore other options. As previously mentioned, BMP-6 and BMP-9 have great osteogenic potential. Because of BMP-6's resistance to antagonist noggin, and BMP-9's resistance to both noggin and BMP-3, these two BMPs offer promising treatments. It was recently shown how transgenic human BMP-2 is at least 100 times more efficient at inducing BMP signaling than rhBMP-2; because of the inefficiency of rhBMP-2, high doses are often prescribed which can cause side effects. (Atasoy-Zeybek et al., 2023) One reason why transgenic human BMP-2 was more efficient at commencing the signaling cascade was because, in the pericellular domain, transgenic BMP-2 is partially resistant to noggin. (Atasoy-Zeybek et al., 2023) Since BMP-6 and BMP-9 are also resistant to noggin, it is possible that lower quantities of

these BMPs could also be applied to induce the same level of signaling. This, in turn, could lead to fewer adverse effects. Clinical studies comparing rhBMP-2, -6, -9 could be conducted to compare the efficacies and risks of these promising BMPs.

Conclusion

With the recent emergence of BMPs, there have been numerous studies comparing the different ligands' osteogenic capabilities and their unique roles in bone healing and formation. BMP-2 has proven to be the most necessary ligand for the initiation of fracture healing. It seems that many of the other BMPs are dispensable, so long as the overall quantity of BMP is sufficient. While BMP-2 and BMP-7 are most used in clinical practice, BMP-6 and BMP-9 offer the most potential in bone healing. Because of their unique resistance to antagonists, they are promising in clinical settings. The use of recombinant BMP-6 or BMP-9 might not have the same adverse side effects as rhBMP-2 seems to have because lower doses could be administered, though more research is needed to clarify this. Ultimately, BMPs are promising phenomena and have potential to be prominent in clinical use.

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Epigenetics and Neurological Disorders By Anika Chakrabarti

Abstract

Epigenetics, with its diverse mechanisms such as DNA methylation, histone acetylation, and ncRNAs, holds significant therapeutic potential for a wide range of disorders and diseases. Its intrinsic adaptability prevents DNA from enduring permanent damage while at the same time, regulating gene expression in reversible and plastic ways. It is a natural and dynamic process that needs continuous regulation for our bodies to function properly. However, this essential machinery can be disrupted by various factors. This paper will explore the molecular and cellular changes that occur in the brain due to epigenetic dysregulation, and how these changes are correlated to neurodegenerative diseases such as Alzheimer's and Huntington's disease.

Introduction

Epigenetics

The central dogma of biology states that DNA is transcribed into RNA, then translated into proteins that carry out various functions. To maintain the inheritance of genetic information, DNA needs to be replicated. To replicate, DNA must first be unwound because it is normally compacted into chromatin. Chromatin is composed of DNA wrapped around histone proteins, forming nucleosomes. Chromatin is compacted to make a structure called chromosomes. Histone proteins help compact DNA and regulate gene expression (Figure 1). When chromatin is condensed, it is called heterochromatin. In heterochromatin, gene expression is repressed as RNA polymerase cannot easily transcribe the genetic information. When chromatin is not condensed, it is called euchromatin, which is the state where gene expression occurs. Various types of RNA are transcribed from DNA, such as coding and noncoding RNAs. Coding RNAs are segments translated to produce a protein, while noncoding RNAs (ncRNAs) do not get translated to make a protein but serve other purposes.

Epigenetic mechanisms, such as DNA methylation and histone acetylation, regulate gene expression without altering the DNA sequence itself, by changing the form of chromatin, either to euchromatin or heterochromatin. Epigenetics is a field of study that investigates how individual genes and large gene networks function at the molecular and cellular level [1]. It focuses on understanding the mechanisms that control gene function, including how genes are turned on and off, and how environmental factors influence gene expression. In epigenetics, genes can be regulated by DNA methylation, histone acetylation, non-coding RNAs, and RNA editing.

Discussion

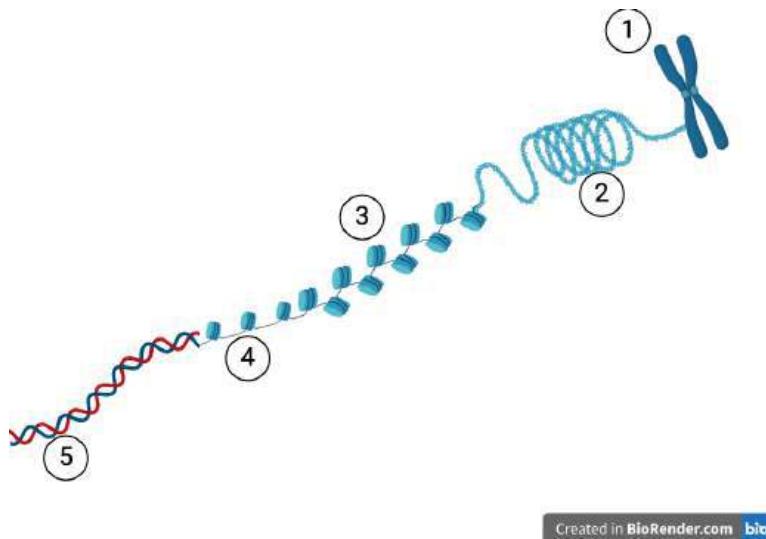


Figure 1. The organization of genetic information. Visual representation of different states that DNA is found in, including 1 (chromosome), 2 (condensed chromatin), 3 (chromatin fiber), 4 (nucleosomes - made up of DNA wrapped around histone proteins), 5 (DNA).

DNA methylation

In DNA methylation, methyl tags are added to the chromatin, causing it to condense. When the chromatin is condensed, enzymes cannot access the DNA to transcribe and translate the information, leading to gene repression. DNA methyltransferase enzymes (DNMTs) are the primary enzymes that catalyze the transfer of a methyl group on the chromatin. DNMTs are expressed throughout neural development and in the mature stem cell generative zones that mediate ongoing neurogenesis. In neurons, DNA methylation prevents premature neural stem cell maturation [1]. DNMTs are regulated by DNA methylation and physiological interactions, promoting neuronal survival, plasticity, and proper neural stem cell maturation [1].

Genomic imprinting is another instance of gene methylation and was the initial epigenetic phenomenon discovered in human diseases. In an imprinted gene, one of the two parental alleles is active, and the other is inactive as a result of DNA methylation [2]. It marks DNA in a sex-dependent manner, resulting in the differential expression of a gene depending on its parent of origin [3]. For example, some of the genes on chromosome 15 are paternally or maternally suppressed, and one allele is active over the other. A defect in the active allele of the imprinted gene results in the loss of expression, which is found in neurodevelopmental diseases such as Prader-Willi syndrome (PWS) and Angelman syndrome (AS) [2]. These diseases are similar in the way that both diseases represent the loss of the same gene expression, but PWS occurs when the paternal gene is active but defective, and AS occurs when the maternal gene is active but defective.

Histone acetylation

Histone proteins can have an acetyl group added to them, a process called acetylation. Histones normally have a positive charge because of their lysine and arginine residues. Acetylation usually occurs at lysine residues. Acetyl groups are negatively charged. Thus, when acetyl groups are added to lysine residues, they neutralize the positive charge, causing the histones to move away from the DNA, which has a negative charge. As a result, the chromatin relaxes. The neutralization of histone tails makes them more available for transcription and translation (Figure 2). This process is facilitated by histone acetyltransferase enzymes (HATs). HATs are essential in normal and malignant hematopoiesis.

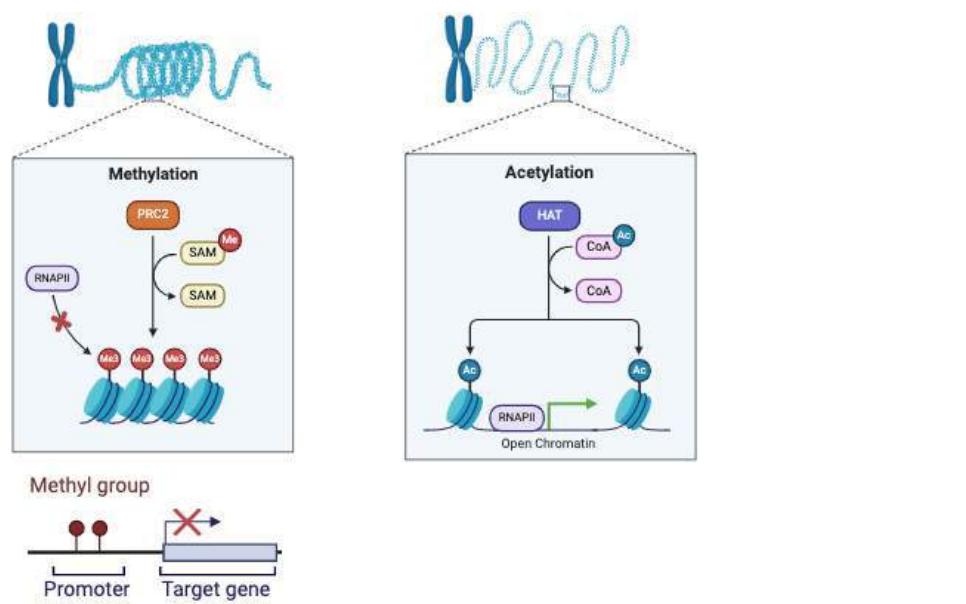


Figure 2. Differences in the effect of DNA methylation (left) and histone acetylation (right) on gene expression. Methyl groups added to the chromatin cause the chromatin to condense. PRC2, a type of DNMT, adds a methyl group. As a result, RNAPII, a type of RNA polymerase that transcribes a target gene is unable to attach to the promoter, and the target gene is not transcribed. When histone proteins are tagged with acetyl groups from coenzyme A, the chromatin is relaxed, enabling RNAPII to attach to the promoter and transcribe the target gene.

Non-coding RNAs

There are several types of non-coding RNAs such as miRNAs, and snoRNAs. Non-coding RNAs can increase or decrease gene expression. Non-coding RNAs (ncRNAs) do not code for proteins. They promote developmental, plasticity, and homeostatic processes [1]. ncRNAs can regulate the activity of other genes by binding to other RNAs to block their expression or mark them for degradation, which decreases gene expression. Additionally, ncRNAs can modify the structure of chromosomes, making genes easier to access for transcription. Chromatin remodeling enzymes can bind to ncRNA to facilitate chromatin

remodeling. ncRNAs influence gene expression by targeting common regulatory proteins to DNA regulatory elements such as PREs and TRES, transcribed as ncRNAs themselves [1].

miRNAs are regulatory ncRNAs that inhibit stability or repress translation of target RNAs. They pair up with their targets to repress their expression and can mark them for degradation, leading to less protein production. Brain-specific miRNAs have specialized roles in neural development, adult homeostasis, and plasticity. A single miRNA may differentially repress or activate as many as 1000 target genes with RNA-binding proteins at untranslated regions or additional regulatory sites [1].

Small nucleolar RNAs (snoRNAs) promote developmental and adult functional complexity by acting on chromosomes, and affecting processes such as genomic imprinting, RNA splicing, transcription, translation, cell cycle progression, and DNA repair [1]. Longer ncRNAs are involved in genomic imprinting, X chromosome inactivation, and serve as sites for miRNAs and snoRNAs. These different classes of ncRNAs help organize the regulation of neural development and local protein synthesis required for synaptic plasticity [1]. These epigenetic mechanisms need to be regulated and function properly for cellular and molecular processes to work effectively.

RNA editing

RNA editing is a process in which RNA modifies and regulates protein-coding genes. It is important in many processes, including neural transmission and presynaptic vesicle release. RNA editing can change the profiles of miRNA targets and can impact every step in the production, processing, and stabilization of mature miRNAs [1]. They can modify miRNAs, target genes, and other non-coding RNAs. By dynamically and reversibly altering bases, RNA editing can adjust the expression profiles and functions of protein-coding genes and non-coding RNAs [1].

RNA editing is mediated by adenosine deaminases acting on RNAs (ADARs). These enzymes swap out one nucleotide for a different one, subsequently changing the sequence's identity. In mammals, there are 3 ADAR enzymes: ADAR1 and ADA2, which are preferentially expressed, and ADAR3, which is restricted to the nervous system [1]. ADARs regulate and manage complex patterns of site-specific editing of individual RNAs, leading to multifaceted and functional consequences. Adenosine deaminases acting on tRNAs (ADAT1-3) modify codon recognition in the process of mRNA decoding, promoting and enabling protein diversity in the developing and adult brain. The gene products that result from RNA editing play various roles in neurodevelopment and adult regulatory functions, including neuronal homeostasis, neural network plasticity, and the epigenetic modulation of learning and memory [1].

Regulation of epigenetic mechanisms by cell and environmental cues

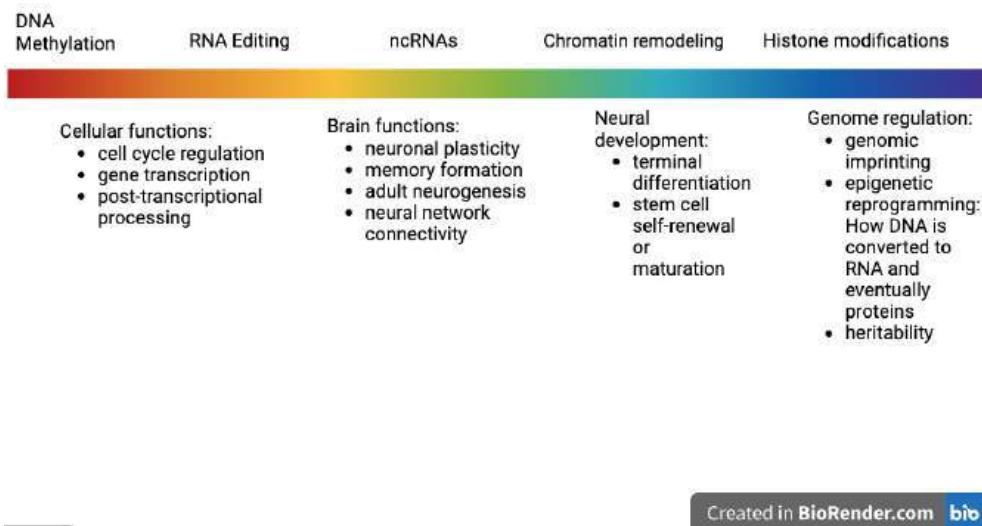


Figure 3. The spectrum of epigenetic mechanisms and some examples of what processes they encompass.

Epigenetic mechanisms are all connected, therefore mechanisms are on a spectrum and processes can fall under more than one mechanism. Adapted from [1].

How epigenetic mechanisms get dysregulated

The various epigenetic mechanisms previously described can all be dynamically changed or influenced by environmental factors as well as genetic cues. The dynamics refer to its ability to move between states and changes over time, known as plasticity. The biological definition of plasticity is that organisms have systems and processes that can change their gene expression based on their environment or circumstances. In neurons, plasticity refers to the consistent and necessary regulation of essential mechanisms. Without regulation, these mechanisms would be unable to control the required cellular and molecular processes [1,4].

Epigenetics is an example of plasticity, as it can alter gene expression without changing the DNA sequence. Epigenetics is continuously happening in normal human cells, while irreversible gene regulation systems like CRISPR Cas-9 do not occur naturally in human cells, but can be used in a therapeutic approach. Plasticity is important to acknowledge from a therapeutic perspective. CRISPR is used for therapeutics involving permanent changes, which are not always aligned with biology's needs. Targeting epigenetics because of its plasticity may be a better strategy.

Two of the ways that epigenetic mechanisms can get dysregulated are through DNA methylation inhibitors and environmental cues.

Presence of inhibitors of DNA methylation

Examples of inhibitors of DNA methylation are cytidine analogs 5-azacytidine and zebularine, as well as nucleoside analogs that sequester DNMT enzymes after being incorporated into DNA. When administered into the brain tissues of mice and rats, inhibitors that do not allow DNMT enzymes to transfer methyl groups onto the chromatin disrupt synaptic plasticity and hippocampal learning and memory [4]. DNA methylation inhibitors can reactivate genes that should be silenced, leading to unintentional and overexpression expression of certain genes.

Environment and lifestyle

There is increasing evidence that several lifestyle factors can influence epigenetic patterns. These factors include diet, obesity, level of physical activity, tobacco, smoking, alcohol consumption, environmental pollutants, and stress. Most studies have focused on the effects of these factors on DNA methylation, and only a few studies examine their effects on histone modifications and ncRNAs (Figure 4). Since genetic factors control energy balance and body weight, dietary components like macronutrients that affect DNA methylation could play a role in the development of obesity. Previous research has suggested that DNA methylation is sensitive to environmental stress during early development and later in life. There are epigenetic biomarkers for obesity, such as methylation patterns of obesity-related genes like *FGF2*, *PTEN*, *CDKN1A*, and *ESR*, suggesting a correlation between obesity and changing levels of methylation [5].

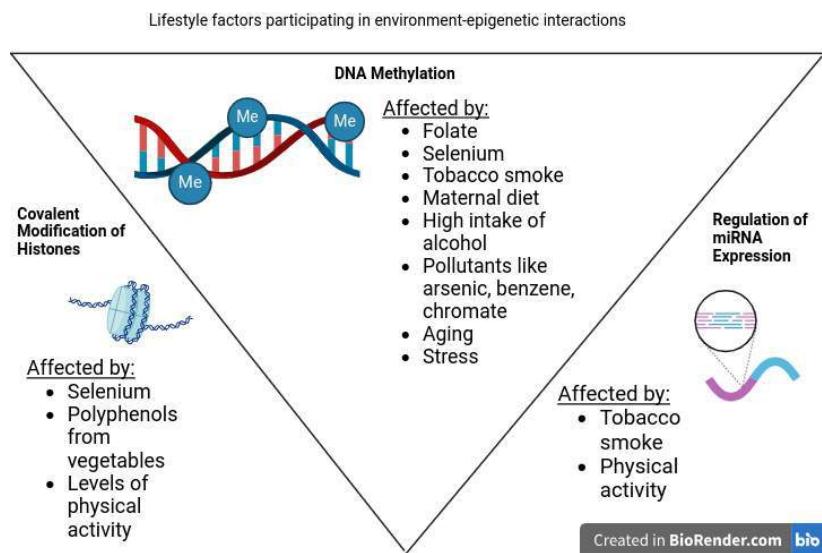


Figure 4. Lifestyle factors that participate in environment-epigenetic interactions. DNA methylation, histone modifications, and the regulation of miRNA expression can be affected by various lifestyle factors. Adapted from [5].

How dysregulation of epigenetic mechanisms contributes to factors linked to Alzheimer's and Huntington's

Alzheimer's disease

Recent studies have suggested a link between dysfunctional epigenetics and the death of neurons, contributing to Alzheimer's disease (AD). AD is the most common form of dementia and affects the elderly population. It is characterized by ongoing and progressive neurodegeneration in specific regions of the brain, including the hippocampus, temporal lobe, frontal lobes, and frontal cortex [6]. This degeneration leads to memory impairment and progressive cognitive dysfunction. This disease is associated with the development and accumulation of amyloid β ($A\beta$) peptide in the brain, which is caused by hyperphosphorylated tau proteins within the neurons [6]. Individuals with AD may experience symptoms such as mood disorders, unpredictable mood swings, reduced self-care, linguistic difficulties, social isolation, and depression.

The role of genetic factors in the development of AD has been established in around 70% of the cases and involves multiple genes. Mutations in genes that regulate the production of $A\beta$ peptide (*PSEN1*, *APP*, *PSEN2* genes) have been identified as the cause of early onset AD, accounting for 1% of cases [6]. The cause of the remaining cases is not fully understood. Researchers have found that mutations in the gene *APOE* are a major risk factor for the development and progression of late-onset AD (LOAD), but mutations in *APOE* alone cannot explain the development and progression of LOAD [6]. At LOAD loci, the genes encode proteins that are involved in inflammatory pathways, cholesterol metabolism pathways, and endosomal vesicle recycling pathways. However, individually, none of these pathways are considered a major risk factor for the development and progression of AD. While the pathogenesis and symptoms of AD have been established, the pathways that lead to these symptoms and the pathogenesis of AD are still not well understood, and there is currently no cure for AD. AD is a result of a complex interplay between genetic and environmental factors, therefore, the pathogenesis of AD could be explained by dysregulated epigenetic mechanisms.

Dysregulated epigenetic mechanisms in AD include DNA hypermethylation, deacetylation of histones, and a general repressed chromatin state. It is important to remember that the chromatin structure becomes tightened (into heterochromatin) due to various epigenetic factors like methylation, which ultimately leads to the repression of gene expression. In AD, the methylation levels of the amyloid precursor protein (APP) promoter region in the temporal lobe are significantly lower compared to those in healthy individuals [6]. This lower amount of methylation results in higher expression, leading to increased protein production and worsening of the condition due to protein aggregation. Studies have shown that AD brains exhibit a large number of differentially methylated (DMRs) or hydroxymethylated (DhMRs) regions compared with control brains. This suggests that the dysregulation of epigenetic mechanisms can potentially serve as a biomarker for downstream correlated factors in AD. Other research findings indicate that enhanced acetylation of histone H4 occurs at the lysine 12 (H4K12ac) residue during the early stages of amyloid protein aggregation in the brain [6]. Given the shared

symptoms of cognitive impairment seen in amnesia, change observed during amnesia may be relevant to AD. For example, acetylation of histone H4 at the lysine 12 (H4K12ac) has been observed during amnestic mild cognitive impairment, indicating its potential as an early-stage biomarker for AD. The protein BACE1 is responsible for the generation of A β peptide in the brain and is characterized by regulated miRNAs in the brain and blood of AD patients. It is important to note that the role of epigenetics in AD is considered as downstream and correlated to AD, rather than being a cause.

Huntington's disease

Huntington's disease (HD) is a genetic disorder that primarily affects medium spiny neurons in the striatum. This condition causes the brain cells to gradually lose function and die, impacting the areas of the brain responsible for controlling voluntary movement and memory. Symptoms of HD include uncontrollable movements and changes in thinking, behavior, and personality, which worsen over time [7].

Huntington's disease is caused by a genetic change in the gene *HTT*, resulting in unstable expanded CAG repeats (>35-39 repeats) and producing a mutant protein (mHtt) with a toxic polyglutamine (polyQ) tract. The *HTT* gene is responsible for making a protein called huntingtin, which is essential for the proper functioning of neurons. Individuals with HD lack the necessary genetic information to produce the huntingtin protein. Consequently, the abnormal shape of these proteins leads to the destruction of neurons, causing them to die. The mutation responsible for Huntington's disease can be inherited in an autosomal dominant pattern. If one parent has HD, there is a 50% chance their child will also develop the disease.

Studies have shown significant changes in gene transcription in the brains of individuals with HD [8]. This demonstrates how disruptions in RNA editing and ncRNAs can contribute to neurological diseases. It is important to note that research investigating the correlation between dysfunctional epigenetic mechanisms and the disease indicates that these mechanisms are more of a downstream effect, rather than the root cause of the mutation of the *HTT* gene. In the brains of individuals with Huntington's disease, there is a re-expression of Hox genes and other homeobox genes. This causes the transcription mechanisms in Huntington's disease neurons to resemble those of immature neurons [9], suggesting impaired transcriptional mechanisms. In cellular systems with overexpressed mutant HTT, extensive changes in histone acetylation levels have been observed. Increased H2A ubiquitylation (H2Aub) was found at down-regulated genes in HD R6/2 mice. Changes in DNA methylation in response to mutant HTT were found at both proximal and distal regulatory regions of genes. A large proportion of the genes that displayed altered expression due to the expression of mutant HTT also exhibited changes in DNA methylation, indicating a potential causal relationship.

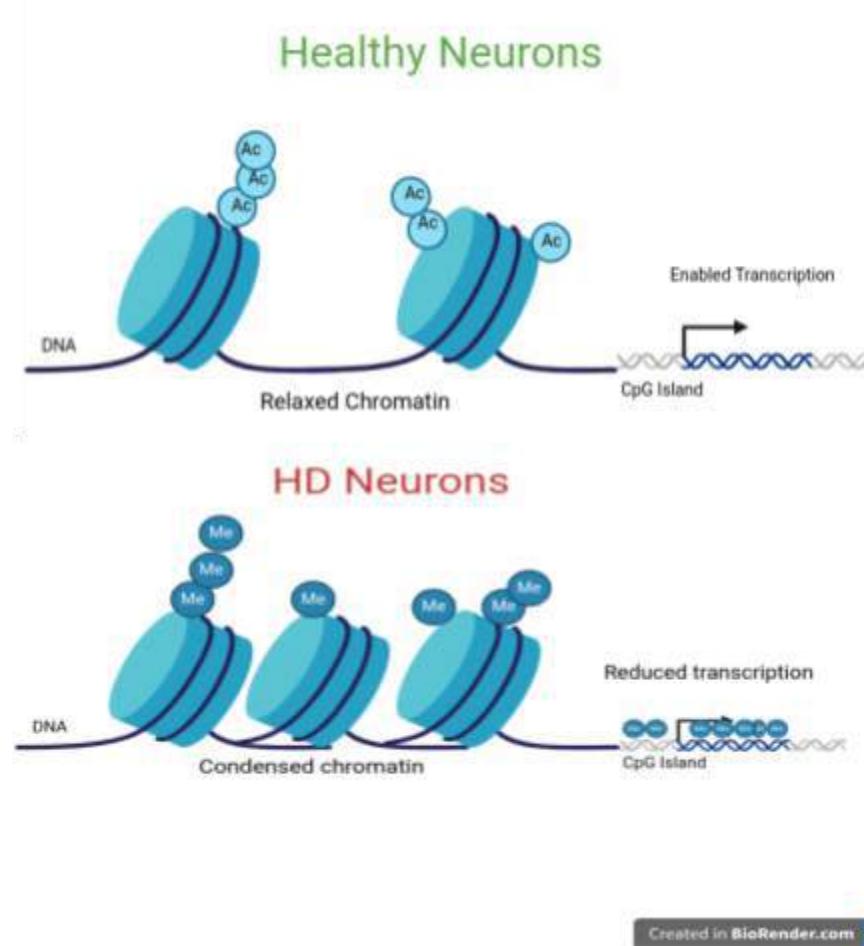


Figure 5. Differences of epigenetic mechanisms active in healthy neurons compared to the neurons of Huntington patients. In healthy neurons, genes can be transcribed at a higher rate due to the acetylation of histone proteins. In neurons of Huntington patients, it was observed that due to the unusually high number of methylation on the chromatin, there was a reduced rate of transcription on the CpG island. CpG islands are areas on the genome that contain a lot of cytosine and guanine nucleotides. Adapted from [10].

Conclusions

The diverse and meticulous mechanisms of epigenetics such as DNA methylation, histone acetylation, ncRNAs, and RNA editing, can regulate gene expression without needing to make changes to the DNA blueprint itself. Prospects suggest that epigenetics could be leveraged for tailored medical approaches targeting specific, extensively researched conditions. Each individual possesses a distinctive epigenetic profile that can change for their specific needs and requirements. Nevertheless, there are lingering questions pertaining to the efficacy of therapeutic intervention in epigenetics and the potential risks associated with interfering with this intricate system, given its inherent connection with other essential molecular and cellular processes.

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Glossary

Chromatin: chromatin is the material that makes up chromosomes, composed of DNA wrapped around histone proteins.

Euchromatin: the uncondensed form of chromatin, where RNA transcription is accessible for gene expression.

Heterochromatin: the condensed form of chromatin, caused by methyl groups being added onto the chromatin. RNA transcription is not accessible, and gene expression is repressed.

Methylation: an epigenetic mechanism where methyl tags are added to the chromatin, causing it to condense; resulting in the repression of gene expression.

DNA methyltransferase enzymes (DNMTs): the primary enzymes that catalyze the transfer of a methyl group onto the chromatin.

Histone acetylation: an epigenetic mechanism where acetyl groups are added onto histone proteins; chromatin relaxes, making the DNA accessible for transcription, and promoting gene expression.

Histone acetyltransferase enzymes (HATs): the enzymes that facilitate the addition of acetyl groups onto histone proteins.

Non-coding RNAs: ncRNAs are RNA segments that do not code for proteins. Instead, they can regulate the activity of genes by binding to other RNAs. ncRNAs influence gene expression and promote plasticity and other homeostatic processes.

miRNAs: microRNAs are a type of ncRNA that regulate gene expression. miRNAs can repress or activate target genes by working with RNA-binding proteins.

snoRNAs: small nucleolar RNAs are a type of ncRNA that promotes developmental and adult functional complexity. In eukaryotes, snoRNAs serve in modifying ribosomal RNA (rRNA).

RNA editing: a process in which RNA is used to modify and regulate protein-coding genes;; useful in processes such as neural transmission and presynaptic vesicle release.

ADAR enzymes: adenosine deaminases are enzymes that mediate RNA editing by acting of RNAs. These enzymes swap out one nucleotide for a different one, changing the sequence's identity.

Plasticity: organisms being able to change their gene expression based on their environment or circumstances; reversible and dynamic.

DNA methylation inhibitors: DNA methylation inhibitors disrupt the transfer of methyl groups onto chromatin, disrupting synaptic plasticity and hippocampal learning and memory. DNA methylation inhibitors can reactive genes that should be silenced; overexpression and unintentional expression of certain genes.

Alzheimer's disease: the most common form of dementia that affects the elderly population; characterized by ongoing and progressive neurodegeneration in specific regions of the brain; this degeneration leads to memory impairment and progressive cognitive dysfunction.

Amyloid β peptide: a protein fragment derived from a larger protein called amyloid precursor protein (APP); accumulation of A β peptide in the brain is associated with Alzheimer's disease.

Huntington's disease: a genetic disorder that causes brain cells to gradually lose function and die, impacting the areas of the brain responsible for controlling voluntary movement and memory.

HTT gene: the HTT gene codes for the Huntington protein. A mutation in the HTT gene is the cause of Huntington's disease.

Homeobox genes: a group of genes that regulate development in organisms, including cell differentiation and morphogenesis.

A Comprehensive Review of DNA-Based Gene Editing Therapies Targeting Neurodegenerative Diseases By Dhivya Muthupalaniappan

Abstract

Neurodegenerative diseases such as Huntington's Disease, Alzheimer's Disease, Parkinson's Disease, and Amyotrophic Lateral Sclerosis have been on the rise as average life spans have begun to increase in the 21st century. All of these diseases can be sporadic or inherited, both due to genetic mutations, and many scientists are investigating ways in which DNA-targeted gene editing therapies can be used to correct these mutations. Both CRISPR-Cas9 and zinc finger nucleases are techniques under investigation, in hopes that they may provide disease-modifying treatments for these diseases. One of these techniques has already experienced real world success in the field of gene editing, with the CRISPR-Cas9 technique becoming FDA (Food and Drug Administration) approved recently. Here, the viability of these techniques to treat neurodegenerative disorders is analyzed, and induced pluripotent stem cell research is also presented. Additionally, while there are not yet any FDA approved DNA-based gene editing therapies for the diseases stated above, the evidence reviewed here suggests the potential to develop an effective therapy in the near future.

Introduction

Neurodegenerative diseases (NDDs) have been recognized as a leading cause of mortality since the 20th century, and much research regarding treatments and cures for these diseases has been done. However, very few potentially disease-modifying therapeutics have reached patients. In this article, the potential efficacy of future DNA-based gene therapies for Huntington's disease, Alzheimer's disease, Parkinson's disease, and Amyotrophic Lateral Sclerosis will be analyzed, and suggestions regarding future research will be made. Specifically, the primary focus of this article will be on the potential for gene editing treatments to address the known genetic causes of these neurodegenerative diseases and the utility of induced pluripotent stem cell research to demonstrate the potential efficacy of these treatments .

Gene editing therapy involves modifying a gene to correct a disease-causing mutation. This can be achieved via clustered regularly interspaced short palindromic repeats-CRISPR associated protein 9 (CRISPR-Cas9) technology or zinc finger nucleases (ZFNs). The steps for the CRISPR-Cas9 technique follow. First, a target mutant DNA sequence is identified for editing. Then, a complementary strand of RNA called a guide RNA (gRNA) is designed to bind to this target DNA sequence, and the gRNA is combined with the Cas9 protein, which is a nuclease that cuts both strands of the DNA, initiating modification of the gene. Next, via viral vectors, lipid nanoparticles, or direct injection, this complex is introduced into cells and the gRNA leads the way to the target DNA sequence, allowing the Cas9 protein to cut the target DNA. Following that, the double-stranded cut in the DNA triggers endogenous repair mechanisms such as homology-directed repair. For homology-directed repair to replace the excised mutant DNA, a source of unmutated wild type DNA is required. In the case of an

autosomal dominant mutation, the unmutated wild type complementary strand provides the template to replace the excised mutant DNA. On the other hand, in the case of a recessive mutation, an exogenous source of wild type non-mutant DNA must be provided to the homology-directed repair mechanism as a component of the therapy. It is important to keep in mind that while this technique may provide great successes, off-target effects may occur, most commonly because the guide RNA may have sequences that partially match other genomic loci in the DNA causing unintended Cas9-mediated DNA cleavage (Wang et al.).

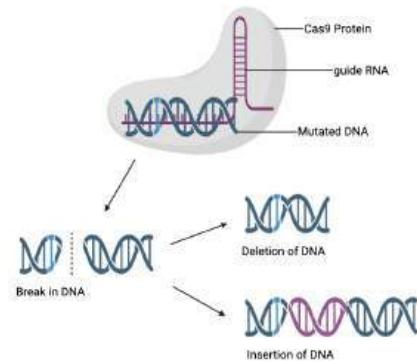


Figure 1: A visual depiction of the CRISPR-Cas9 technique.

The first successful application of CRISPR-Cas9 occurred in the treatment of Sickle Cell Disease (SCD). In December of 2023, Casgevy, the first FDA approved CRISPR-Cas9 gene editing therapy, was authorized for treatment of patients aged 12 or older. In SCD, an inherited mutation of the β -globin gene causes hemoglobin molecules to misfold, impairing the binding and distribution of oxygen around the body. Casgevy corrects the mutation by restoring the proper formation and function of hemoglobin (Singh et al.).

Gene editing can also be done using ZFNs. ZFNs are artificial proteins engineered to bind to a specific target DNA sequence in cells and elicit DNA cleavage nearby. To achieve this, zinc finger domains, which bind specific DNA sequences, are fused to the FokI nuclease domain, which non-specifically cuts the DNA nearby. This complex is then introduced into cells along with modified genetic material. Once the DNA is cut, the homology directed repair process is activated, replacing the mutant DNA using the modified available genetic material template as described above. Like CRISPR/Cas9, this process will yield a new cell lineage with a wild type gene, of course with the possibility of off-target effects as well (Carroll).

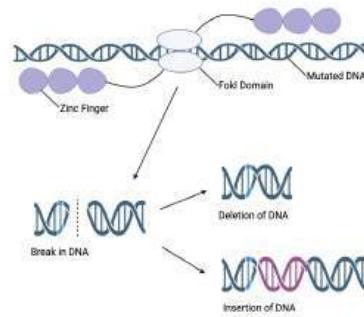


Figure 2: A visual depiction of the Zinc Finger Nuclease technique.

In 2018, Sangamo, a company researching ZFNs for Mucopolysaccharidosis, or Hunter's Syndrome (HS), announced positive results with one of their therapies, SB-913. In HS, the level of glycosaminoglycans (GAGs) in the body is elevated due to a loss-of-function mutation in the IDS gene. This gene encodes the enzyme called iduronate 2-sulfatase (I2S), whose purpose is breaking down glycosaminoglycans (GAGs). Sangamo's ZFN treatment, SB-913, was associated with reduced urinary levels of GAGs, suggesting that I2S function had been restored via the treatment (Harmatz et al.).

While both the CRISPR-Cas9 technique and ZFNs are intended to yield similar results, there are a few distinguishing factors that set these two apart. The differences in these methods are due to differences in selecting and synthesizing guide RNAs vs engineering zinc-finger DNA binding domains as the gene-targeting component. CRISPR-Cas9 is cheaper and faster to implement, and can target multiple genes simultaneously, but has a higher risk of off-target effects. However, ZFNs are more difficult and expensive to design, but have higher specificity and therefore a lower risk of off-target effects. As seen, there isn't an optimal option between the two techniques; the approach being used is largely based upon the uniqueness of the target DNA sequence and the level of possibility of unwanted DNA cleavage.

Induced pluripotent stem cell (iPSC) research has also become a major part of the NDD treatment discovery field. iPSCs are completely differentiated somatic cells that are programmed to return to the immature, stem cell states of themselves, and once done, they are capable of differentiating into several different cell types. To model disease cell biology, iPSCs are harvested from patients with NDD-derived genetic mutations. Because these cells are already mutated, the gene editing techniques described above can be tested upon these cells to determine the viability of these techniques.

Among the neurodegenerative diseases with known genetic causes are Huntington's Disease (HD), Alzheimer's Disease (AD), Parkinson's Disease (PD), and Amyotrophic Lateral Sclerosis (ALS). The characteristic symptoms of these diseases reflect the types of neurons that degenerate earliest in the course of each disease. Huntington's disease (HD) is an exclusively hereditary and invariably fatal NDD caused by an expansion of trinucleotide cytosine adenine guanine (CAG) repeats in the Huntingtin (HTT) gene. Typically, individuals with 35 or less repeats of this sequence show no symptoms of HD and do not have this disease, whereas those with 36 or more repeats have a higher risk of developing HD. In HD, the earliest affected neurons are medium spiny neurons of the striatum, which are critical for motor and cognitive brain function. HD presents as a mid-life decline in motor or cognitive skills, with or without psychiatric symptoms. Symptoms may include chorea, which are involuntary, unpredictable movements, clumsiness, difficulty concentrating, impaired judgement, depression, or psychosis.

AD, PD, and ALS primarily occur sporadically, without a clear monogenic pattern of familial inheritance. Alzheimer's disease (AD) is the most common cause of dementia and the most prevalent NDD. AD's neuropathology is characterized by the deposition of plaques, composed primarily of the Amyloid-beta (A β) peptide. Rare, monogenic, heritable Alzheimer's is caused by mutations in the Amyloid Precursor Protein (APP) gene, which encodes the protein

from which the Amyloid-beta peptide is derived, or the Presenilin 2 (PSEN2) gene, which encodes one of the proteases that cleaves APP to generate Amyloid-beta. In addition to these rare monogenic forms of Alzheimer's, the risk of sporadic AD is increased 2-3 fold by inheritance of the ε4 allele, one of four alleles of the Apolipoprotein E gene. In AD, the earliest affected neurons are in the entorhinal cortex, which is critical for new memory formation. AD primarily affects a person's cognitive abilities, including short term memory loss, progressing to frank dementia, characterized by confusion remembering the current time and place, personality changes, and eventually difficulty with movement and coordination.

Parkinson's disease (PD) is the second most prevalent NDD, and rare, monogenic causes of PD include mutations in the alpha-Synuclein (SNCA) and leucine repeat kinase-2 (LRRK2) genes. In PD, the earliest affected neurons are dopaminergic neurons of the substantia nigra, which are critical in motor control. PD primarily slows and impairs initiation of movement, and can also impair cognitive function and cause behavioral changes. For instance, a person with PD may experience difficulty with movement, memory and attention, or experience a tremor, depression, or fatigue.

Amyotrophic Lateral Sclerosis (ALS) is a NDD in which upper and lower motor neurons degenerate. Mutations causing rare, monogenic forms of ALS occur in more than 40 genes, including point mutations in the Cu/Zn Superoxide Dismutase (SOD1) gene and hexanucleotide (GGGCC) repeat expansions in the Chromosome 9 Open Reading Frame 72 (C9orf72) gene. Those with ALS typically experience a rapid onset of weakness in the hands, feet, arms, and legs, or in the muscles involved in speech and swallowing. Additionally, patients with ALS invariably die 2-5 years after diagnosis due to respiratory paralysis.

Discussion

Huntington's Disease

HD is a well researched NDD in terms of gene editing therapy treatment. As stated above, a mutation in the HTT gene, called mutant HTT (mHTT) is thought to cause this disease, and fixing this mutation by removing the excessive trinucleotide CAG repeats or suppressing this gene can help manage the symptoms of HD.

One example of this comes from an *in vivo* study that demonstrated this successfully in HD mouse models. Via an adeno-associated virus and the use of viral vectors, the CRISPR-Cas9 complex was introduced into the brains of 9 month old mice with two identical copies of mHTT with 140 CAG repeats to perform gene editing. In this study, the mHTT gene was suppressed, and the resulting data suggested that this could be a potential therapeutic strategy to treat HD. Both the levels of aggregated mHTT protein, caused by the mutation, decreased, and motor function in areas such as balance and grip improved. Additionally, it was noted that there were some off-target effects to the mice to the wild type HTT gene in the first study, but a subsequent study determined that using an alternative Cas9 protein which only cuts one strand of DNA at a time as opposed to both like in the first study can make this technique safer and more specific to

use. However, it is worth mentioning that the mice in the experimental group of this experiment did not recover as well as those in the control group, which may serve as a minute worry, despite the seemingly overall success (Rohn et al.).

Another study aiming to delete excessive CAG repeats did so by using the CRISPR-Cas9 technique in both wild type and mutant copies of HEK293 cells as well as mice. Scientists created 4 gRNAs to specifically bind to the target DNA sequence in exon 1 of the HTT gene. Doing so displayed positive results as astrocytes that are typically quite active in patients with HD were alleviated and most other areas of the gene were unaffected. Inevitably though, there were some off-target effects that led to the loss of wild type HTT, which ultimately had negative effects on the experimental mice group. Additionally, it was also noted that the efficiency of mHTT expression reduction varied between individual mice, which is undesirable (Fields et al.).

Alzheimer's Disease

AD has mutations such as those of the PSEN2, APP, and APOE genes associated with it. Research regarding gene therapies as well as iPSCs has been done to study this disease, and it is seen that modifications to these existing genes can serve as a therapeutic strategy for AD.

A study using the CRISPR-Cas9 technique sought to correct the PSEN2 gene mutation in neurons derived from iPSC cells. This was done by obtaining cells from an individual carrying the PSEN2 N141I mutation, reprogramming these cells to iPSCs, and differentiating them into basal forebrain cholinergic neurons, which are commonly affected neurons in AD. The study resulted in the normalization of the A β 42/40 protein ratio, which is typically off balance with higher levels of the A β 42 protein in patients with AD. Therefore, this suggests that the technique used here could serve as a treatment option for AD patients (Rohn et al.).

Another study aiming to disable the Swedish APP mutation attempted to do so in patient-derived fibroblasts. These scientists used the CRISPR-Cas9 technique as well, and also yielded a positive result. They noted that after completing their gene therapy treatment, fibroblasts secreted only 60% of A β protein, which is desirable since this is the protein that toxicologically aggregates in the brains of AD patients and this percentage is typically higher in these patients (Rohn et al.).

Conversely, a study utilizing ZFNs attempted to convert the APOE4 allele, which is associated with increased risks of AD, to the safer APOE2 or APOE3 alleles in the APOE gene in iPSC-derived neurons as well. It was observed that doing so prevented pathology linked to APOE4 in AD, which signifies a positive result (Rohn et al.).

Parkinson's Disease

PD is linked to mutations in the SNCA and LRRK2 genes with some research studies being done to explore how gene therapy can aid in this situation. To date, studies have only tried to modify parts of these genes and have succeeded in reducing and delaying PD pathology.

A study utilizing the CRISPR interference technique, which silences genes without affecting DNA, tried to inhibit SNCA expression and α -syn aggregation via gene editing and

DNA methylation. In this in vivo study, PD mouse models were used, and many positive results were recorded. It was noted that there was significant improvement in motor performance, balance, and coordination, and the amount of α -syn aggregation was greatly down-regulated. This proves that this technique yields many benefits and could be translated to other non-human primates and human patients as a possible treatment (Kong et al.).

Another study aiming to correct the LRRK2 mutation, which is one of the most prevalent causes of both familial and sporadic PD, used CRISPR-Cas9 on isogenic cell lines to edit the mutant LRRK2 gene. Dopaminergic toxicity is typically observed in PD patients, but after this gene editing therapy was used, an immense decrease in neurite complexity was observed. Additionally, researchers also determined that there was a reduction in the prevalence of familial PD as well, which implies that this treatment could also be a good option for PD patients if it proves successful in humans (Mansour and El-Khatib).

Amyotrophic Lateral Sclerosis

ALS is also a highly studied disease with both gene editing and iPSC research exploring different therapies to treat it. Currently, there are mutations associated with the C9orf72 gene, which has an extremely excessive amount of 4 guanine, 2 cytosine (G4C2) repeats in it, and the SOD1 gene, which creates misfolded proteins in its mutated form.

An in vivo study involving ALS mouse models used an adeno-associated virus and CRISPR-Cas9 gene editing to delete the hundreds to almost thousand extra repeats of the G4C2 sequence in the C9orf72 gene. Having succeeded in doing so, the scientists recorded positive results such as the fact that there was a reduced level of RNA Foci, which typically toxicologically aggregate in cell nuclei when C4G2 repeats are high. Additionally, it was also noted that dipeptide repeat protein aggregation was also lowered, which usually happens in the condition mentioned prior as well. Therefore, because aggregation levels of both of these proteins were lowered, this technique could serve as a possible treatment (Miccio et al.).

Another in vivo study also using ALS mice models attempted to edit the SOD1 gene via an adeno-associated virus too. With the treatment administered to them, the mice displayed decreased expression of SOD1 in their spinal cords, an increased number of motor neurons, delayed onset of ALS, and increased survival rates, all of which were reversed for mice in the control group. Two subsequent studies also completed three years after the fact confirmed these results as well. However, a limitation to this study was that this technique was only performed on ALS mice models before the mice exhibited symptoms of ALS, so it is uncertain whether or not this treatment would work after symptoms are shown (Fang et al.).

Conclusion

For now, progress being made with CRISPR-Cas9 is sufficient, but it seems to be that there are quite a few off-target effects when using this technique. Because ZFNs are more specific than CRISPR-Cas9 since they are less likely to have unintended DNA cleavage, it could be helpful to use them for the gene editing portion of a treatment, following the discovery of a

desirable outcome with the use of the CRISPR-Cas9 technique. In other words, CRISPR-Cas9 is easier and more cost-effective to use, so a treatment utilizing this technique should be determined first. Once a desirable outcome is exhibited to the targeted DNA sequence with this technique, regardless of the amount of off-target effects, a ZFN can be designed exactly for the target DNA sequence. Because ZFNs have higher specificity, the off-target effects should not be present with a ZFN. Therefore, because the efficacy of the treatment was confirmed with CRISPR-Cas9 and a specific ZFN is designed to replicate the effects of the original gene editing treatments without off-target effects, this type of gene editing treatment should theoretically work. Furthermore, success with both CRISPR-Cas9 gene editing and ZFNs has been shown in the past with techniques regarding SCD and HS. Therefore, although it will require a great amount of time and effort, gene editing therapies using these techniques should be attainable for the diseases examined here.

Progress with individual diseases is also moving along quickly. For HD, it has been observed that gene editing can be harnessed to suppress or remove mHTT, but the main problem with this is that off-target effects to the wild type HTT gene are also being seen. As stated above, this could theoretically be resolved by using ZFNs to complete gene editing work as opposed to CRISPR-Cas9 since ZFNs are more specific, although this has not explicitly been tried yet. However, other than that, it seems as if researched treatment options are working well. They have been tested and tried upon mice, and after doing so on other non-human primates and seeing success, human testing and treatment release may follow for HD.

As for AD, most research has been done on human-derived iPSCs. This research has resulted in positive outcomes with A β protein aggregation levels being reduced, which implies a major hallmark of this disease being resolved, but there has been limited success beyond this level in terms of gene editing. In regards to next steps, AD mouse models could be used to analyze the success rates of current iPSC treatments to see if any are successful. Following that, these treatments could also be translated to other non-human primates and humans if seen as beneficial.

Additionally, the reasoning for the order of iPSCs to mice to non-human primates to humans for treatment testing follows: cells are the least risky test subjects in regards to ethical codes. Next, mice are quite easy to breed and model diseases in, and they share about 85% of their DNA with humans, which makes them optimal to test treatments on. Following that, non-human primates such as chimpanzees share almost 98-99% of their DNA with humans, which means the way they react to treatments would be quite similar to a human's reaction, making them ideal for treatment testing too. Finally, once successes have been seen in mice and non-human primates, it makes sense to test upon humans, since a treatment has a low likelihood to be fatal to humans if it has made it to this stage. Furthermore, all animal testing is done by a code of ethics, so an animal's wellbeing is still kept in mind while scientists administer their treatments.

For PD, after gene editing therapy was used to edit either the SOD1 or LRRK2 genes, the pathology of this disease was either greatly slowed or stopped. Again, treatments for this disease

have been tested on cell lines and mice models so far, so since positive results have been shown, it could be possible to analyze whether or not these methods could be used on other non-human primates to see if results remain consistent.

In terms of ALS, success in managing the pathology of this disease has been shown with iPSCs and gene editing research. However, for one of the studies mentioned above, there was a concern as to whether or not the tested treatment would work in all ALS mice models since the treatment tested was done in not-yet-symptomatic mice and the scientists still needed to explore if this treatment would work in more advanced pathologies of ALS where the mice were symptomatic. Completing this treatment as well as the other treatments tried upon iPSCs in mice who show symptoms of ALS such as balance deficits and muscle twitching may reveal if the current options are sufficient. This could lead the way for future research indicating whether currently successful treatments can be translated to other non-human primates or whether new treatments need to be developed to be tested on symptomatic ALS mice models.

NDDs are meticulously being researched every day and more and more treatment options and facts about them are being discovered. Gene editing therapy is one of the most explored ways to treat NDDs as it has shown significant progress in methods to treat various diseases. With a growing amount of research being done in this field, treatments or cures for all of these devastating diseases will hopefully be discovered soon.

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Evaluation of Environmentally Friendly Deicing Agents Compared to Current Road Salt

By Myounghoon Chung and Yoonseo Kim

Abstract

Road salts like calcium and sodium chloride significantly impact the natural environment and human health and contribute to the corrosion of both metal and pavement. Consequently, tests have been undertaken to determine which deicing agent could expedite the ice-melting process, with the aim of discovering a safer alternative. The initial hypothesis posited that salt would exhibit the most dramatic reduction in ice melt time. However, it was anticipated that all variables would positively affect the ice melting speed. The results revealed that Calcium Chloride demonstrated the swiftest melting speed, averaging just 76 minutes. Salt closely followed with an average of 80 minutes, while sand and the absence of a deicing agent yielded the lengthiest durations at 142 and 146 minutes, respectively. These findings suggest the potential for applying eco-friendly deicing alternative.

Introduction

Calcium chloride and sodium chloride are the most utilized deicers and are commonly discovered anywhere on the road in winter. They are excellent at melting ice and snow and have low freezing points. It even has a minimal expense, making it productive and ideal for deicing (Jamshidi et al., 2020; Leggett et al., 2020). However, they carry unpleasant side effects. They destroy the roads and cars and make roads even more slippery in certain circumstances (Craig and Zhu, 2018). They leave the ice melted and in a liquid state and then freeze again if the weather is extreme. Calcium chloride is also unsafe for human bodies, and sodium chloride has a substandard impact on plants in the surrounding area, and they both pollute waterways (Hinsdale, 2019). Therefore, it is necessary to find a way to melt ice in place of road salt in a more environmentally friendly way.

Some road salts, such as calcium chloride, might not be safe for both the environment and the human body. Non-hydrated salt with strongly hygroscopic properties can present many hazards. By drying up moist skin, calcium chloride can go about as an aggravation. Disintegrating exothermically, solid calcium chloride can cause burns in the mouth and esophagus if it is to be ingested. Also, concentrated solutions or solid items may cause gastrointestinal bothering or ulceration if ingested (Jamshidi et al., 2020). Calcium chloride is used in concrete mixes to accelerate the initial setting, but chloride ions lead to corrosion of steel rebar, which means it should not be used in reinforced concrete. The anhydrous type of calcium chloride may likewise be used for this reason and can give a proportion of the moisture in the concrete (Redland et al., 2020).

At low concentrations, chloride is generally benign, but as concentrations rise, it may be toxic to oceanic creatures, including plankton and fish living in inland lakes. These ecological changes can greatly have an influence on water quality. Road salts could harm amphibians,

plants, and creatures if they end up in freshwater bodies by disturbing their osmoregulation capacity (Learn, 2022).

Salinization (increasing salinity) and increased metal leaching are ongoing problems throughout North America and European fresh waterways. In highway deicing, salt has been associated with the corrosion of bridge decks, motor vehicles, reinforcement bars, wire, and unprotected steel structures used in road construction (Liu et al., 2021).

Surface runoff, vehicle spraying, and windblown actions also affect soil, roadside vegetation, and local surface water and groundwater supplies. Although evidence of environmental loading of salt has been found during peak usage, the spring rains and thaws usually dilute the concentrations of sodium in the area where salt was applied. Chloride is corrosive. Like chloride-based deicers, acetate-based deicers affect asphalt pavement. The damage comes through a combination of chemical reactions, emulsification, distillation, and stress that stacks up in the asphalt (Redland et al., 2020).

Research Hypothesis

Calcium chloride and Sodium Chloride will melt the ice in the shortest amount of time, while all other deicers will cause the ice to melt faster than ice standing by itself.

Materials and Methods

Control group: Ice (no deicing agent)

Experimental group:

Calcium chloride and Sodium chloride

Baking Soda

Rubbing alcohol

Vinegar

Sand

Coffee grinds

Water

Sugar

Beet juice

Procedure

Salt first dissolves in the film of liquid water that is always present on the surface (because it's a salute), lowering its freezing point below the temperature of the ice. Ice in contact with salty water melts, creating more liquid water, dissolving more salt, causing more ice to melt, and so on. The reason is that the acetic acid lowers the melting point, meaning that the ice cube will melt at a colder temperature. Therefore, the ice cube will melt faster with a lower melting point (since carbohydrates or sugars can lower melting temperatures, it might be possible to use wastewater from fruits or vegetables).

These are materials needed for one set (6 ice cubes) of the test, not the whole experiment.

6 bowls

Ice cube tray (size or shape does not matter too much as long as the right amount of water is added)

Tap water (120 milliliters)

freezer

Measuring cup for milliliters

A spot with room temperature (20~22 degrees Celsius)

60 milliliters of a single deicing agent (none, salt, water, sugar, etc.)

1. Fill a measuring cup to the 20-milliliter mark.
2. Add the 20 milliliters of tap water into every single cube on the ice tray
3. Repeat until 6 ice cubes are filled
4. Freeze in the freezer for 7 hours
5. Place them in individual bowls (at room temperature) with the side with the largest surface area facing down
6. Use another measuring cup and put 10 milliliters of the deicing agent on the top surface of the ice
7. Wait and record the amount of time they took to melt the ice cube completely
8. Move on to the next set of trials by repeating the same steps
9. When finished with the second set then, change the deicing agent and repeat

Data

(at room temperature)

(Hour: min)

Ice by itself

1	2	3	4	5	6
2:17	2:13	2:49	2:35	2:19	2:21

trial 2

2:39	2:42	2:22	2:22	2:12	2:15
------	------	------	------	------	------

salt (10 millimeters)

1	2	3	4	5	6
1:14	1:52	1:24	1:31	1:02	1:14

trial 2

1:03	1:19	1:07	1:17	1:25	1:26
------	------	------	------	------	------

water (10 millimeters)

1	2	3	4	5	6
1:40	1:58	2:15	1:37	1:50	2:07

trial 2

1:29	2:01	1:38	1:39	1:41	2:06
------	------	------	------	------	------

sugar (10 millimeters)

1	2	3	4	5	6
1:27	1:49	1:58	2:03	1:15	1:49

trial 2

1:26	1:32	1:42	1:29	1:39	1:23
------	------	------	------	------	------

Baking soda (10 millimeters)

1	2	3	4	5	6
1:45	1:31	1:55	1:37	1:42	1:28

trial

1:51	1:43	1:43	1:48	1:40	1:35
------	------	------	------	------	------

Sand (10 millimeters)

1	2	3	4	5	6
2:31	2:13	2:22	2:16	2:28	2:10

Trial 2

2:15	2:34	2:18	2:23	2:26	2:27
------	------	------	------	------	------

Calcium chloride (10 millimeters)

1	2	3	4	5	6
---	---	---	---	---	---

1:30	1:24	1:08	1:17	1:21	1:11
------	------	------	------	------	------

1:15	1:05	1:12	1:19	1:23	1:02
------	------	------	------	------	------

Coffee Grinds (10 millimeters)

1	2	3	4	5	6
1:34	1:37	1:52	1:58	1:37	1:42

1:47	1:42	1:45	2:01	1:41	1:57
------	------	------	------	------	------

Vinegar (10 millimeters)

1	2	3	4	5	6
1:30	1:59	1:34	1:38	1:46	1:46

trial2

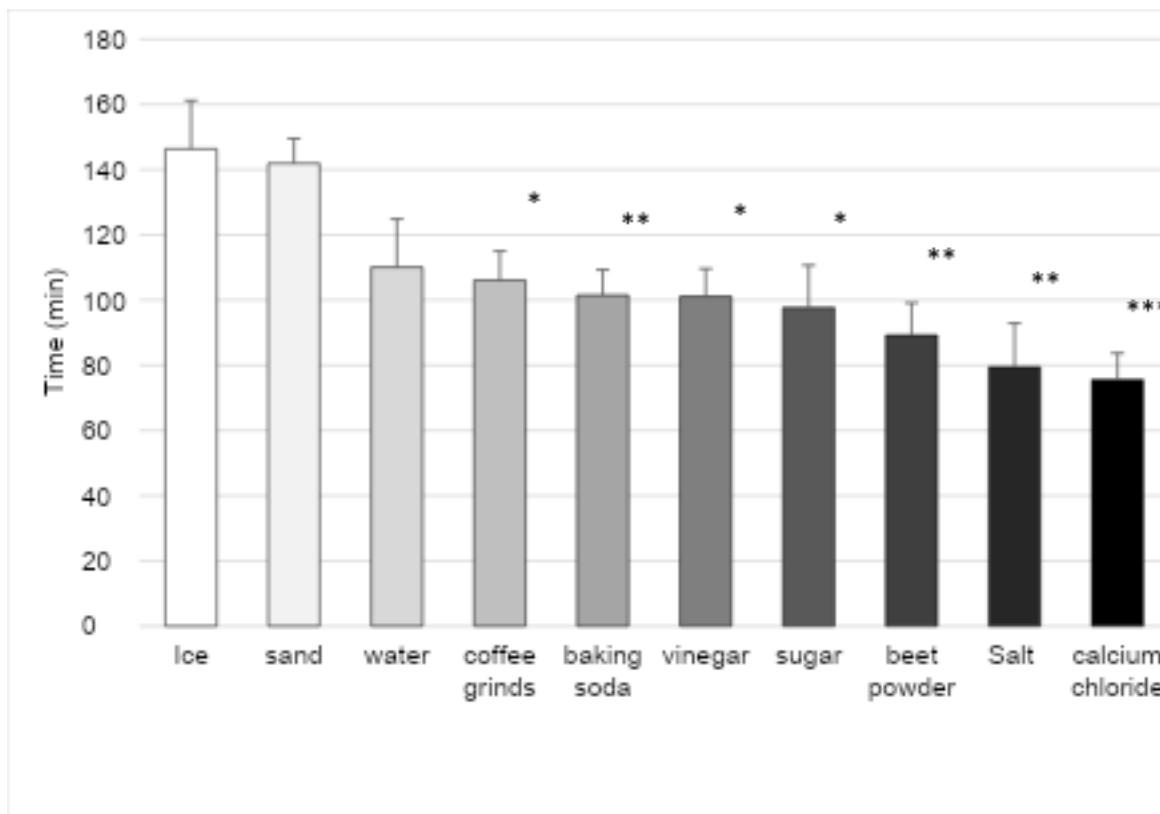
1:42	1:48	1:36	1:34	1:33	1:47
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Beet powder

1	2	3	4	5	6
1:14	1:33	1:26	1:29	1:39	1:39

trial 2

1:40	1:31	1:31	1:31	1:19	1:29
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Results

The statistical analyses were performed on 6 independent values with duplicates, and statistical significance was determined using one-way analysis of variance (ANOVA) followed by posthoc Dunnett's test (SAS 9.4) to compare the different treatments compared to ice control (p-value of 0.05 or less was considered statistically significant). In addition, the data were analyzed using Tukey's test to determine statistical significance between the groups.

Most deicers had no extensive gap between their trial times and had consistent data, landing roughly average. Despite having the same measurements, they did not stay within 20 minutes. The control experiment showed a melting time of 146 ± 14.8 minutes. As expected, salt and calcium chloride demonstrated the fastest melting times of 79.5 ± 13.3 minutes ($P < 0.01$) and 75.5 ± 8.1 minutes ($P < 0.001$), respectively. Other agents, such as baking soda and beet powder, showed significantly reduced melting times compared to the control: baking soda (101.5 ± 7.7 minutes, $P < 0.01$), beet powder (89.2 ± 9.8 minutes, $P < 0.01$), coffee grounds (106.0 ± 8.9 minutes, $P < 0.05$), vinegar (101.0 ± 8.5 minutes, $P < 0.05$), and sugar (97.6 ± 13.0 minutes, $P < 0.05$).

The variants with the fastest average speed were calcium chloride, salt, and beet powder. Calcium chloride quickly frames saline solution, which rapidly liquefies the ice by bringing down the freezing point of water. Calcium chloride draws in moisture because of its hygroscopic properties, which help it form brine more quickly than other ice melters (Hinsdale, 2019). It

generally contains ideal blends that soften ice viably. The salt works in a similar manner in that it lowers the freezing point. Beet powder can also make brine quickly, and the beet contains sugar, which can lower the freezing point of the ice (Redland et al., 2020; Fischel and Branch, 2001). The two significantly slow data came from sand and ice on their own. Ice must melt on its own from room temperature, and the water must be created by the melted ice. However, as the ice starts melting, it starts picking up pace more rapidly as more water forms. While sand is widely used on the road for snow, its main purpose is to create friction; therefore, it does not include many properties that help melt ice. Data from sugar to water did not have a crucial variance in time as they all had similar averages, having a range of 12 minutes.

Conclusion

In conclusion, salt dramatically accelerated the ice melt speed and came close to calcium chloride with an average speed of 80 minutes. However, holding an average of 76 minutes, calcium chloride had the most drastic change in time out of all the variants. As proposed in the hypothesis, all deicers did speed up the ice melt process. Sand held the slowest time out of the variables in melting the ice and was not much faster than ice by itself.

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A Study on the Effectiveness of Antidepressants in Improving Worker Productivity through Analysis on the Management of Depression and Patient Outcomes in Different Countries By Wen Hao Chong

Abstract

There has been a rise in anxiety disorders in fast-paced societies, which can affect productivity in the workplace. (Fava) Reduced productivity in important public services like healthcare could cause a domino effect and lead to a decrease in standards of living. Insight into antidepressant consumption (AC) is important in examining the societal importance of improving depression management and patient outcomes. This study examines the effectiveness of antidepressants by exploring the relationship between AC rates and the management of depression in different countries. The analysis is centred around the Human Development Index (HDI), analysing healthcare system efficiency, standard of living, and levels of knowledge acquisition as key metrics. This study examines data across three countries, Iceland, United Kingdom (UK), and South Korea, to assess the impact of increased AC (measured in Defined Daily Doses per 1000 inhabitants (DDD)) on the chosen sectors, alongside indicators of productivity such as Gross Domestic Product (GDP) growth rates and GDP per capita. The findings show that while rising AC (eg. from 95 DDD in 2007 to 157.3DDD in 2022 in Iceland) enhances worker productivity in the healthcare sectors of the analysed countries and improves those citizens' overall standards of living, the AC trend coincides with a decline in the quality of education systems. This correlation between AC and worker productivity is valuable for healthcare providers, giving better understanding on the effect of antidepressants. Moving forward, stricter regulation of antidepressant prescriptions could be helpful especially for teenagers or children receiving education (due to the negative correlation observed).

Introduction

Antidepressant prescriptions for young adults and teens have grown nearly 64% since 2020. (Vogel) COVID-19's healthcare pressure, together with an increasingly busier lifestyle in many fast-paced societies has led to an increase in depression and anxiety problems, which have increased reliance on antidepressants. (Fava) Happening alongside the growth in AC are growing societies and economies, which can be due to countries' strengths in various sectors, one example being healthcare. HDI can be used to measure antidepressants' effect on patient outcomes and the management of depression. It is important in analysing socioeconomic conditions which are correlated with mental health outcomes such as the rates of AC. (United Nations Development Programme) The HDIs of three nations – Iceland, the UK, and South Korea will be examined in this study. The former two are among the nations with the highest rates of AC, while the latter is among the lowest (see Fig. 1). Although Latvia (country in Europe) has a DDD more than South Korea (country in Asia), investigating two different regions, Asia and Europe, can provide more insight into the differing cultures of societies which might affect AC rates. On the other hand, by comparing the AC rates and worker productivity of

Iceland and the UK, two European nations, it is possible to investigate whether countries' locations (geography) plays a role. Although a worker's physical health is crucial to their overall well-being, the main focus of this study will be mental health and how it affects patient outcomes.

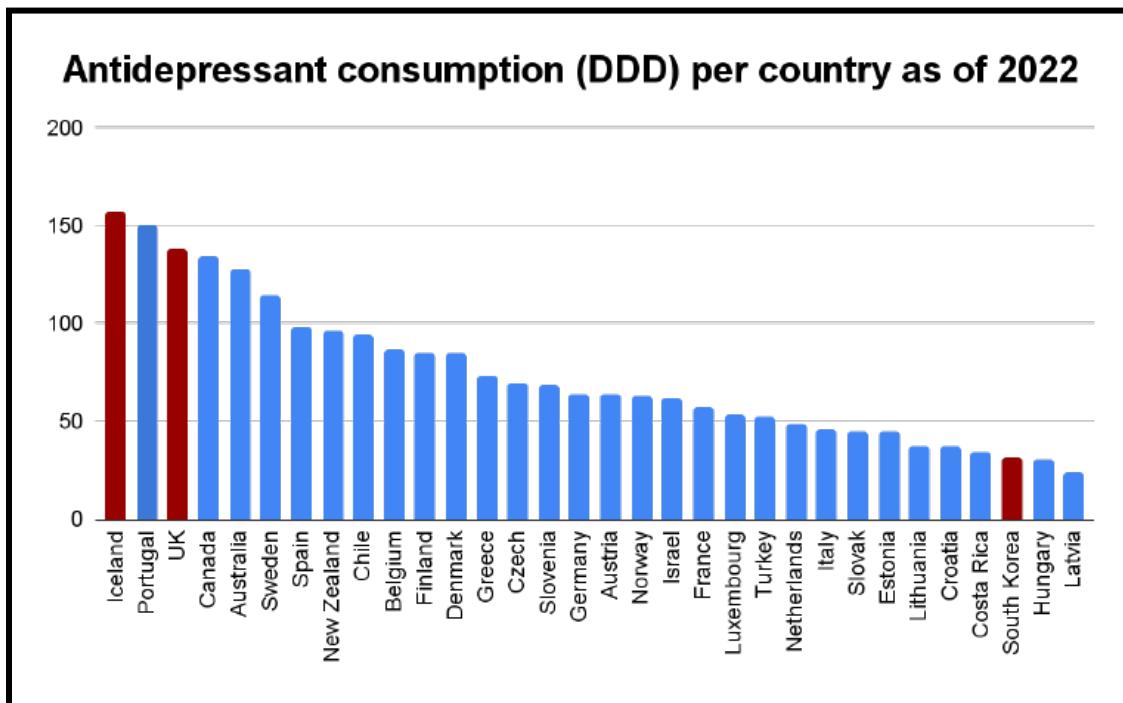


Fig. 1. Antidepressant consumption (DDD) per country in 2022 showing Iceland and UK being the high ranking countries, while South Korea being ranked one of the lowest (countries of interest marked out in red)

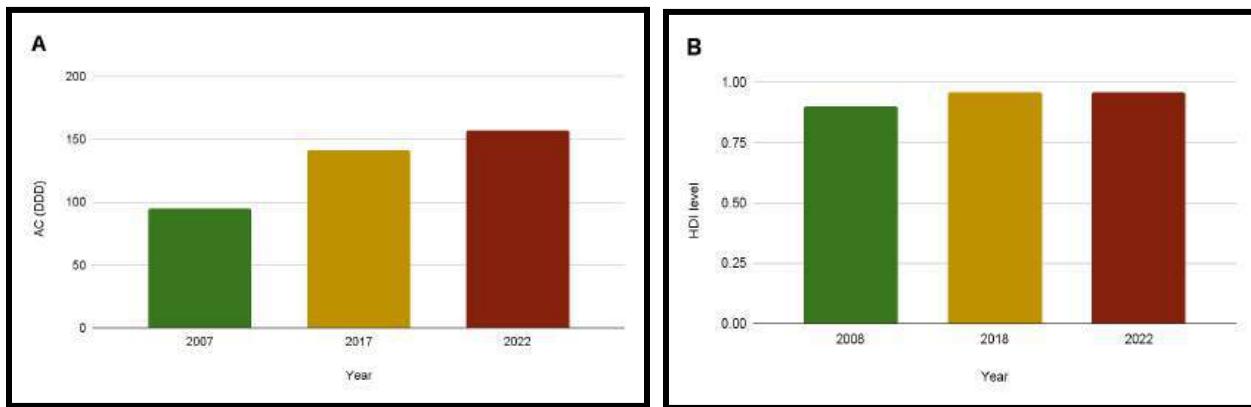
However, the three HDI components alone cannot fully measure the usefulness of antidepressants on patients. While the factors influencing HDI might correlate with AC, the relationship may not be as straightforward as one might expect. Countries with a higher HDI like Iceland (which ranked 3rd in 2022) typically have better healthcare access, education, and social services, leading to greater diagnosis of mental health conditions. This may cause higher AC due to more available treatment options. In contrast, in lower HDI countries like Myanmar (which ranks 144th in 2022), limited access to mental health care might cause underreporting and lower AC despite mental health challenges. This study will thus categorise the factors affecting worker productivity into primary and secondary factors. The primary factors are the three core factors mentioned above (i.e. factors influencing HDI): healthcare standards, standard of living, and knowledge acquisition. The secondary factors will include various relevant physical and environmental elements, such as level of happiness, suicide rates, working hours, and technological and infrastructural advancements, which interact with the primary factors to influence overall productivity. With global AC rates continuing to rise, this trend is often associated with an assumption of enhanced quality of life. However, to date, there is a lack of empirical evidence investigating this claim. This review thus seeks to analyse the various factors

related to AC rates and determine how they affect patient outcomes, focusing on the synergistic effects between the primary and secondary factors.

The effect of increased AC on productivity and quality of life will be measured through countries' overall GDP growth rate and GDP per capita. GDP growth measures the increase in total value of goods and services produced within a country over a period, showing overall productivity. (Fernando) GDP per capita measures economic productivity relative to the population size, reflecting the standard of living and economic well-being of individuals. (Brock) In other words, this measure can be an indication of the effectiveness of antidepressants in maintaining worker productivity. It also reflects how effectively resources are used to address mental health challenges, linking AC to economic outcomes.

Countries' AC rates, HDI rankings, and GDPs

2008 was chosen as the starting point for this investigation due to the occurrence of major socio-economic events like the global financial crisis. (Erkens) This period impacted mental health greatly due to changes in healthcare policies and prescription practices. (Christodoulou) Sustained improvements in mental health infrastructure and advancements in pharmaceutical therapies were signs of economic stability until 2018. (Reinhart) Data from this period provides insights into AC during a time of relative economic stability. By 2022, the focus had shifted to the COVID-19 pandemic, and data from this year would be especially helpful in exploring the impact of public health crises in shaping mental health management and AC. Together, these three years show three different contexts of mental health management and AC across different nations, showing their influence on patient outcomes over time.



*A. AC of Iceland from 2007 to 2022, in DDD.
B. HDI levels of iceland from 2008 to 2022.*

As the country consistently ranked as having the highest rates of AC, Iceland is particularly worthy of study. Due to limited data availability, this study uses DDD data for Iceland from 2007 and 2017, as they are the closest years to 2008 and 2018 respectively (see Fig. 2A). Iceland's AC rate (DDD per 1000 inhabitants) in 2008 was 106, (Thengilsdottir, et al.) which increased to 141.4% by 2017, (OECD) and rose further to 157.3 in 2022. (Mikulic)

Iceland's 3rd place HDI ranking in 2022 is higher than many other developed countries, including the UK (15th) and South Korea (19th). (Qery) This high ranking has been consistent and increasing throughout the years. Iceland's HDI level was 0.902 in 2008, (countryeconomy.com) which rose to 0.959 in 2018, and remained constant in 2022. (see Fig. 2B) Icelanders have been enjoying high standards of living. Their workers are also shown to be satisfied with their working conditions.

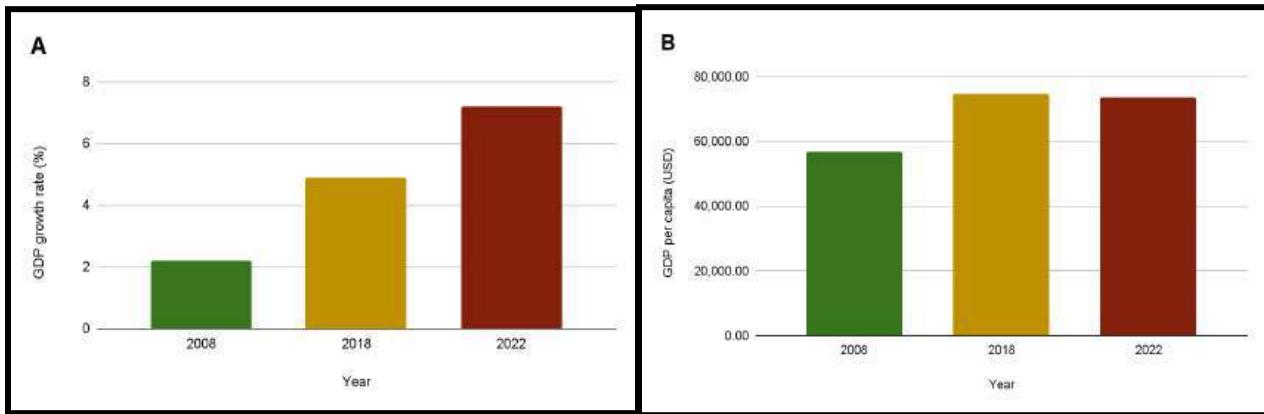


Fig. 3.

- A. *GDP growth of Iceland from 2008 to 2022, in %.*
 B. *GDP per capita of Iceland from 2008 to 2022, in USD*

Over the same time period, Iceland's overall GDP growth was 2.2% in 2008 before rising to 4.9% in 2018. Although the 2020 COVID-19 pandemic affected Iceland's growth rate, it has been improving steadily since, reaching 7.2% in 2022. (World Bank national accounts data) Moreover, Iceland's GDP per capita rose from 56,943.40 USD in 2008 to 74,452.19 USD in 2018, before falling slightly to 73,466.8 USD in 2022. (World Bank national accounts data) (see Fig. 3A and Fig. 3B) Overall GDP per capita over the years shows positive signs despite the recent drop which can be attributed to the pandemic.

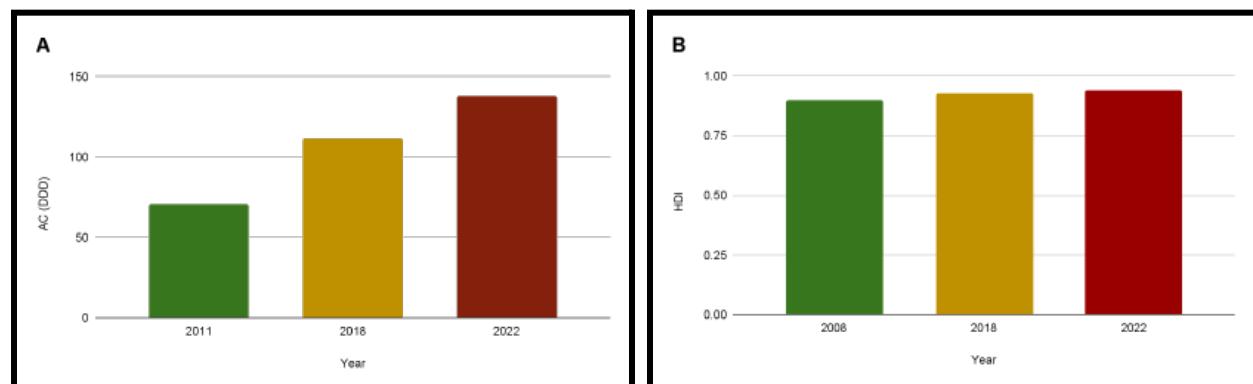


Fig. 4.

- A. *AC of UK from 2011 to 2022, in DDD.*
 B. *HDI levels of UK from 2008 to 2022.*

The UK also ranks within the top 3 countries for rates of AC (in 2022), (Mikulic) with 70.7 DDD in 2011, which further increased to 111.6 in 2018, before increasing to 138.2 in 2022. (see Fig. 4A) Over the same time period, the UK experienced a much larger increase in AC compared to Iceland. UK's HDI was 0.900 in 2008, which increased to 0.929 in 2018, and continued to grow until 0.940 by 2022. (see Fig. 4B) (countryeconomy.com)

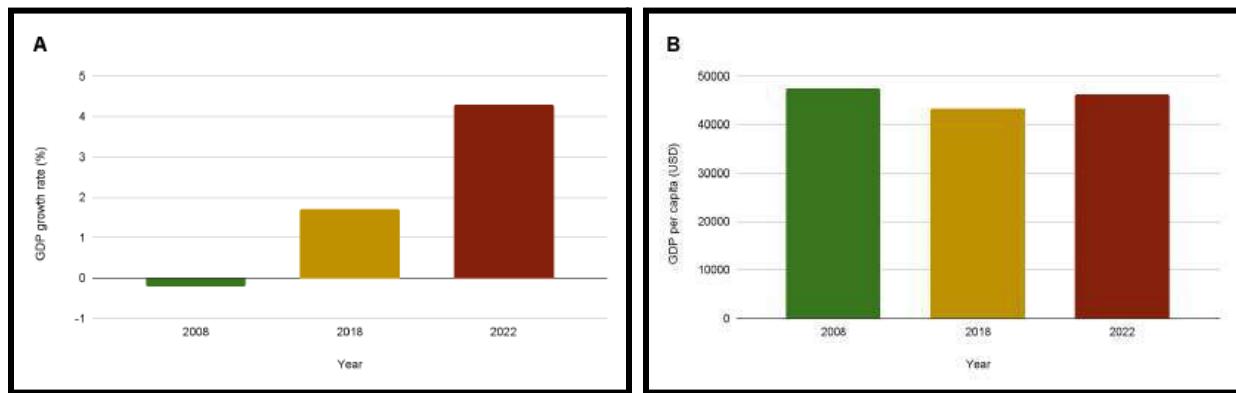


Fig. 5.

- A. GDP growth of UK from 2008 to 2022, in %.
 B. GDP per capita of UK from 2008 to 2022, in USD.

Unlike Iceland's steady growth rate, the UK's GDP growth has experienced fluctuations through the years. Its growth was -0.2% in 2008, before increasing to 1.7% in 2018. This further increased to 4.3% in 2022, reflecting the UK's economic growth. (Clark) Across the same time period, the UK's GDP per capita decreased from 47,396.12 USD in 2008, to 43,203.81 USD in 2018, before rising to 46,125.26 USD in 2022. (see Fig. 5A and Fig. 5B) (World Bank national accounts data, and OECD National Accounts data files)

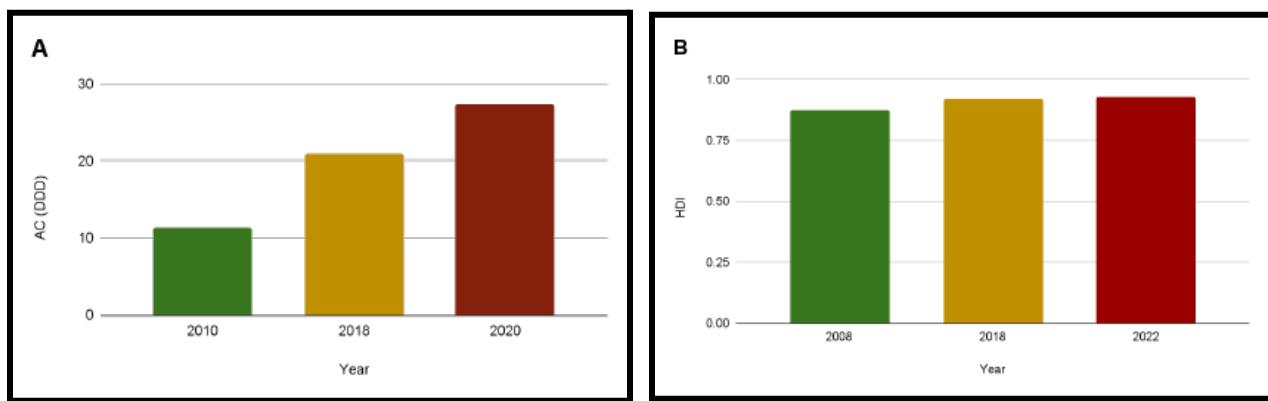


Fig. 6.

- A. AC of South Korea from 2010 to 2020, in DDD.
 B. HDI levels of South Korea from 2008 to 2022.

In contrast to Iceland and the UK, South Korea is a country which ranks lowly in AC rates, despite an overall increase of 142.48% from 11.30 DDD in 2010 to 21.00 DDD in 2018 and to 27.40 DDD in 2020 which suggests growing antidepressant use. (see Fig. 6A)(Oxford Martin School) South Korea's HDI in 2008 was 0.875, which increased to 0.919 in 2018, before further increasing to 0.929 in 2022. (see Fig. 6B)(countryeconomy.com)

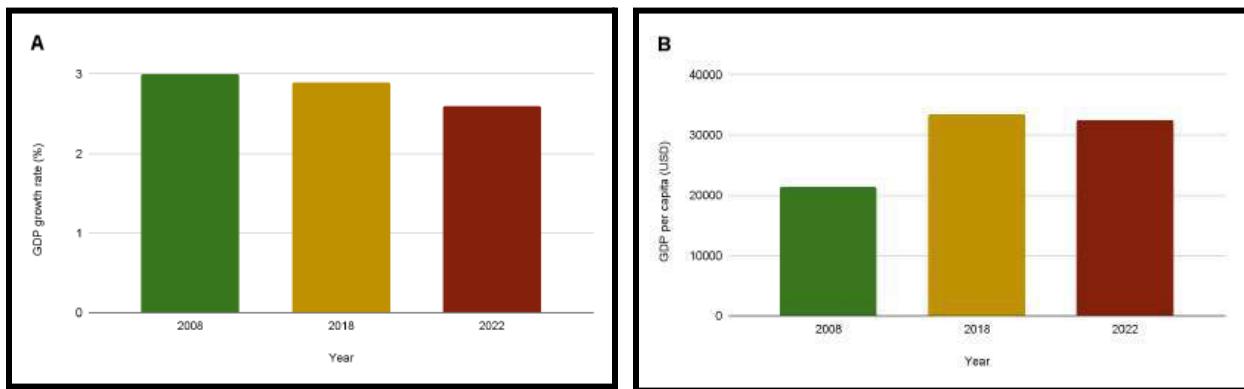


Fig. 7.

- A. GDP growth of South Korea from 2008 to 2022, in %.
 B. GDP per capita of South Korea from 2008 to 2022, in USD.

Unlike Iceland and the UK which have shown growth in GDP, South Korea's GDP growth rate in 2008 was 3.0%, which dropped slightly to 2.9% in 2018, and further decreased to 2.6% in 2022. (World Bank) However, GDP per capita increased over the years, from 21,350.43 USD in 2008, to 33,447.16 USD in 2018, before experiencing a slight decline to 32,422.57 USD in 2022. (see Fig. 7A and Fig. 7B) (Macrotrends)

Healthcare systems

The accessibility of healthcare services impacts employee productivity. About 5.4% of all workers worldwide, or 7.8 million people, missed work in January alone in early 2022 due to health-related issues. (Stafford) Better access to healthcare services increases the chances that workers will address health issues promptly. This raises the amount of preventative care and lowers sick leave, which contributes to employee productivity. (Gulliford)

Healthcare systems are supported by its workforce, and the number of healthcare professionals is needed for a system's capacity to meet the needs of a country's citizens. (Bureau) The healthcare workforce must be able to deliver accessible and quality care because it directly influences the efficiency of other sectors. (Mosadeghrad) Other factors like availability and adequacy of healthcare services, public satisfaction, and the general medical needs of the population must also be taken into account when evaluating healthcare systems. Analysing both workforce size and broader public health context is thus necessary.

Iceland's healthcare system is generally highly efficient thanks to a large labour force. The number of practicing physicians increased from 3.4 per 1,000 people in 2000 to 3.9 in 2019, ("Physicians (per 1,000 People) - Iceland | Data.") while nurses and midwives grew from 14.0 to

16.3 per 1,000 people between 2000 and 2020. (“World Bank Open Data.”) Reports of unmet medical needs are also low; only 3% of citizens reported such issues in 2018, less than half of the EU average of 6.8%. (*State of Health in the EU*) This not only supports effective mental health interventions, but also correlates with increased AC (DDD), which as mentioned above grew from 106 in 2008 to 157.3 in 2022, suggesting that Iceland’s healthcare system could be a contributing factor towards higher worker productivity due to its increasingly better management of mental health.

A similar trend between healthcare efficiency and AC can be seen for the UK. Its healthcare sector productivity rose by 0.7% and labor inputs in healthcare increased by 2.3% in 2018 as AC rates similarly grew over this same period. (Lewis) UK’s National Health Service (NHS) has also shown growth. Between 2000 and 2019, the proportion of practicing physicians rose from 2.2 to 3.0 per 1000. (Yang) The proportion of nurses and midwives per 1000 persons increased from 7.3 to 8.8 throughout that time. This enables more efficient handling of various medical requirements. However, 4.6% of people in 2019 reported having trouble accessing healthcare, which could mean that certain populations, especially those living further from cities still face difficulties. However, the UK’s healthcare system shows clear evidence of productivity which could be made more sustainable in the long-run by better accommodating more disadvantaged citizens.

South Korea’s universal healthcare system, organised through the National Health Insurance Service (NHIS), ensures near-complete medical coverage for its citizens. (Ahn) Its efficiency can be seen through the country’s low burden of circulatory diseases. (Kim) Through the NHIS, antidepressants can be effectively prescribed in order to support mental health. This contributes to societal gain and economic productivity. The efficiency of healthcare and management of health problems has helped maintain productivity, as evidenced by the improvements in workforce and infrastructure over the years. From 2000 to 2021, the number of doctors per 1,000 citizens nearly doubled from 1.4 to 2.6. (English site Ministry of Health and Welfare) Between 2002 and 2021, the number of nurses per 1,000 rose from 4.2 to 8.4. South Korea has a high ranking in healthcare access ratings due to its universal NHIS coverage. It is worth noting that a country may achieve a high Human Development Index (HDI) even in the absence of primary factors (robust healthcare infrastructure, sustainable standard of living, or productive knowledge acquisition). This is where the analysis of secondary factors (indirectly related to human behaviour) becomes crucial, as it allows analysis of the impact of the primary factors on HDI. Healthcare expenditure and life expectancy can be used to evaluate healthcare systems’ productivity.

When healthcare professionals pass away, they cease contributing to their sector. The assessment of productivity therefore must take into account life expectancy.

Iceland not only has had one of the highest life expectancies globally, but its life expectancy has risen from 79.1 years in 2000 to 82.77 years in 2020. (O’ Neill) This was accompanied by an increase in health expenditure from 8.2% in 2008 to 8.77% in 2018. (“Health Expenditure as a Share of GDP, 2018 (or Nearest Year.”) Similarly, the UK has made

improvements in its healthcare sector on paper, notably in service delivery and population health outcomes; as health expenditure rose from 9.6% of GDP in 2010 to 10.3% in 2020, life expectancy increased from 79.60 years in 2008 to 81.26 years in 2018. (O' Neill) South Korea experienced a similar trend, as health expenditure increased from 5.9% of GDP in 2010 to 8.4% in 2020 while life expectancy increased to reach 83.6 years in 2021—higher than both Iceland and the UK. This is in contrast to a lower value of 79.6 years in 2008. (L. Yoon)

It must be reiterated that AC itself does not seem to have any direct impact on the healthcare system. However, it can be said that when healthcare professionals consume antidepressants, the result will improve their productivity and delivery of health services. Healthcare workers face high demands and stress as a part of their professional life. (Dr A. Mark) Healthcare careers are considered to be the hardest. Aspiring medical workers face various challenges while the training, burnout due to highly stressed workplaces has been normalised, and long medical training. For instance, the healthcare system in the UK is facing serious problems like overcrowding, lack of funds, issues like waiting lists and staff shortages. In order to keep the entire workforce efficient, management is important. Antidepressants can play a big part in doing so. The efficient distribution of antidepressants through efficient health systems can contribute to improved workforce well-being and productivity, continued economic growth and social welfare. In any case, the healthcare system of countries like the UK is showing positive growth patterns. Thus, there is a good chance it may remain sustainable for a longer period, as long as medical professionals' well-being is taken into account. To ensure that the healthcare productivity of these three countries continues to grow, it is all the more important to mitigate possible mental health problems in this sector, while not relying on antidepressants in the long-run.

Quality of life

Quality of life, as a measure of societal well-being, can be determined by several components (eg. self-reported happiness). (Medvedev) Due to its positive effects on individual well-being and societal productivity, work-life balance is a key determinant of quality of life. (Bhende) Another metric is suicide rates - high suicide rates are associated with stressors such as poor work-life balance, inadequate mental health care, and economic pressures, while low suicide rates may reflect high quality public health systems, availability of mental health support, and positive work conditions including work-life balance in a country, signalling a high quality of life for citizens of that country. (Fu et al.) Countries that prioritise work-life balance and mental health services tend to report both higher life satisfaction levels and lower suicide rates, demonstrating the interplay between mental health, happiness, and societal well-being in measuring a nation's health and prosperity.

Iceland was reported as the third-happiest country in the world in 2023, with a World Happiness Report score of 7.525. (Saunders) This is the second year in a row that Iceland has achieved third place. In terms of working environment, Iceland's average weekly working hours has decreased 9% over the decade, from 38.7 hours in 2010 to 35.5 hours in 2022. (Dyvik)

Iceland's recent four-day work week trial has also proven to be a huge success, as participants (more than 1% of Iceland's total working population) reported decreases in stress and increases in energy levels, which facilitated improved focus and higher productivity. The positive experience made Iceland one of the leaders in applying the four-day working week. It demonstrates that Iceland's working hours are well-received, and thus contribute positively to workers' productivity. (Joly et al.) Iceland's suicide rate decreased from 12.7-12.8 in the 2000s (World Health Organisation) to 8.6 in 2022. (Nordic Council of Ministers) Given the rise in AC over the same period of time, the role antidepressants play in improving mental disorders can be hypothesised.

In the UK, although the decrease in work hours has been relatively minor, decreasing by just 0.6% from 32 hours a week in 2008 to 31.8 hours in 2022, four-day work week pilots have been relatively successful. (Joly et al.) 92% of the 61 UK companies involved in a six-month pilot intend to continue with the shorter working week. Suicide rates also decreased from 10.9 to 8.4 per 100,000 people from 2010 to 2022, which can be explained by improvements in mental health services. We can observe a significant change towards a more supportive and productive work environment in the UK.

Between 2010 and 2022, the average workweek in South Korea dropped from 47.1 to 39.3 hours. (Park et.al) The government allowed flexible schedules and introduced a 52-hour maximum work week policy. Reports of higher employee happiness and work-life balance correlate with less societal pressure and higher productivity. Unfortunately, despite these improvements, the work-life balance in South Korea is relatively poor. Ministers in South Korea have recently unveiled plans to reform its cap on maximum hours, proposing for employees to work longer hours, and arguing that the change will encourage households to start a family. (Gordon) South Korea's push for a record 69 hour workweek means that four-day work weeks, which have been proven successful in European countries, are simply impossible. Increased working hours have led to fatigue and burnout, with a 2020 survey revealing that 70% of Korean office workers suffered from burnout over a given one-year period. (Shim) Suicides are a major public health challenge. Intense pressures faced by both adults and youths have also led to high suicide rates in South Korea. In 2010, the suicide rate was 31.2 per 100,000 people, and although this decreased slightly to 25.2 in 2022, (L. Yoon) suggesting progress, it is still one of the highest rates among OECD countries. (Statistics Korea Statistics Research Institute.)

Overall, the evidence suggests that AC has the potential to improve people's quality of life in general. Decreased suicide rates and better work-life balance in Iceland and the UK indicate that antidepressants benefit people. Long work hours and high suicide rates are still problems in South Korea. Nonetheless, South Korea's lowering suicide rates align with increased ACs, suggesting antidepressants' increasingly beneficial effects on reducing social stressors. Mental health therapies can be a key factor in improving the quality of life for both individuals and the workforce, as seen by the relationship between antidepressant use and improvements in more general social indicators.

Similar to the analysis of healthcare efficiency, a country may achieve a high HDI even in the absence of primary factors (robust healthcare infrastructure, sustainable standard of living, or productive knowledge acquisition), suggesting the need for analysis into the secondary factors. With regards to quality of life, a key factor influencing this metric is countries' technological readiness.

Workers' access to technology is strong in Iceland, with the country ranking 24th in Network Readiness Index (NRI) in 2024 above much larger countries like Spain (26th) and the Russian Federation (38th). (World Intellectual Property Organisation) This is in spite of Iceland's small population of 395,733 people (as of 2024) (Worldometer) and geographical distance from technological superpowers like the United States and China. (Roucek)

As a technologically advanced country, the UK is 8th on the 2023 Network Readiness Index (NRI). (World Intellectual Property Organisation) This is higher than other similarly developed economies like Japan and Australia, which ranked 12th and 15th, respectively. Moreover, the UK ranked 5th on the 2024 Global Innovation Index (Iceland only ranked 25th). (World Intellectual Property Organisation) Between 2011 and 2022, the number of IT workers in the UK dropped from 483000 to 101700. (Borgeaud) Despite this, UK's IT sector has improved steadily, with investments in the sector growing tenfold from £1.2 bn in 2010 to £11.3 bn in 2020. (Skelton) This expansion in spite of the decrease in available workers indicates the technological progress of the UK.

South Korea's 5th ranking in the 2023 NRI, highlighting its highly accessible technology infrastructure. (World Intellectual Property Organisation) South Korea's advanced technology sector has helped the country maintain its edge in digital readiness. South Korea is recognised as a global leader in Information Communications technology (ICT) due to its strong technological penetration rates. Importantly, the ICT industry accounts for 13% of the country's GDP, and is a sector that the nation heavily relies on. (Kang) In 2022, South Korea's total production of the ICT industry reached a record KRW 560 trillion, indicating South Korea's strong technological readiness.

Through the analysis on the countries' technological advancements, it can be theorised that the technological position of the countries' could have a role to play in their improving productivity. The strong technology would not only have enabled better productivity in workplaces, but would also have allowed for more efficient access to online and social media platforms which could have a significant role in peoples' quality of life. (Roy Rillera Marzo, et al.)

Education and knowledge acquisition

Iceland's education system has shown signs of decline in recent years. Although primary education remains nearly universal, with around 90% of children aged 6 to 16 attending school and around 90% progressing to secondary education, (Ministry of Education, Science and Culture) performance in the 2022 PISA assessment fell significantly. Icelandic students scored 459 in mathematics, 436 in reading, and 447 in science, well below the OECD averages of 472,

476, and 485 respectively, and a clear regression from the 2018 results; these results represent the lowest performance recorded for Iceland. (PISA database) The percentage of students achieving at least Level 2 proficiency in mathematics has dropped to 66%, below the OECD average of 69%. Socioeconomic disparities, especially among immigrant students, have worsened this situation, with immigrant students scoring 37 points lower on average than non-immigrant students. Upper secondary completion rates have also stagnated, and retention in key subject areas remains a concern. Even though Iceland remains committed to inclusivity and lifelong learning, these trends suggest a declining education efficiency for its students, and a need for education reform to prevent further deterioration.

The UK's education system, although still maintaining strong enrollment rates and a high participation rate in tertiary education, has shown concerning signs of decline in recent years. Firstly, UK students, who performed above OECD average in the 2018 PISA assessments, showed significant decline in the 2022 assessment as they scored below the OECD average. (Norden) This is also illustrated by the fact that in 2019, only 5% of primary schools met the government's target of 90% of students reaching the expected standard in core subjects. (Andrews) High teacher turnover rates, inequitable learning gaps, and absenteeism also remain significant causes for concern. (Menzies) These point to systematic flaws in the education system.

South Korea is famous (and perhaps notorious) for its demanding educational standards and strong emphasis on attainment – which are not dissimilar to cracks appearing. Almost every child is enrolled in primary school with an enrolment of around 99.9%, secondary education with an enrolment of about 97%, and the high school dropout rate is remarkably low at 2.7%. About 70% of the population is enrolled in tertiary institutions. With regards to South Korean students' 2022 PISA scores, their score of 527 points was much higher than the OECD average of 472 points in mathematics, with similar above-average performance in reading and science. (OECD) Despite South Korea's better performance in comparison to other countries, its performance in comparison to previous years has declined, with a score of 546 in mathematics in 2009, with higher scores in reading and science in 2009 as well. (L. Yoon) South Korean students have faced increasing pressure, with young Koreans on treatment for stress and depression having risen by 32% in the past five years, this national record in 2023 having never been seen before. (LaCroix International) The fact that there is less than 1 psychiatrist per 10,000 inhabitants worsens the situation, with many youths struggling to cope with mental challenges without help from professionals.

It is worth taking into account the effect of the Covid-19 pandemic on countries' declining education systems in recent years. However, surveys and research carried out suggest that although the pandemic would have made education more challenging, it did not have a serious effect on the knowledge acquisition of students, (Pillai) given the countries' technological advancements (see section on Quality of life) and adaptability of their healthcare systems (see section on Healthcare systems).

Despite all 3 countries (being first-world countries) showing a reasonable education system, standardised tests like PISA scores among other statistics show several declines in the education systems, which coincide with rising AC. Unlike nations' healthcare systems and quality of life, the flaws of ACs can be seen through analysis on the countries' education systems. It can be hypothesised that the increased reliance on antidepressants may be increasing stress and burnout among both students and educators, leading to a deterioration in educational quality. This correlation underscores the urgent need to address both the mental health crisis and the educational decline, as these challenges threaten the long-term sustainability and productivity of these nations' education systems.

Discussion

Among the three factors identified—healthcare systems, quality of life, and education and knowledge acquisition—this study has found that an increase in AC occurs alongside improvements in healthcare systems and quality of life. The strong, long-term economic (GDP) growth in the countries (except South Korea, whose decrease was marginal in comparison to its increase in AC) aligns with the increase in the availability of healthcare professionals, together with better life expectancy, and stronger funding from third party organisations. The strengthening economy across all 3 countries also aligns with the increasingly positive quality of life amongst workers in all 3 countries, which can be attributed primarily to better work-life balance, with high consumption rates suggesting accessible and functioning healthcare services. Similarly, although antidepressants significantly improve standard of living by alleviating symptoms of depression and enabling individuals to participate more fully in social activities, the study found a correlation between increased AC and decline in the quality of education systems.

The use of antidepressants does have its restrictions. For example, it has been known that antidepressants can have severe side effects when taken in high doses, such as mood swings, nausea, and headaches. (Carvalho, André F., et al) In addition, antidepressants may also be subject to the placebo effect. The placebo effect is a phenomenon that describes improvements in symptoms associated with the taking of medication, but in reality, an inactive substance or a placebo is being taken rather than an actual medication. (Papakostas, Yiannis G., and Michael D. Daras) This can be because of positive expectations, good doctor-patient relationships, or even biological mechanisms like neurotransmitter release, which could ease symptoms of depression. Furthermore, ethical issues can be involved in the mental health treatment of patients, overprescription can potentially pose long-term health risks, and also carries a risk of addiction and dependence, particularly from some classes of antidepressants. (Hengartner)

Alternative mental health treatments may also be feasible: for example, therapy, mindfulness seminars, and workplace guidelines supplementing the use of antidepressants, though ideally should be held as a solo option prior to antidepressant prescription. (Maj, Mario, et al.) This is in consideration of negative side effects of antidepressants as previously stated.

While improvements in healthcare and lifestyle are clearly desirable in themselves in addition to the benefits to other aspects of standard of living that they bring, they can come at the

expense of other areas, like children's education. Although there seems to be a correlation between the use of antidepressants and better healthcare systems or overall well-being, the evidence is not conclusive. It is clear that further research is essential to understand and address these complex issues. As this study only focused on the key parameters impacting worker productivity, future works can discuss how the change in AC is related to other parameters not discussed in this study. Besides, future model experiments in populations or communities with lower and/or lowering AC would be helpful for assessing the effect of antidepressants. Moving forward, healthcare intervention through the stricter regulation of antidepressant prescriptions could be helpful towards certain populations of a country, especially for teenagers or children who are still receiving education (due to the negative correlation observed). Antidepressant prescriptions by clinicians as a treatment for severe depression or related issues, rather than being relied on as a 'coping mechanism' for minor anxiety problems, could have a positive impact on sectors like education.

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Net Neutrality or Net Neutering – How Controlling the Internet Comes with a Price

By Jacob Brill

Abstract

This article explores controversial topics in the net neutrality debate raising critical questions about the role of government in regulating Internet Service Providers (ISPs) to ensure a free and open internet. Most people agree that internet service providers (ISPs) shouldn't be allowed to slow down certain websites, block access to content, or give faster speeds to those who pay extra. But figuring out how to enforce these rules has sparked plenty of debate. This paper takes a closer look at how net neutrality has evolved in the United States, focusing on the Federal Communications Commission's (FCC) shifting policies, the role of politics, and the impact on everyday internet users and ISPs. Moments like the 2008 Comcast case and the FCC's Open Internet Order highlight just how tough it is to navigate the legal and political challenges. Ultimately, the paper argues that Congress needs to step in with straightforward, fair legislation to require transparency and stop unfair ISP practices. By locking in basic protections while allowing space for new technology to grow, Congress could cut through the gridlock, rebuild trust in how the internet is managed, and make sure it stays open and innovative for everyone.

Almost all internet users and other stakeholders instinctively support the concept of "net neutrality" under which Internet service providers (ISPs) must provide access to online content and services without blocking or throttling traffic or engaging in other discriminatory practices. Hardly anyone thinks it would be reasonable for ISPs to prevent consumers from visiting the websites of their choosing or to give preferential treatment to particular companies (such as favoring Netflix over Hulu). But there has been a long-simmering debate over what role the government should play in ensuring adherence to those consensus principles. Should the Federal Communications Commission (FCC) regulate ISPs as "common carriers" under a utility model of regulation under Title II of the Communications Act of 1934 to safeguard net neutrality, or should it apply "light touch" regulation under Title I of that statute and rely on market forces to prevent abusive practices? (Kimball 5-8; Stiegler 11-13) Consumer advocates have emphasized that the internet is too important to leave unregulated. In contrast, ISPs have argued that, while they do not object to net neutrality mandates in particular, the FCC's imposition of a common carrier framework would result in vast overregulation that undermines ISPs' incentives to build faster and more extensive broadband networks and to continue innovating. For two decades, industry participants, consumer groups, academics, and others have grappled with these contrasting perspectives, and the FCC has flip-flopped with changes in political leadership. To ensure practical net neutrality rules without constant back and forth regulation that ISPs or consumers fear, Congress should enact *transparent* legislation that fosters innovation and leads to clarity and the FCC and policymakers must strive to discourse the debate from its politically divisive past.

Transparency is not just a foundational principle but a dynamic mechanism for effective net neutrality regulation. Through mandating that ISPs openly disclose their network

management practices, Congress can empower consumers and policymakers with critical information while avoiding overregulation that might stifle innovation. But to fully understand this regulatory challenge, it is essential to examine the FCC's evolving approaches to net neutrality and the legal classifications shaping its authority. (Marsden 36)

Due to the complex interplay of economic, political, and legal factors at stake in this debate, principle net neutrality concepts are often quite arcane. John Eggerton, a reporter focused on media regulation noted, “[t]here are multiple layers to the debate — political, technical and legal — with politics threatening to trump the other two facets.” (Eggerton 16) The history of net neutrality dates back to the early 2000s. Early calls for FCC intervention led to a landmark speech by Chairman Michael Powell in 2004, identifying “Four Internet Freedoms” relating to choice and competition. The FCC then issued a 2005 Policy Statement setting forth early net neutrality principles. At that point, the FCC had treated internet access as an “information service” under the Telecommunications Act of 1996, and the classification was not controversial. (Marsden 29-30) It was a 1998 Report to Congress written during the Clinton administration that treated internet access as an information service, and Republican administrations (including under Chairman Powell) agreed that the information service classification was appropriate as a legal and policy matter. The Supreme Court ultimately upheld that classification in a case called “Brand X,” in 2005. This legal battle over the classification of broadband was critical because it determined what power the FCC could exercise: Under the information service classification, the FCC had limited authority to impose net neutrality mandates or other rules, but if the agency classified internet access as a “telecommunications service,” that would mean ISPs would be regulated much more extensively as common carriers. (Kimball 45-47) Reflecting on this, Sona Sotomayor, a telecommunications lawyer, noted, “Brand X as I understood it was a question of which government agency would regulate. ... We’re talking about Congress’s interpretation and Congress’s ability to alter the court’s understanding by altering the statute if it chooses.” (“Sotomayor Says Congress Must Set Net Neutrality Policy” 16) Even towards the beginning of the net neutrality debate during the Brand X case, congress’ loose legislation has created unnecessary confusion on how to enforce certain regulations. But supporters of these contrasting legal approaches began to agree that, regardless of how internet access was classified, some form of government oversight with a focus on transparency was appropriate to ensure that net neutrality principles would be preserved. During the early years of the net neutrality debate (2000-2009), the FCC was under republican control and over time the democratic party formed different views in which they’d later strive to enforce leading to politically divided orders and rules.

At a minimum, most advocates and stakeholders agreed that the FCC should require ISPs to disclose what practices they employed, so if they blocked or throttled traffic, consumers and policymakers would not be left in the dark but the problem continues that the FCC struggles in enforcing rules as Congress fails to provide strong legislation for the FCC to rely on. One of the most pivotal moments underscoring the need for such “transparency” came in August 2008, when the FCC issued its “Comcast Order.” That order found that Comcast had violated net

neutrality principles by blocking BitTorrent and P2P file-sharing applications. Comcast's interference with BitTorrent traffic spurred a public backlash leading to more of a political illusion and illuminated the potential for ISPs to misuse their power as gatekeepers of internet access. (Marsden 30) But the court of appeals held that the FCC could not punish Comcast because it had not put binding rules in place. It was a very controversial case in the debate timeline as ISPs found the FCC to be overstepping their jurisdiction. Tim Doyle, an author in net neutrality, notes FCC Commissioner Robert McDowell, ““McDowell doubted the commission’s ability to continue to set precedent in regulating the Internet. The commissioner noted that the FCC cannot make the instantaneous decisions necessary to regulate the Internet.”” (Doyle) When Comcast blocked BitTorrent traffic, it "spurred a public backlash and illuminated the potential for ISPs to misuse their power" (Marsden 31). Without mandatory disclosure, such practices would remain undetected, undermining consumer trust.

Scholars argue that transparency alone can deter ISPs from engaging in discriminatory behavior. As Kimball observes, “Transparency rules empower consumers to hold ISPs accountable, reducing the need for stricter regulations – [which are unnecessary.]” (Kimball 48) Paul Kirby, a senior editor of Wolters Kluwer’s Daily, cited a discussion from Frannie Wellings, telecom counsel to Sen. Byron L. Dorgan, describing her viewpoint on the senators’ stand against transparent litigation, “[w]hile my boss is appreciative of developments in the issue [toward consensus], he still feels that legislation is necessary. She also said that a “fifth principle”, added to the FCC’s existing four broadband principles, to bar unreasonable discrimination “or something similar” is needed.” (Kirby 8) Senator Dorgan notes that he not only sees a need for more legislation by congress but also feels that the existing foundational principles don’t fully address net neutrality issues such as unreasonable discrimination hinting that maybe the FCC’s current legislation isn’t transparent either. With the relatively simple fix of enacting stronger legislation, Kimball and Senator Dorgan agree that by codifying transparency requirements, Congress can strike a balance, bringing accountability while avoiding the heavy-handed regulation ISPs fear.

The FCC’s repeated attempts to regulate net neutrality reveal just how deeply the issue has become politicized, with each administration’s approach reflecting its partisan priorities. In 2010, under President Obama, the FCC issued the Open Internet Order, which sought to prevent ISPs from blocking or discriminating against lawful online content. However, the Order relied on a contested interpretation of Section 706 of the Telecommunications Act of 1996, leading to skepticism about its legal viability. John Eggerton noted that “two out of three [judges] appeared to have problems with the nondiscrimination portion of the FCC’s order,” as it effectively treated ISPs as common carriers while maintaining their classification as information service providers. (Eggerton 14) Predictably, the appellate court invalidated the Order, marking an early example of how unresolved legal ambiguities allowed political ideology to shape the FCC’s actions. According to Robert Zelnick, a political journalist, “[t]raditionally the Internet’s tradition of self-governance stems from the philosophies of many of its founding fathers, that this new frontier should remain free and unfettered by government intrusion. One of the most famous

rallying cries for Internet autonomy came from cyber-libertarian and former Grateful Dead lyricist John Perry Barlow.” (Zelnick 135) The public picked sides quickly whether they respected Barlow or the newly appointed FCC chairman every new presidency and throughout the following years, regulation changes highlighted the regressive effect that politics has had on the net neutrality debate.

The political landscape shifted dramatically with each new administration, turning net neutrality into a symbol of broader ideological conflicts rather than a straightforward policy issue. Robert Zelnick describes this phenomenon as a mix of “political illusion” and “alarmism.” Under President Obama, Democrats championed net neutrality as vital for protecting a free and open internet, positioning it as a safeguard against the unchecked power of ISPs. Republicans, led by President Trump’s administration, viewed these regulations as excessive government interference that stifled market innovation. Ajit Pai, Trump’s FCC chairman, spearheaded the 2017 Restoring Internet Freedom Order, which rolled back the 2015 rules by shifting ISPs back to Title I classification and adopting a light-touch regulatory approach. Conservatives praised this as a victory for internet freedom, while Democrats and consumer advocates condemned it as prioritizing corporate interests over consumers. This ongoing political back-and-forth deepened divisions, turning discussions into partisan soundbites rather than productive conversations. The cycle of reversals has left consumers confused and eroded trust, underscoring the need for Congressional action to establish lasting clarity.

The stakes grew even higher when Republican Chairman Ajit Pai took control of the FCC during the Trump administration. In 2017, Pai’s Restoring Internet Freedom Order dismantled the 2015 rules, arguing that deregulation would encourage investment and innovation, a sentiment embraced by many Republican policymakers. The policy shift, upheld by the D.C. Circuit, highlighted how net neutrality had become a political tug-of-war, leaving consumers uncertain about the future of internet governance. As Robert Zelnick aptly observed, the debate had devolved into a partisan “political grab bag” rather than a thoughtful discussion focused on preserving the internet’s vitality (Zelnick viii).

Zelnick’s critique of the regulatory back-and-forth has its roots in a statute that does not expressly determine the classification of broadband or the extent to which (if at all) net neutrality should be required by the FCC, or left to the marketplace. Given that net neutrality has widespread support and appears vital to the continued vibrancy of the internet, Congress must step in to resolve the lingering uncertainty about the FCC’s role and give them the stature to rely on. Much of the fighting over arcane classification issues could have been avoided if Congress originally specified the ground rules itself rather than relying on an administrative agency to decide the core questions without clear guidance from the legislature. While Congress has stepped in minimally throughout the past decade, at this juncture, Congress needs to specifically enact a statute that preserves transparency and prohibits blocking, throttling, or paid prioritization of internet traffic. This way cases such as the Comcast 2008 case, can be limited because ISPs are forced to be held more accountable as congress legislation is clear for them to follow and at the same time the FCC can’t “overstep” their power. Some argue that Congress

should refrain from legislating net neutrality, suggesting that rigid laws might struggle to keep pace with the rapid evolution of technology and could unintentionally hinder innovation in the internet sector. They also claim that competition within the market is a more effective way to ensure fair practices without government overreach. Yet, relying on market forces alone has proven ineffective, as ISPs have a history of engaging in practices like throttling and prioritizing paid content. A thoughtfully designed law, paired with periodic reviews is needed to address these concerns by allowing for flexibility and adaptation to consistent technological advancements. Furthermore, politics reflects a great deal of tension in the net neutrality debate. The politicization of net neutrality underscores a deeper issue though: the lack of stable, consistent regulation that prioritizes the public good over partisan agendas. Some argue that the back-and-forth between administrations reflects healthy democratic debate, but in reality, it has eroded trust and made the internet's future uncertain. Only clear, balanced legislation from Congress can cut through the gridlock, providing the strong net neutrality rules we need to protect consumers, encourage innovation, and keep the internet open and fair for everyone.

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Volatility and Return Spillovers in Global Banking By Aritro Chakravarty

Abstract

The study examines the interconnectedness and risk transmission mechanisms of major global financial institutions by examining volatility and return spillover. The study investigates the interdependencies and volatility spillovers of banks in the United States, the United Kingdom, France, Germany, Canada, Australia, Brazil, China, Japan, and India by utilizing daily return data from 10 prominent global banks, spanning the years 2009–2024. The Granger causality tests suggest a causal relationship between numerous pairs of financial institutions. The results suggest a substantial presence of volatility spillovers, notably among banks in the United States, the United Kingdom, and Canada. The findings emphasize the need for global risk management strategies.

Keywords Volatility, return, spillover, world banks

Introduction

In the current interconnected global economy, financial institutions, notably those in the banking sector, are encountering an increasing number of cross-border risks. The importance of understanding cross-border volatility and return spillovers has been emphasized by a number of financial crises in recent decades. These spillovers not only reflect the interconnectedness of global financial markets, but they also serve as a means for risk transmission.

These spillovers show how connected the world's financial markets are, and they also help move risk from one market to another. The aim of this study is to shed light on the trends and factors that affect how volatility moves through the international banking system by examining the relationship between banks from the USA, US, UK, France, Germany, Canada, Australia, Brazil, China, Japan, and India.

Policymakers, investors, and financial regulators need to understand this dynamic in order to improve financial stability.

This study contributes to existing literature by focusing on interdependencies among global banks over the period from 2009-2024, covering the recovery from the global financial crisis, various market challenges, and the effect of the COVID-19 pandemic. Specifically, the study highlights the role of Granger causality in identifying predictive relationships and spillover effects, offering insights into how past volatilities in one market can influence others. The results of this study have an important effect on risk management and hedging strategies. This research provides valuable guidance for the development of strategies to strengthen the global banking system and navigate future crises by emphasizing the interconnectedness of major financial institutions.

This topic is crucial as it allows us to recognize systemic risks in global banking stemming from our interconnectivity. We have examined the cross-border effects of ten of the biggest international banks. The results

have shown that there are strong links between international banking systems. identifying these links could help policymakers or investors to develop better risk management tools. The primary objective of this research is to analyze cross-border risk in global banking and highlight interdependencies to inform policy and enhance financial stability. This paper proceeds as follows: Section 2 provides information on the existing literature, Section 3 highlights the empirical findings, and Section 4 concludes the paper.

Literature Review

The volatility spillover in financial markets has been extensively examined, yielding insights into systemic risks and market dynamics across many countries and institutions. Elyasani et al. (2015) investigated volatility spillovers within banking sectors amid the global financial crisis. It was agreed that US banks played a big role in spreading volatility. Whether Japanese banks stayed closed off. Their findings further underscore the interdependencies between the banking and insurance sectors. Corsetti et al. (2005) examined the Asian financial crisis, highlighting volatility spillover across regions. Forbes and Rigobon (2002) contended that market independence during crises is called as contagion. Aloui et al. (2011) examined the influence of oil price volatility on stock returns in both established and emerging markets. Between 2005 and 2010, it was acknowledged that oil price volatility had a substantial impact on developed markets. Guo et al. (2021) emphasized the influence of geopolitical factors on the COVID-19 pandemic, demonstrating significant volatility contagion between the United States and China. Syllignakis and Kouretis (2011) identified a notable link between CDS spreads and stock returns in emerging European markets during the financial crisis. In order to assess volatility contagion among global markets, Diebold and Yilmaz (2009) implemented a variance decomposition approach. They underscored the dynamic nature of global interconnectedness. The function of universal bank lenders during financial crises was examined by Van Rijckeghem and Weder (2003). Although the impacts were less pronounced during the Mexican and Russian crises, significant volatility transmission was observed during the Thai financial crisis. Subburayan (2023) investigated the volatility spillover between the BSABankex index and the stock prices of Indian banks. They emphasized significant causal relationships, particularly for ICICI and Kotak, from 2018 to 2023. De Bruyckere et al. (2013) demonstrated that there were substantial spillover effects between sovereign entities and institutions in Europe during the financial crisis. Betz et al. (2016) developed a quantile-based methodology to assess systematic risk in European institutions and sovereign entities. This methodology demonstrated an increase in risk during the sovereign debt crisis. In order to examine the volatility contagion from the US equities market to the Japanese and six Pacific-Basin markets, Ng (2000) employed ARCH models. Choudhry and Jayasekera (2014) conducted an investigation into the spillover effects within the banking sector during the global financial crisis. The findings suggest that the contagion dynamics have shifted from minor to larger economies during the crisis. Wang et al. (2018) carried out an investigation into the volatility spillovers in the Chinese banking system, which emphasized the interdependence of banks during the crisis. Jiang et al. (2012) investigated

the impact of volatility contagion in stock markets on news announcements from the United States and Europe. Scheduled news was proven to diminish volatility. Yang and Zhou (2017) showed global volatility spillovers to the United States. Wang et al. (2021) examined the interconnections of returns and volatility among Chinese financial organizations. They underscored the significance of small to medium-sized banks in managing systemic risk. Rehman and Vo (2023) looked at how integrated big global banks are. Significant integration was observed between Citibank and Deutsche Bank, including diversification potential between Citibank and HSBC.

Empirical Evidence

Data

We drove the data from Google Finance for selected individual banks such as JPMorgan Chase & Co for USA, BNP Paribas SA for France, HSBC Holdings plc for UK, Commonwealth Bank of Australia for Australia, Itau Unibanco Holding SA ADR for Brazil, Royal Bank of Canada for Canada, Deutsche Bank AG for Germany, Industrial & Commercial Bank of China Ltd for China, Mitsubishi UFJ Financial Group Inc for Japan, State Bank of India for India covering daily frequency for selected period from 1 Apr 2009 to 18 Oct 2024.

Descriptive Statistic

The price, return, and volatility of individual banks are presented in figure 1, figure 2, and figure 3 respectively.

Figure 1. Price Data for World Bank

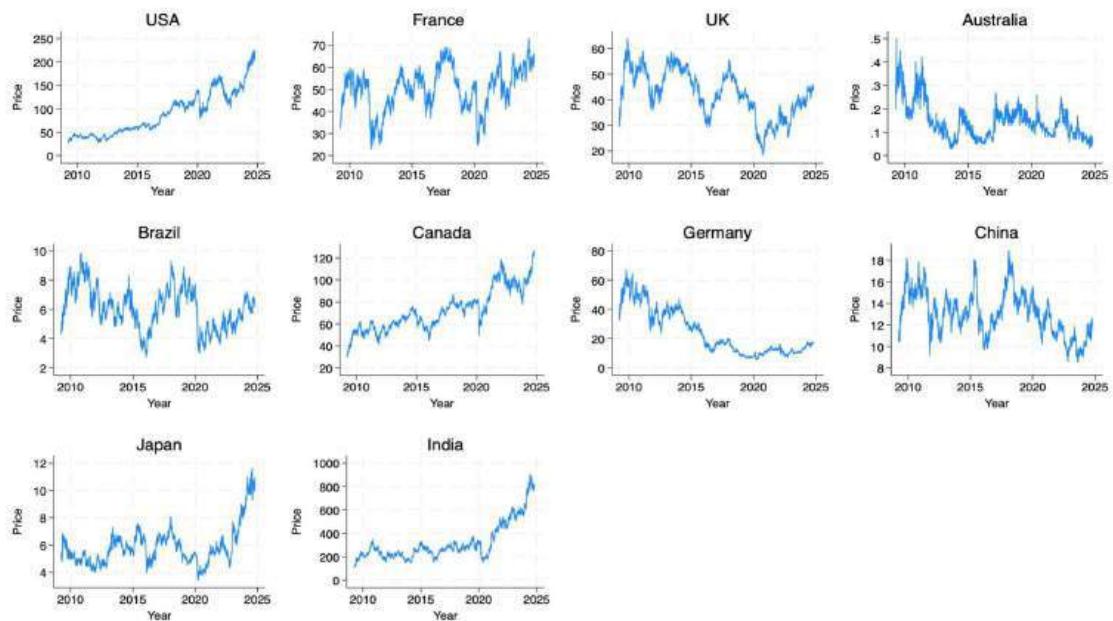


Figure 2. Return Data for World Bank

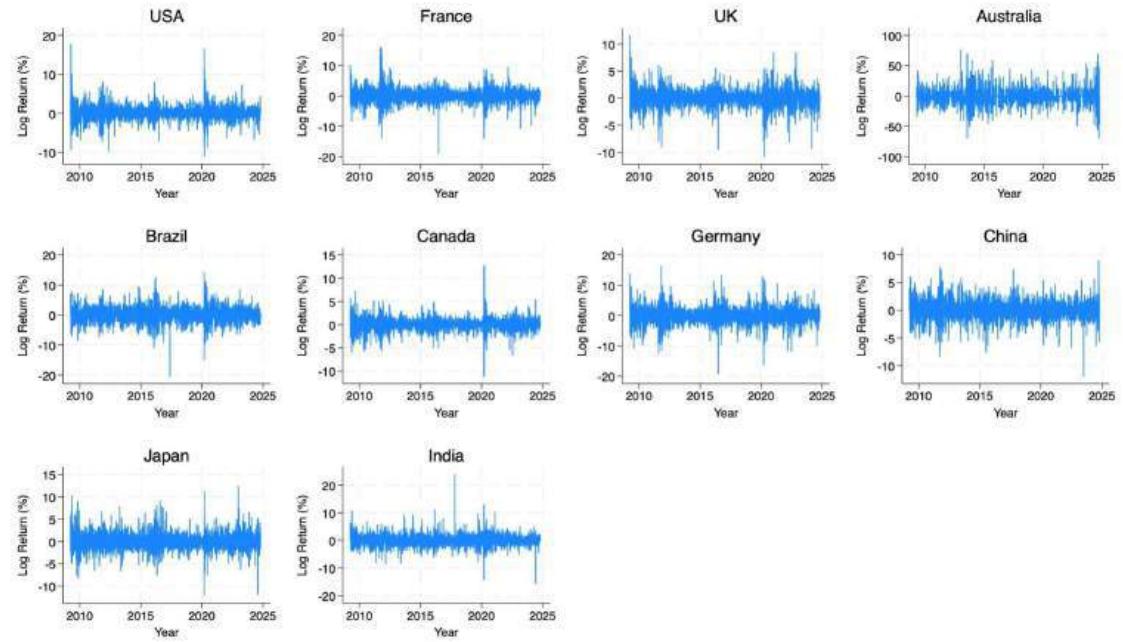


Figure 3. Volatility Data for World Bank

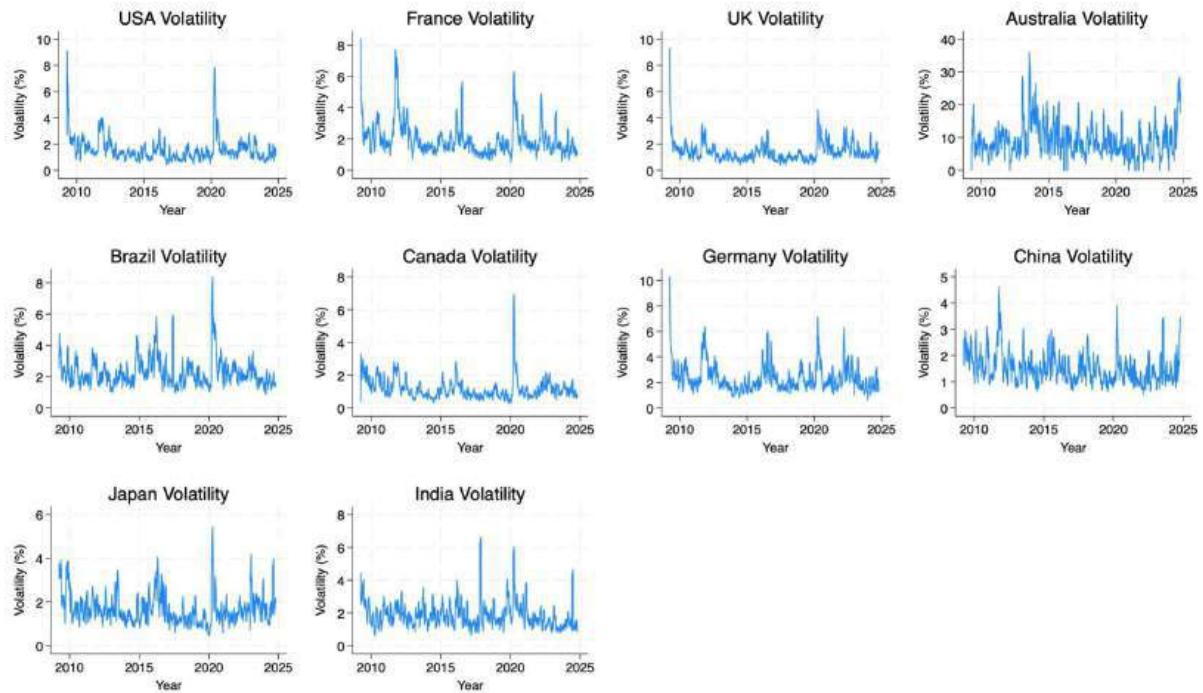


Table 1. Descriptive Statistics

Variable	Obs	Mean	Std. Dev.	Min	Max
USA log return	5642	.0359	1.3337	-11.1232	17.7266
France log return	5642	.0343	1.6313	-19.1166	15.9031
UK log return	5642	.0174	1.1535	-10.8101	11.571
Australia log return	5642	-.0444	7.6559	-69.3147	76.214
Brazil log return	5642	.0331	1.8209	-20.3739	14.2083
Canada log return	5642	.0206	1.0026	-11.1272	12.7567
Germany log return	5642	.0064	1.9072	-19.2333	16.2562
China log return	5642	.0023	1.2152	-11.9103	8.9412
Japan log return	5642	.0102	1.3449	-12.1439	12.3572
India log return	5642	.0347	1.5037	-15.5532	23.8393

This table provides descriptive statistics for many different banks from all over the world. The log return of USA has 5642 observations with a mean of .0359 and a standard deviation of 1.3337, ranging from a minimum of -11.1232 to a maximum of 17.7266.

The log return of France has 5642 observations with a mean of .0343 and a standard deviation of 1.6313, ranging from a minimum of -19.1166 to a maximum of 15.9031.

The log return of UK has 5642 observations with a mean of .0174 and a standard deviation of 1.1535, ranging from a minimum of -10.8101 to a maximum of 11.571.

The log return of Australia has 5642 observations with a mean of -.0444 and a standard deviation of 7.6559, ranging from a minimum of -69.3147 to a maximum of 76.214.

The log return of Brazil has 5642 observations with a mean of .0331 and a standard deviation of 1.8209, ranging from a minimum of -20.3739 to a maximum of 14.2083.

The log return of Canada has 5642 observations with a mean of 0.0206 and a standard deviation of 1.0026, ranging from a minimum of -11.1272 to a maximum of 12.7567

The log return of Germany has 5642 observations with a mean of .0064 and a standard deviation of 1.9072, ranging from a minimum of -19.2333 to a maximum of 16.2562.

The log return of China has 5642 observations with a mean of .0023 and a standard deviation of 1.2152, ranging from a minimum of -11.9103 to a maximum of 8.9412

The log return of Japan has 5642 observations with a mean of .0102 and a standard deviation of 1.3449, ranging from a minimum of -12.1439 to a maximum of 12.3572

The log return of India has 5642 observations with a mean of .0347 and a standard deviation of 1.5037, ranging from a minimum of -15.5532 to a maximum of 23.8393

Table 2. Descriptive Statistics for Volatility

Variable	Obs	Mean	Std. Dev.	Min	Max
USA volatility	3913	1.595	.919	.3865	9.0904
France volatility	3913	1.9796	1.0448	1.0448	8.3962
UK volatility	3913	1.4249	.7131	.3657	9.3006
Australia volatility	3913	9.2706	5.0977	0	36.0214
Brazil volatility	3913	2.2987	.9054	.8703	8.3754
Canada volatility	3913	1.1945	.6545	.293	6.9455
Germany volatility	3913	2.387	1.0549	.6265	10.2808
China volatility	3913	1.5401	.5883	.5071	4.6256
Japan volatility	3913	1.7001	.6779	.4847	5.4343
India volatility	3913	1.8822	.7708	.6466	6.6181

The volatility of USA has 3913 observations with a mean of 1.595 and a standard deviation of .919, ranging from a minimum of .3865 to a maximum of 9.0904

The volatility of France has 3913 observations with a mean of 1.9796 and a standard deviation of 1.0448, ranging from a minimum of 1.0448 to a maximum of 8.3962

The volatility of UK has 3913 observations with a mean of 1.4249 and a standard deviation of .7131, ranging from a minimum of .3657 to a maximum of 9.3006

The volatility of Australia has 3913 observations with a mean of 9.2706 and a standard deviation of 5.0977, ranging from a minimum of 0 to a maximum of 36.0214

The volatility of Brazil has 3913 observations with a mean of 2.2987 and a standard deviation of .9054, ranging from a minimum of .8703 to a maximum of 8.374

The volatility of Canada has 3913 observations with a mean of 1.1945 and a standard deviation of .6545, ranging from a minimum of .293 to a maximum of 6.9455

The volatility of Germany has 3913 observations with a mean of 2.387 and a standard deviation of 1.0549, ranging from a minimum of .6265 to a maximum of 10.2808

The volatility of China has 3913 observations with a mean of 1.5401 and a standard deviation of .5883, ranging from a minimum of .5071 to a maximum of 4.6256

The volatility of Japan has 3913 observations with a mean of 1.7001 and a standard deviation of .6779, ranging from a minimum of .4847 to a maximum of 5.4343

The volatility of India has 3913 observations with a mean of 1.8822 and a standard deviation of .7708, ranging from a minimum of .6466 to a maximum of 6.6181

Findings

Table 3. Granger causality Wald test

Equation	Excluded	chi2	df	Prob>Chi2
USA_volatility	France_volatility	2.432	2.432	2.432
	UK_volatility	33.092	2	0.000
	Australia_volatility	2.682	2	0.262
	Brazil_volatility	0.895	2	0.639
	Canada_volatility	15.910	2	0.000
	Germany_volatility	17.678	2	0.000
	China_volatility	3.625	2	0.163
	Japan_volatility	19.688	2	0.000
	India_volatility	3.667	2	0.160
France_volatility	USA_volatility	0.160	2	0.923
	UK_volatility	18.675	2	0.000
	Australia_volatility	0.627	2	0.731
	Brazil_volatility	1.902	2	0.386
	Canada_volatility	11.441	2	0.003
	Germany_volatility	4.677	2	0.096
	China_volatility	5.492	2	0.064
	Japan_volatility	3.128	2	0.209
	India_volatility	1.548	2	0.461
UK_volatility	USA_volatility	3.982	2	0.137
	France_volatility	4.106	2	0.128

	Australia_volatility	2.055	2	0.358
	Brazil_volatility	0.418	2	0.811
	Canada_volatility	15.005	2	0.001
	Germany_volatility	4.936	2	0.085
	China_volatility	0.459	2	0.795
	Japan_volatility	8.454	2	0.015
	India_volatility	3.272	2	0.195
Australia_volat~y	USA_volatility	7.763	2	0.021
	France_volatility	3.709	2	0.157
	UK_volatility	1.057	2	0.590
	Brazil_volatility	2.861	2	0.239
	Canada_volatility	1.536	2	0.464
	Germany_volatility	0.279	2	0.870
	China_volatility	4.271	2	0.118
	Japan_volatility	5.249	2	0.072
	India_volatility	1.257	2	0.533
Brazil_volatility	USA_volatility	0.272	2	0.873
	France_volatility	7.369	2	0.025
	UK_volatility	4.875	2	0.087
	France_volatility	7.369	2	0.025
	UK_volatility	4.875	2	0.087
	Australia_volatility	0.009	2	0.995
	Canada_volatility	0.274	2	0.872
	Germany_volatility	2.582	2	0.275
	China_volatility	4.867	2	0.088
	Japan_volatility	6.986	2	0.030

	India_volatility	5.488	2	0.064
Canada_volatility	USA_volatility	4.026	2	0.134
	France_volatility	7.411	2	0.025
	UK_volatility	0.010	2	0.995
	Australia_volatility	3.190	2	0.203
	Brazil_volatility	9.478	2	0.009
	Germany_volatility	0.315	2	0.854
	China_volatility	9.618	2	0.008
	Japan_volatility	10.962	2	0.004
	India_volatility	3.272	2	0.195
Germany_volatile~y	USA_volatility	0.338	2	0.844
	France_volatility	4.941	2	0.085
	UK_volatility	23.022	2	0.000
	Australia_volatility	0.738	2	0.691
	Brazil_volatility	7.989	2	0.018
	Canada_volatility	9.262	2	0.010
	China_volatility	2.267	2	0.322
	Japan_volatility	2.428	2	0.297
	India_volatility	0.876	2	0.645
China_volatility	USA_volatility	10.342	2	0.006
	France_volatility	7.888	2	0.019
	UK_volatility	0.064	2	0.968
	Australia_volatility	1.006	2	0.605
	Brazil_volatility	0.163	2	0.922
	Canada_volatility	3.891	2	0.143
	Germany_volatility	2.719	2	0.257

	Japan_volatility	1.599	2	0.450
	India_volatility	3.416	2	0.181
Japan_volatility	USA_volatility	4.287	2	0.117
	France_volatility	8.815	2	0.012
	UK_volatility	1.449	2	0.485
	Australia_volatility	0.278	2	0.870
	Brazil_volatility	9.343	2	0.009
	Canada_volatility	5.008	2	0.082
	Germany_volatility	4.752	2	0.093
	China_volatility	3.907	2	0.142
	India_volatility	5.242	2	0.073
India_volatility	USA_volatility	12.713	2	0.002
	France_volatility	0.385	2	0.825
	UK_volatility	0.982	2	0.612
	Australia_volatility	4.167	2	0.124
	Brazil_volatility	6.052	2	0.049
	Canada_volatility	1.791	2	0.408
	Germany_volatility	3.170	2	0.205
	China_volatility	0.597	2	0.742
	Japan_volatility	5.626	2	0.060

Table 3 present Granger Causality Tests examine the causal relationship between the volatility of individual banks for ten different countries. Since the p value is lower than 0.10, we reject the null hypothesis. If there is a significant volatility spillover between 2 banks, the corresponding p value is highlighted in bold. For example, there is a significant causal relationship between the volatility of the USA and the volatility of the UK with a p value of 0.000. This means volatility of UK causes volatility of USA, suggesting that the past values of volatility of UK can help predict volatility of USA. This relationship suggests that the volatility of these 2 markets is connected.

Conclusion

This study examines the interdependencies among the world's largest financial institutions. Volatility spillovers affect banks in both developed and developing countries. The results indicate significant connections between banks in the US, UK, and Canada. The historical volatility of one bank can be utilized to predict the future volatility of another, as demonstrated by the Granger Causality Test. These results show that risk management methods need to think about how risks might spread across borders and financial institutions. This has big implications for policymakers and investors.

These results are crucial because they show that risk management strategies for both policymakers and investors should take into account how effects might spread across borders and financial institutions. Policymakers should focus on building strong structures to track and reduce spillover effects, which will help maintain global financial stability. In a world that is becoming more connected, investors can make better decisions about how to diversify their portfolios and handle risk factors.

Future studies may explore sector-specific or regional spillovers, further enhancing our understanding of the complexities of global financial markets.

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Have Anti-Racism Movements Reduced Racism? By Danny Chu

Introduction

“I have a dream today. I have a dream that one day this nation will rise up and live out the true meaning of its creed; We hold these truths to be self-evident: that all men are created equal”. Sixty years ago, Dr. Martin Luther King Jr. delivered the famous speech “I Have a Dream” to fight against racism. In the past years, various anti-racism movements including the civil rights movement, the Anti-Apartheid Movement, and Black Lives Matter vigorously fought against racism. Have these anti-racism movements reduced racism?

Racism can be traced back to anti-Jewish racism in the 3rd century BCE, developing in European imperialism and the slave trade. In the 19th and 20th centuries, there was racial segregation in the United States and apartheid in South Africa. In recent years, it has become harder to ascertain modern racism which may be in the forms of implicit, subconscious, or unconscious racial discrimination.

In the history of fighting against racism, anti-racism movements have improved to reduce racism, but the contemporary anti-racism movements have made racism more complicated. More deliberate resolutions of anti-racism to reduce racism shall be explored in the future.

Early Movements of Anti-Racism

The early movements of anti-racism in history had an undeniable impact on reducing racism. The origin of anti-racism was spread from Europe to America after the discovery of the New World with the new humane values to criticize the colonists’ “cruelty and tyranny” in dealing with indigenous people such as American natives and slaves. (Pagden, 1992). The further anti-racism has won the abolitionist movement in England, the United States and throughout the world with the belief in freedom and equality for all people. However, racial discrimination such as racial segregation and supremacism still existed in the 20th century. Can you imagine that certain people are forbidden to go to the same restaurant, and children are not allowed to go to the same school only because of their skin color? Can you believe that people could be arrested for refusing to give up their seats on buses only because of their race? In the 1960s, numerous civil rights movements successfully fought for desegregation, labor rights, right to vote and other civil liberties. Racial segregation was outlawed in the Civil Rights Act of 1964 in the United States. In 1950 the European Convention on Human Rights was adopted, which was widely used on racial discrimination issues. (European Court of Human Rights, 2011). The United Nations adopted the definition of racial discrimination in the “International Convention on the Elimination of All Forms of Racial Discrimination” in 1966. (Office of the High Commissioner for Human Rights, 1965).

Development of Anti-Racism Movements

With the development of anti-racism movements in the contemporary period, the impact of reducing racism has become more complicated and acknowledged. Although anti-racism

movements promoted great impact in extensive aspects in legislation, employment and education, earlier violent and aggressive forms of racism have evolved into more complicated forms of prejudice in the contemporary era, which makes it more difficult to obtain satisfactory resolutions against racism. In 2014, Eric Garner, an African American suspected for committing a crime, was killed in New York City after a New York City Police Department Officer put him in a banned chokehold while arresting him. (Williams, 2015). Thereafter, Ezell Ford was shot and killed by the Los Angeles Police Department officers, then Akai Gurley, Tamir Rice, Michael Brown, Freddie Gray, George Floyd ... all these African American were killed by police officers. Black Lives Matter Movement brought a surge of protests, rallies and mass mobilization and renewed the anti-racism protests in the United States and later spread globally. Although the primary concerns of the Black Lives Matter movement are police brutality and racially motivated violence against black people, such movement also increased the concerns and acknowledgement of race conflicts. In 2014, two New York Police Department officers Rafael Ramos and Wenjian Liu were shot and killed in Brooklyn, New York. In 2016, Micah Xavier Johnson, a 25-year-old veteran, shot and killed five Dallas Police Department officers because he was angry over police shootings of black men. Following this, Blue Lives Matter became a countermovement in the United States supporting law enforcement officers and advocating that those who are prosecuted and convicted of killing law enforcement officers should be sentenced under hate crime statutes. (Duignan, 2020). Meanwhile, in response to Black Live Matter, other activist groups created "White Lives Matter" and "All Lives Matter" with the belief that we are all human beings and all lives shall be treated equally. At this point, it has become challenging to measure the direct effect on reducing racism by the anti-racism movements.

Complication of Contemporary Racism and Anti-Racism Movements

In order to further reduce racism, the complication of anti-racism shall be explored deliberately. While the core value of anti-racism movements is to pursue "equality" in race, it may cause a controversial effect depending on the ways to interpret "equality" – equality in opportunity or equality in outcome. In 2013, the litigation against Harvard University by Students for Fair Admission in the United States is a typical reflection about such contradictions. The lawsuit claimed that Harvard imposes a soft quota of "racial balancing" that artificially depresses the number of Asian-American applicants admitted to Harvard. (Hsu, 2018). Students for Fair Admission alleged that Asian American applicants have the lowest chance of admission of all racial groups in the United States, despite scoring highest in all objective measurements. (Arcidiacono, 2019). Although Harvard argued that its admission philosophy of considering race as one of many factors in its admissions policy complies with the law, the Court ruled that race-based admissions adopted by Harvard University were unconstitutional under the Equal Protection Clause of the Fourteenth Amendment of the Constitution. According to the majority opinion of the court, the use of race was not a compelling interest, and the means by which the school attempted to achieve diversity bore little or no relationship to the purported goals. (Baio, 2023). While the colleges try to reach equality in the result of diversity, the cost to sacrifice the

equality in opportunity of students of a certain race is not upheld by the majority of the judges and has not reduced racism either. If anti-racism movements focus too much on equality in outcome and disregard equality in opportunity, it is risky to depress the efforts of all races to work hard for equal opportunities and promote social progress. It may also lead to more bias and hidden racism.

Conclusion

The effectiveness of the anti-racism movement in reducing racism depends on various factors including legislation, justice system, economic development, education and cultural ideology. From this phenomenon, statistics may show a higher percentage of poverty and criminal rate in certain areas with habitations of certain races which caused racial discrimination. But in essence, the effective way to reduce racism is to break the race barrier and treat everybody as an individual, not a race. If the contemporary anti-racism movements focus on promoting the fight for equality of all individuals, it will get more support from all races and reduce racism more effectively. The complication of anti-racism movements needs the efforts and wisdom of all human race. The dream of Dr. Martin Luther King Jr. shall be continued and carried on: let us dream that one day every individual shall be treated equally, whether the color is white, black, yellow or brown; let every individual bloom in a free and equal life to make a beautiful and colorful world!

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Optimal Human Population By Kyle Li

Introduction

As a result of the industrial revolution, the global population has skyrocketed from 1 billion people in 1800 A.D. to over 8 billion people today.¹ Over this period, new technology paved the way for staggering economic growth and an increase in the global standard of living. However, the population growth that has come with this high production level has caused many societal problems. From an environmental standpoint, exponential population increase has contributed to issues like climate change, resource depletion, and pollution.² Socially, poverty has been on the rise, with more and more families falling into extreme poverty.³ The world is indeed overpopulated, but by how much?

Although a large human population isn't the sole cause of environmental and social issues, a large population only exacerbates problems. Given the fact that technological development is unlikely to significantly mitigate environmental pressure,⁴ the optimal population must prioritize environmental sustainability for future generations. While a smaller population does sacrifice total economic growth, it ensures environmental stability as well as improving global living standards. This essay argues that a population of 4 to 5 billion people will maximize these factors.

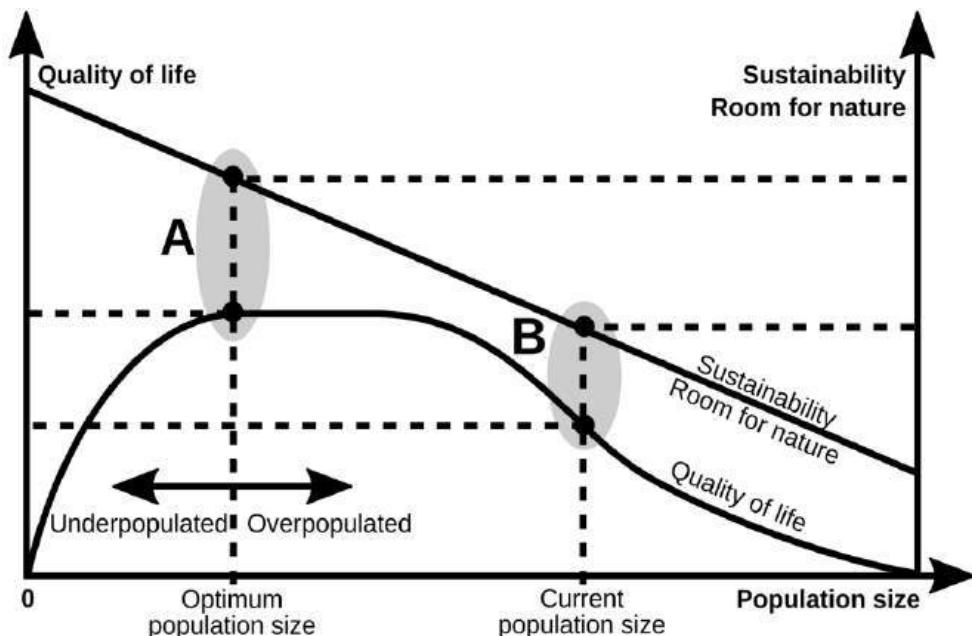


Figure 1: Relationship between population size, quality of life, and environmental sustainability⁵

Environmental Sustainability

As showcased by the graph, the growing global population negatively affects environmental health. With the level of production and consumption that is normalized today in

developed and developing countries, the planet cannot regenerate the resources that humans use each year.⁶ In many parts of the world, economic growth is taking precedence over environmental health. India, for example, contains 18% of the world's population but only 2.4% of the total land area on Earth. To support India's large population density, the use of chemicals and pesticides for agriculture has been increasing, which puts tremendous pressure on land.⁷ While this large population has spurred India's economy, which has the fifth largest GDP in the world,⁸ its GDP per capita is a mere 2,389 dollars, ranked 120th in the world.⁹ Energy demand has multiplied India's use of coal, from 32.2 million tons in 1950 to almost 1 billion metric tons in 2023.¹⁰ This is a trend that is not just present in India. In the United States, the second largest carbon emitter in the world, both population and consumption are growing. In 1970, the average American consumed 2054 calories daily. That number jumped to 2501 in 2010. American industry and transportation accounted for almost 3 billion metric tons of CO₂. Estimates reveal that humanity would need 5 Earths to sustain the population if everyone lived like the average American.¹¹ Humanity only has one Earth, and all humans deserve a good quality of life, so a smaller population is desperately needed to prevent sacrificing consumption patterns. As the U.S. population is expected to increase by another 70 million over the next 40 years, and as the global population is expected to rise to 10 billion in the next century,¹² the current population is not environmentally sustainable. Without a population change, global temperatures are estimated to rise 3 degrees Celsius by the end of the century, which would result in consequences like water scarcity, severe flooding, and rampant forest fires.¹³

Using carbon dioxide emissions as a measurement of environmental sustainability, the goal is to achieve net zero emissions. This is where the amount of carbon output equals the amount of carbon absorbed by trees, bodies of water, and other carbon sinks.¹⁴ Scientific consensus and the Paris Agreement state that in order to prevent global warming from exceeding 1.5 degrees since pre-industrial times, global emissions need to be reduced by 45% from 2010 levels by 2030 to achieve net zero by 2050.¹⁵ Given that the average worldwide carbon footprint is 4.7 tons per person,¹⁶ and that humans emitted 37.4 billion tons of CO₂ in 2023,¹⁷ a population of around 4.4 billion people would satisfy the Paris Agreement. To reach net zero immediately, the global population would need to be around 500 million, but this is assuming that population decline is the only way to cut CO₂ emissions.¹⁸

Ultimately, a global reduction in carbon emissions is not solely determined by population. An optimal global population can only supplement other factors like technological developments and government policies. Unfortunately, up until the 1990s, climate change policies have been practically nonexistent.¹⁹ By microeconomic laws, the social cost of emitting greenhouse gasses is far greater than the private cost of running a power plant, which causes a negative externality.²⁰ This means that too much of a product is produced for societal health, but the EU is making significant progress to close the gap between the marginal social cost and the marginal private cost of production. Some 20 European nations are implementing carbon taxes that put a much-needed price on mass greenhouse gas emissions.²¹ Policies like this are effective, as EU emissions in 2022 were 32.5% less than total emissions in 1990.²² Outside of Europe, countries

like New Zealand and the U.S. are experiencing a decline in emissions despite a growing population, which deflates the carbon footprint.²³ Additionally, some countries are moving towards renewable energy instead of fossil fuels. In 2020, renewable energy made up 29% of global electricity, and this number is rising.²⁴ Renewable energy grew a staggering 50% in just 2023, with China's wind turbine additions rising by 66%.²⁵ Uruguay alone uses 98% renewable energy.²⁶ As these trends inevitably continue, the world's carrying capacity will increase and could accommodate up to 5 billion people.

The environmental benefits of a smaller population are endless. A smaller market results in less total consumption and less greenhouse gas emission. Biodiversity will bloom and Earth will undergo reforestation. Sea levels will stabilize and forest fires will become less frequent. Air pollution and diseases will diminish, resulting in an overall healthier population.²⁷

Economic Growth

Generally, environmental damage and economic growth have a direct relationship.²⁸ Think of India, China, and every industrialized country in the world. All of these nations to some extent sacrificed environmental health for a booming economy, and a large workforce fueled this economic growth. But as developed nations are shifting towards knowledge economies, a large working class is not as important to economic growth anymore. In the long run, productivity is more important than population growth for economic growth.²⁹ Finland and Sweden, countries with high living standards that will soon experience population decline, are investing in education and innovation to bolster their economies. China's GDP will continue to rise despite reaching peak population.³⁰ Despite marginal population changes, these effects showcase that a population decline doesn't necessarily entail an economic collapse. A significant decrease in population to 4.5 billion will result in a smaller aggregate economy, as both supply and demand decrease, but the real GDP will rebound in the future. Eventually, long-run aggregate supply (LRAS), which represents full employment output, will shift to the right due to a rise in productivity rather than a boom in population.³¹

As the supply of laborers goes down, productivity becomes more important in companies. The decreased reliance on labor fosters innovation and technological advancements as companies need to find an alternative. Additionally, education opportunities will be more present because of higher wages and lower fertility rates, as parents invest more in fewer children. With the rise of human capital in a smaller population, the labor force participation rate should rise, stimulating economic growth.³² Following macroeconomic laws, an increase in productivity per worker and income per worker will shift aggregate demand (AD) and short-run aggregate supply (SRAS) to the right, indicating economic growth. This rise in productivity is not to say that the economy will not suffer from a large population plummet, as a population of 4 billion people will certainly have a smaller GDP than a population with 8 billion people. But as human capital becomes more widespread, innovation will not stall and economic growth will occur.

Standard of Living

Historically speaking, a rise in population has corresponded with a rise in living standards.³³ While a larger population ensures a larger aggregate economy, it is not the direct cause of the rise in living standards over the last 100 years. In developed countries, empirical data shows that greater population growth results in less GDP per capita growth.

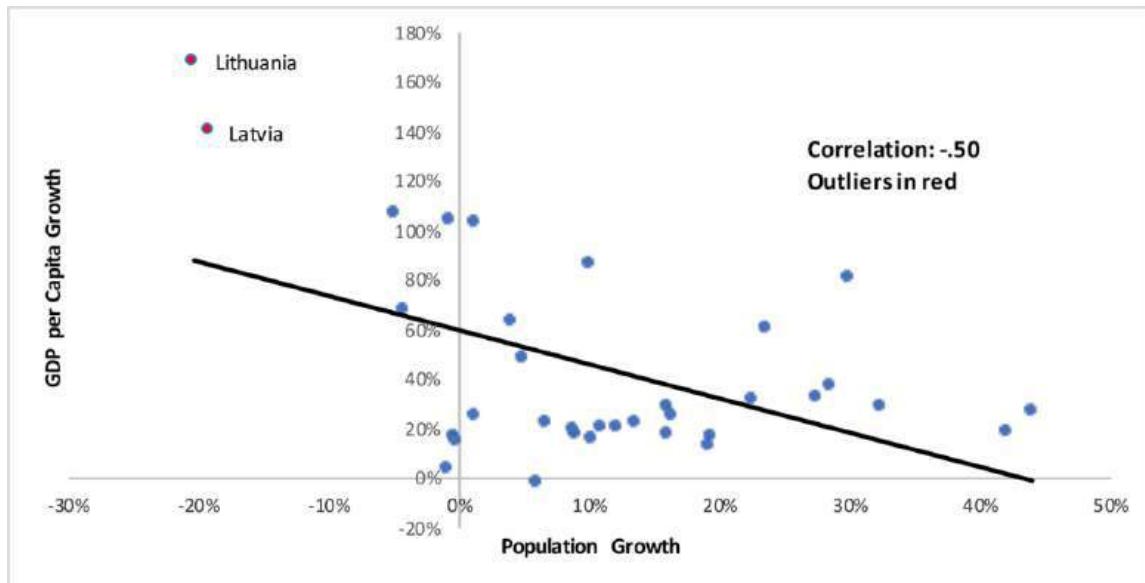


Figure 2: Higher population growth is correlated to lower GDP per capita growth in developed nations³⁴

The graph indicates that a population decline positively affects quality of life. Throughout history, it has been technological developments driven by human capital that have been driving up standards of living, not population growth.³⁵ Population growth was just a result of improved technology, and now that fertility rates are going down in high-income countries, the supply of labor is steadily decreasing. This results in higher wages where people have more disposable income, hence the rise in GDP per capita.³⁶ Despite only having an annual population growth rate of 0.76% from 1990-2015, China experienced an average annual GDP per capita growth rate of 8.72%.³⁷ More broadly, research shows that relatively low fertility rates support greater material standards of living.³⁸ On the contrary, countries with high fertility are struggling with extreme poverty and low living standards.

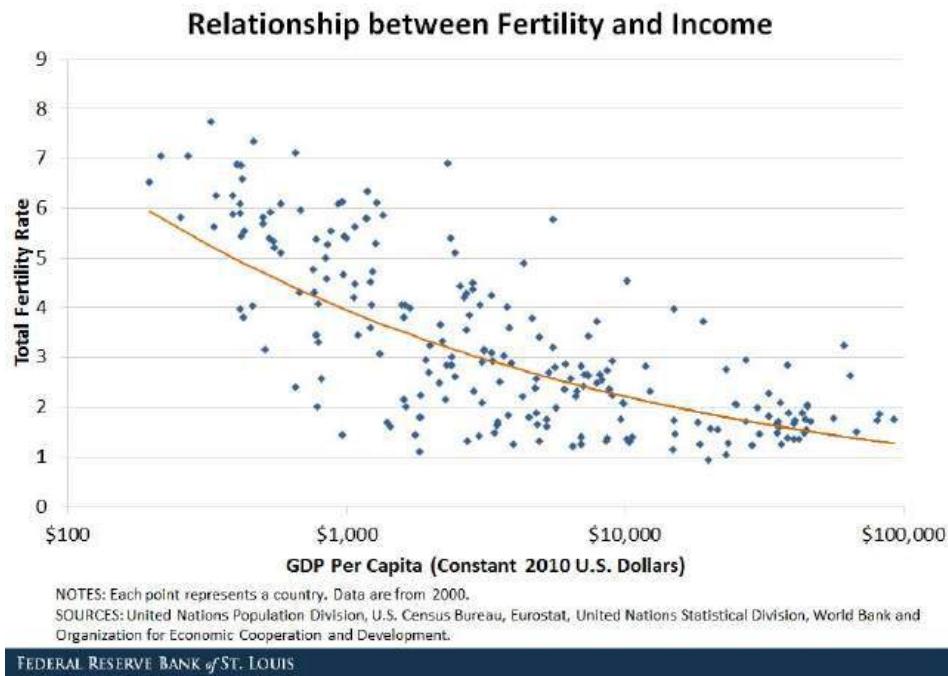


Figure 3: GDP per capita and fertility rates have an inverse relationship³⁹

Those nations with low GDP per capita and high fertility are generally least developed countries (LDCs), most of which are African nations.⁴⁰ Africa's average GDP per capita is around 2,000\$ USD⁴¹ while the world average is around 13,000\$,⁴² but the African population is expected to more than triple over this century.⁴³ Underdeveloped nations like those in Africa simply cannot handle such a drastic population growth. Studies show that by 2075, African food production can only provide for 1.35 billion out of an estimated 3.5 billion people.⁴⁴ Making things worse, a population rise will put immense pressure on Africa's dilapidated infrastructure.⁴⁵ While a large African population can catalyze the eventual modernization of the continent, existing poverty would be further exacerbated. An ideal population in these high-fertility countries would minimize unemployment and poverty to allow the population to grow alongside infrastructural improvements.

Once again, a population change cannot singlehandedly eliminate problems, but it can ameliorate poor living standards. About 11 million youth enter the workforce each year, yet only 3 million jobs are created.⁴⁶ In addition, about 60% of the African population faces moderate to severe food insecurity.⁴⁷ An optimal population for LDCs would be 30-50% of the current population or 264-440 million people. While this would hinder economic growth because of the scarcity of workers, the main roadblock to African modernization is its failure in government policies. LDCs are generally being held back by violent conflicts, lack of education, and government corruption.⁴⁸ These factors have nothing to do with population growth and decline, so the optimal population will have a slightly negative effect on total GDP, but a major leap in

GDP per capita. This will ensure that population growth will not outpace food production and job creation in already poor areas.

Conclusion

While developed and underdeveloped nations face different problems, a smaller global population benefits the entire world. In summary, the optimal global population is 4-5 billion people, which maximizes the global population to preserve economic growth while ensuring environmental sustainability and a rise in standards of living. In this optimal world, humans will achieve net-zero carbon emissions in the next 30 years. Economic growth will be fueled by widespread education instead of sheer population size, and quality of life will be much higher worldwide.

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On the International Criminal Court: US ratifying the Rome Statute

By Sajda Aboushabana

Introduction

The concept of international law was introduced to the world back in World War II after the conflict between the Allied powers and the Axis powers ended. Subsequently, the Nuremberg and Tokyo Trials from 1945 to 1948 were a way of holding Germany and Japan accountable for their actions by putting the people behind atrocities like the Holocaust and the Pearl Harbor attack on trial for their actions. At the time, international criminal law was an untapped domain, with permanent tribunals not existing until the eventual creation of courts such as the International Criminal Court (ICC). All these courts are founded on the fact that states/countries choose to be a part of them, to create a global environment to punish tyrants who defy the basic mandates of humanitarian regulations. The standards for these crimes are high, and it's rare for these standards to be met. But it can be done and has been reached before in certain cases, in countries that have agreed to be a part of the tribunals. However, some countries such as Israel, Russia, and the United States, (otherwise referred to as the U.S.), still do not recognize these tribunals. Robert F. Drinan, a former U.S. representative and former chair of the Subcommittee on Criminal Justice of the House Judiciary Committee wrote a piece saying "...representatives of the United States expressed fear that U.S. soldiers on peacekeeping missions might be brought before the court on politically motivated charges. This fear is unfounded. The treaty makes it very clear that the ICC will not prosecute any persons if their nation is taking appropriate actions against them" (Drinan). The implications of the U.S. not being a part of these courts allow atrocities such as War Crimes, Crimes against humanity, and Genocide to go unenforced because of the legitimacy and resources the United States provides.

War Crimes

Amnesty International, an organization that investigates the scenes of armed international conflict through on-site and remote investigations to find violations of international law, defines war crimes as "...willful killings, direct attacks on civilians, torture, use of prohibited weapons, the murder or ill-treatment of prisoners of war or others who have been captured, surrendered or injured and crimes of sexual violence" (Amnesty International). For example, during the Nuremberg trials in 1946, the Allied powers, which consisted of the United States, Great Britain, France, and the Soviet Union, came together to create a tribunal that would prosecute Germany for their acts during World War II. But for this specific trial, it was for the worst of the worst. It was for the leaders who were behind the planning and execution of a majority of the violence and colonization that the Nazis were able to enact. Patricia M. Wald, a former Chief judge of the US Court of Appeals for the District of Columbia Circuit wrote how "War crime prosecutions, especially against top leaders who have planned or executed countrywide strategies of abuse, are enormously complex, expensive, and lengthy. Many of the...prosecutions...followed five-year field investigations in which hundreds of witnesses were interviewed, thousands of documents

seized or accessed, and exhumations of mass burial sites conducted and the scattered body parts of thousands of victims collected and analyzed, and their identification attempted" (Wald 1,123). Because of the time and resources these cases demand, large and developed countries are required to take the initiative to prosecute these criminals in the name of keeping peace and delivering justice. For if there aren't, "...if these investigations had to wait until the recuperating war-torn countries had the facilities to undertake them, potential witnesses and documents would likely have been lost and graves vandalized or robbed" (Wald 1,123). During the Nuremberg trials, some charges of War Crimes included: enslaving and creating slave laborers, annihilation, and a myriad of brutal torturing methods. The powerful countries, such as the US being a part of the tribunal and prosecution were a huge advantage to the trials, allowing proper justice to be served to the Nazi leaders. In spite of this, they do not support the legitimacy nor authority of the International Criminal Court because of their belief that military personnel would be prosecuted for crimes. They disapprove of the investigation of themselves and their ally Israel, but encourage the investigation of other countries, such as Russia's Vladimir Putin and his alleged war crimes (Hixon, 23). Having the US be a part of the International Criminal Court allows fair and speedy trials, which are seen to be a priority according to their 5th Amendment.

Crimes against humanity

Article 7 of the Rome Statute, the International Criminal Court's founding treaty, explains the elements for a charge for Crimes against humanity to be "...(1) the commission of the crime as part of a 'widespread or systematic attack;' (2) against a civilian population; (3) with knowledge of the attack [directed against any civilian population]; and (4) involving "a course of conduct involving the multiple commission of acts ... against any civilian population, pursuant to or in furtherance of a State or organizational policy to commit such attack" (Sadat 352). An instance in which this charge was used after the fall of Yugoslavia, during the Bosnian War, where Serbian authorities attempted to systematically remove all Bosnian Muslims out of Bosnia (aka Bosniaks). The technical definition is that they were attempting an ethnic cleansing. They separated Bosniaks into concentration camps of men and women and used tactics such as rape, horrifying living conditions, and violence against the Bosniaks. The leaders, Serbian President Slobodan Milošević, Bosnian Serb President Radovan Karadžić, and Bosnian Serb military officer Ratko Mladić were all charged with crimes against humanity for their atrocities to ethnic groups taking place in Croatia, Bosnia, Kosovo, Serbia and Macedonia (Holocaust memorial day trust). Benjamin B. Ferencz, a former prosecutor at the Nuremberg war crimes trial, made a statement writing that he "...strongly advocate[s] the United States' ratification of the [Rome] treaty creating the International Criminal Court... 'No nation and no person has a sovereign right to commit crimes against humanity with impunity. The best way to protect our military, and the peace of the world, is through universal and equal enforcement of the rule of law for everyone'" (Denver Journal of International Law and Policy 3). Ferencz's point is proven by the US's involvement in the Bosnian War, as they were the prime reason that the Bosnian government was able to defend themselves against the Serbs, and were the reason for an eventual negotiation

between the Bosnian and Serb entities. When we see what the US has been able to do in past global conflicts because of its influence, it benefits the international community by allowing them to join the ICC.

Genocide

Ion Ristea, a professor at the University of Pitesti in Romania explains the high burden that is set to prove the intent for the crime of Genocide. It states that “The offender must intend to destroy the group, the offender must intend that the group be destroyed in whole or in part, and the offender must intend to destroy a group that is defined by nationality, race, ethnicity or religion” (Ristea). A case we can see this in is the Genocide of Rwanda in 1994, a case in which the US was NOT involved. This fact makes a big difference when compared to the cases that have been previously discussed, because of how long the genocide lasted, and how inefficient the legal proceedings were after the fact. Professor Mats Berdal, a professor in the Department of War Studies teaching Security and Development wrote, “The genocide in Rwanda involved the most murderously efficient bout of mass killing in the twentieth century... In little more than a hundred days, more than 800,000 people were slaughtered while, as the developed world, impassive and apparently unperturbed, sat back and watched the unfolding apocalypse or simply changed channels” (Berdal 117). The Rwandan Genocide came into being after the colonialism of European states, which brought political factors like ethnic identification systems that highlighted a clear difference between the groups. This turned Rwandan ethnic groups such as the Tutsis, Hutus, and the Twas to be hostile against each other, and led to the Hutu revolt, starting the attack against the Tutsi people. A peace accord was reached, but later on, the Hutu president was shot down in a plane, which initiated the attacks of physical and sexual violence against Tutsi political enemies and civilians. Because of the sheer volume of defendants that were charged with crimes after the fact, and with no extra resources, the Rwandan society turned to Gacaca proceedings, where three laymen civilians would judge perpetrators in a more efficient fashion. Timothy Longman, a professor of political science and international relations at Boston University explains, “Although gacaca has held many genocide perpetrators accountable and promoted dialogue in some communities, the gacaca process has promoted neither the restorative nor traditional judicial principles its supporters claimed. Instead, gacaca has been a retributive and punitive process used to promote a repressive political agenda and to settle many personal vendettas” (Longman 49). Maya Sosnov from the Denver Journal of International Law and Policy explains that because of the nature of the economy and lack of resources in Rwanda, makes it nearly impossible to prosecute each and every perpetrator, which leads them to Gacaca. However, Gacaca then leads to divided communities by draining financial resources either way (Sosnov 152). Therefore, the United States, a country with a surplus of resources, should join international communities to help countries that are struggling to have proper legal proceedings after a time of war.

Conclusion

Without US participation in the ICC, it allows war crimes such as Crimes against humanity, War crimes, and Genocide to go unresolved globally. By having them as a part of the tribunal, it increases the legitimacy and resources of international law. By not having the United States as a part of the ICC tribunal to help in prosecuting war criminals, we give up the ability to deliver justice in countries that are more susceptible to conflict and don't have as many resources for the eventual legal proceedings. According to White House policy, "Preventing mass atrocities and genocide is a core national security interest and a core moral responsibility of the United States" (US Department of State). However, there are people who will continue to argue against joining the ICC, like frivolous indictments from any country that wants a charge on an American leader. Nevertheless, the US would be able to defend itself easily through defenses like the standard of limitations of the crime, double jeopardy, etc, as in any other case in which one defends oneself from criminal charges. This is assuming that the person is innocent though. If they're truly guilty, then this would allow fair trials for the global community.

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Evaluation of Modern Corporate Social Responsibility By Varsha Jagadeesh

Abstract

Corporate social responsibility (CSR) is defined as the ways in which companies use business practices to benefit society, socially and environmentally, while continuing to pursue their economic goals. In recent decades, society has placed an increased amount of importance on CSR, leading it to become an integral part of a successful business. However, there is a lack of standardization regarding what constitutes an adequate amount of CSR for companies. While some companies implementing CSR into their business models have produced positive change, others have been unsuccessful in producing tangible differences. This paper dissects the differences between authentic and disingenuous CSR efforts and the key factors that lead to genuine CSR impact by analyzing several case studies on prior companies' commitments and execution of various CSR initiatives. Upon analysis, it can be found that the differences in impacts created by authentic and disingenuous CSR initiatives largely depend on the companies' follow-through on their commitments. Implementing legal CSR standards would eliminate the subjectivity around what qualifies as adequate CSR.

Author Summary

Upon doing research about the history of business ethics, I found that there was a gap when it came to what indicates that a company has done enough for the welfare of the environment, its employees, and/or society. I found that companies often distort what impacts they make on the world in order to appear more righteous to gain customers and support. In this paper, I analyze several case studies that detail instances of different companies negatively or positively impacting society or the environment. I discovered that the key difference between real and illusionary impact is whether or not a company alters its business practices to allow for real change. The results show that the social pressure from customers to "be good" is not enough for companies to actually produce genuine impacts, which indicates that there needs to be increased legal measures that force companies to be ethical.

Introduction

Although businesses have existed for many centuries, the idea of companies bearing a responsibility to society gained ground in the 1950s. Society has been steadily increasing the value it places on responsibility and ethics in the capitalist economy and has been gradually implementing reforms to early-day laissez-faire economics (Agudelo et al.). By shifting their priorities to include moral obligation and responsibility, consumers, stakeholders, and shareholders have increased the importance they place on associating with businesses that not only lack harmful practices but have a tangible positive impact on society (Agudelo et al.). As this notion became more widespread, it produced the concept of business ethics, which applies to moral and ethical situations that arise in the business world (Gheraia et al.). In order to maximize profit, businesses are now expected to show some modicum of regard for their planet and

society, or in other words, show that they have regard for the concept of business ethics and actively include it in several facets of their business model – this is the expectation from which corporate social responsibility emerged (Gheraia et al.).

Corporate social responsibility (CSR) is defined as the strides businesses take to benefit society environmentally and socially while continuing to maximize their profit and pursue their economic goals (Gavin). The goal of CSR is to encourage businesses to keep in mind the power they possess over society and their indispensable ability to benefit society when making decisions and creating business models, ensuring that they do not fall into the ruthless nature of capitalism solely to maximize profits. Business ethics and CSR work hand-in-hand to ensure that companies operate with morality and positively impact the world (Gheraia et al.). In recent decades, CSR has gained an increased amount of attention, not only in society but in the business world as well; valuing social welfare has become an integral part of operating a successful business. Business models can exercise CSR in multiple ways, such as environmental, employee, and organizational efforts and philanthropy (Gavin). From a purely performance-based perspective, incorporating CSR in business practices has been proven to increase employee and customer retention, attract investors, and increase company differentiation. Every consumer wants to be a good person or "do good"; one way to achieve that is by consuming products from socially responsible companies. CSR allows companies to profit from that mindset while concurrently bettering society and the environment ("CSR Impact,").

However, there is much subjectivity surrounding CSR, and businesses have been ambiguous between performative and genuine CSR efforts. Part of this issue is a need for standardized CSR metrics. Companies whose motives do not involve social change often make desultory or false CSR efforts and get away with it because there are no legally established requirements and assessments for CSR initiatives. While it is currently understood that companies must integrate some form of CSR into their business model in order to be successful, those efforts do not always provide a true positive impact, calling into question the validity of companies' CSR efforts and the criteria CSR efforts need to meet in order to be legitimized. Even when companies do not hold altruistic motives when implementing CSR, they can still produce genuinely positive impacts with their CSR initiatives. However, for that to happen, there need to be legal CSR standards and heightened regulations to ensure legitimacy. This paper explores various CSR implementations, explicitly looking at sincere implementations and various ways CSR is misused. Upon examining different instances of CSR, this paper discusses what qualifies as genuine CSR and will explore a potential course of action to help mitigate CSR's inherent subjectivity. The conclusions of this paper provide insight into the intricacies of CSR, the different ways CSR can be interpreted, and how to standardize its interpretation and guarantee successful returns.

Background

Modern CSR emerged in the 1950s, influenced by post-World War II social changes that prompted increased academic interest in business ethics (Agudelo et al.). Initially, CSR focused

on addressing resource depletion and environmental issues due to rapid population growth. However, by the late twentieth century, business leaders' social and economic influence gained attention, leading to corporate and philanthropic CSR initiatives (Agudelo et al.). Today, CSR is understood in various ways, from a moral obligation to a marketing strategy. Institutions are the "cultural elements and symbols to which organizations must conform to receive support and legitimacy". Legitimacy does not just imply organizational legitimacy to satisfy the needs of consumers and fulfill their objectives, but it also implies social legitimacy, showing regard for communal welfare. The institutional theory implies that companies must achieve legitimacy to be financially successful, and CSR initiatives are essential to fulfill social legitimacy (Kim & Ha, 2020). Companies often adopt CSR to enhance their legitimacy among stakeholders, even if their efforts lack sincerity, to build loyalty across their customer base. The functionalist approach views CSR communication as signaling commitment without necessarily delivering genuine impact (Schoeneborn et al.). Functionalist ideals can be seen in companies that extensively advertise their CSR efforts to their target audience, with little tangible evidence of accurate CSR returns. The concept of moral licensing, where companies may use past ethical actions to justify future misconduct, illustrates the insincere motives behind CSR (Bouzzine et al; Tamplin).

Similarly, greenwashing can be described as "the practice of promoting environmentally friendly initiatives while engaging in unsustainable business practices" (Tamplin). Greenwashing often results when CSR is used as a marketing tool to boost a brand's image as environmentally friendly and gain loyalty by appearing to be socially responsible. Ultimately, while ideal CSR practices exist, many companies engage in CSR primarily to benefit their profits rather than societal welfare.

Nevertheless, capitalistic motives and genuine CSR efforts do not need to be mutually exclusive; implementing legal CSR standards with metrics becomes very important in this context. Current CSR measurements target impact, which accounts for the "tangible and intangible effects" CSR has on society. Impact metrics include output measurement (which measures the immediate output and their benefit on the targeted parties), outcome measurement (which measures long-term impact/changes), and impact assessment (which analyzes both negative and positive impacts) ("CSR Impact") Because the legitimacy of different companies' CSR initiatives often varies, as seen in the case studies below, there is a need for legal standards and measurable metrics to ensure accountability and genuine positive change.

Case Studies

To examine the differences between insincere and sincere CSR efforts, this paper examines the specific CSR efforts of several companies: Lego, Volkswagen, Garment multinational corporations (MNC) such as H&M, Gucci, Nike, and more, as well as Coca-Cola. Each case study involves a comprehensive analysis of each company's CSR commitments and their follow-through. This paper examines articles and case studies to argue for the implementation of legal CSR regulations in order to mitigate the concept's subjectivity.

Lego

This case study about Lego analyzes a company's CSR commitments and follow-through on environmental CSR efforts. In 2014, Lego partnered with the World Wildlife Fund, making commitments to reduce carbon emissions, utilize renewable energy, and provide resources for their employees and suppliers to engage in environmental sustainability. Lego upheld its vow to reduce carbon emissions and utilize renewable energy by using offshore wind power in Germany and the UK instead of fossil fuels. Lego upheld its vow to engage employees and suppliers in environmental sustainability by establishing an environmental engagement program for its employees to reduce energy use, waste, and water consumption. The company also helped its suppliers partake in the Carbon Disclosure Movement, a global non-profit organization that tracks companies' carbon footprints ("In Partnership with WWF").

Along with these implementations, Lego has vowed to make its packaging and toy materials environmentally friendly (Gavin). To follow through with this, Lego has shrunk its box size among other initiatives and started creating block pieces with sustainably sourced sugar cane rather than petroleum-based plastic (Gavin). Since it joined the WWF in 2014, Lego has improved the energy efficiency of Lego brick production by over 12% ("Lego's efforts"). The company has also invested millions of dollars into researching sustainable toy materials that can eventually be used in production (Gavin).

Volkswagen

Like Lego, this case study about Volkswagen analyzes a company's commitments and follow-through on environmental CSR efforts. In contrast to Lego's CSR initiatives, Volkswagen's case study reveals insincere CSR efforts regarding the environment and fuel emissions. Volkswagen's environmental efforts, specifically the series of events that led to the Volkswagen diesel emissions scandal, exemplify moral licensing and greenwashing. In 2015, the Environment Protection Agency (EPA) noticed that the emissions from Volkswagen's vehicles were exorbitantly high and violated the Clean Air Act (Geuss). Upon further investigation, it was revealed that Volkswagen had been using software for their emissions testing to manipulate their results (Bouzzine et al.). The scandal preceded Volkswagen's public release of their environmental CSR reports detailing how the company had made their cars more environmentally friendly (Bouzzine et al.). Volkswagen illegitimately participated in emissions testing intended to prevent the very outcome of the scandal.

Garment Multinational Corporations

The garment industry has encountered an immense amount of controversy surrounding the treatment of its workers. A case study by Labron et al. from the University of Sheffield examined how different garment MNCs—such as Gucci, Nike, Under Armour, H&M, and other similar entities, upheld their commitment to paying a living wage to their supply chain workers (Labron et al.). This was a significant vow because the garment industry is notorious for treating its workers poorly and outsourcing labor to sweatshops in developing countries.

Firstly, the researchers defined a *living wage* as the money a worker needs to pay for food, healthcare, rent, clothing, and a small amount for education and savings. They then used surveys and public data to track companies' progress toward providing the aforementioned living wage to their customers). The researchers found that the examined garment companies were notably unsuccessful at providing living wages for their workers, mainly because they did not change the parts of their business model that produced the low wages. Instead, they often implemented only nominal adjustments to their supply chain and employee management practices, manipulated the definition of a living wage, and engaged in multiple stakeholder initiatives to delegate their commitments to entities that were unable to effect meaningful changes to the business model, thereby failing to alter employee compensation significantly. For instance, shortly after making their CSR commitment, in order to show proof of their commitment to being responsible, many of the garment companies partnered with ACT, which is a multiple stakeholder initiative that does not precisely require participating companies to reallocate funds to allow for living wages but whose goal is to better employee treatment (Labron et al.).

Overall, the survey data indicated that companies had done little to reallocate the flow of funds in their business model to pay their workers higher wages. The researchers found that the companies were unsuccessful at making meaningful CSR impacts because they were reluctant to reduce purchasing practices because of the pressure they faced to output a large volume of product, resulting in them continuing to exploit their employees and cutting corners in their CSR efforts. The researchers found that, on average, when taking action to uphold their commitment to pay their workers a living wage, the companies left the core parts of their business model that were the root cause of the low wages intact and avoided giving a clear projection or timeline of their results or a plan to display their progress to the public. The researchers concluded that the lack of meaningful, tangible progress from both the companies and their stakeholders indicates the need for more research regarding codes of conduct and assessments to eliminate industries' ability to pay their workers "illegally low wages" and get away with it (Labron et al.).

Coca-Cola

An example of a company whose CSR efforts exemplify the subjectivity that this paper seeks to clarify is Coca-Cola. The company's efforts towards environmental sustainability, positive shareholder relationships, and social change have been both praised and criticized. Two works with different perspectives can be viewed to show this juxtaposition: a case study focusing on Coca-Cola's business ethics by Younas Khan et al. from Ulster University and an evaluation of Coca-Cola's CSR initiatives by LinkCxO, both published in late 2023 (Figure 1).

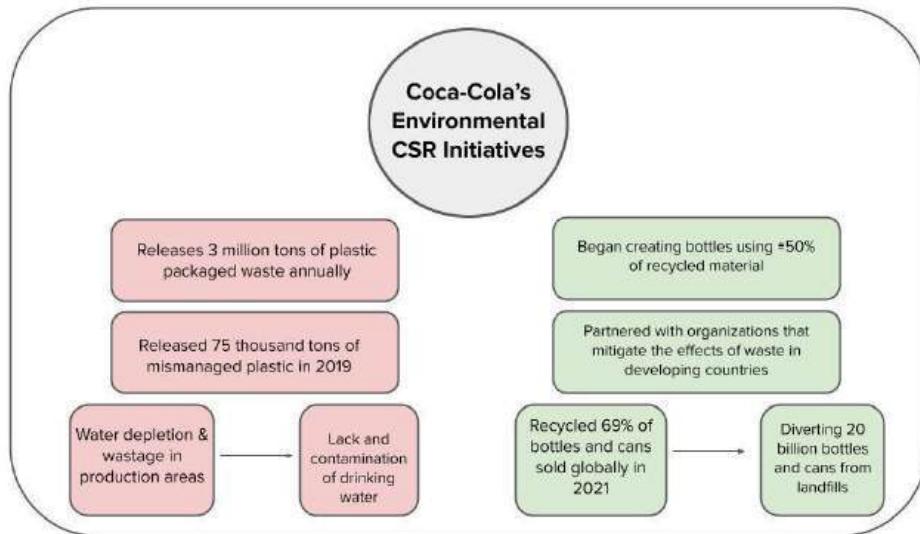


Fig 1: Differing Perspectives on Coca-Cola's Environmental CSR Initiatives Supported By Specific Statistics (Khan et al.; "CSR Unveiled").

The figure above highlights the ambiguity of Coca-Cola's overall environmental CSR impact, where red and green boxes show Coca-Cola's detrimental and beneficial statistics, respectively. The efforts of Coca-Cola's recycling initiatives were presented by LinkCxO in 2021; however, in the same year, the Earth Island Institute filed a lawsuit against Coca-Cola, accusing them of greenwashing their sustainability efforts ("Coca-Cola Company Accused"). According to the case, the institute accused Coca-Cola of misrepresenting the recyclability of their bottles, claiming that the company said their bottles were "100% recyclable" even though most bottles are not recycled. The case was brought to the federal court. However, it was dismissed because the court found that it did not violate the Consumer Protection Procedures Act, an act designed to protect consumers from unlawful, misleading business practices ("DC Consumer"). It was dismissed because Coca-Cola's statement about the recyclability of their productions was merely an aspiration or a goal, and the amount of Coke bottles that go into landfills did not serve as evidence of Coca-Cola "misleading" their customers ("Coca-Cola Company Accused").

Next, Khan et al. found Coca-Cola accused of racial discrimination, biased and prejudicial employee treatment in their Colombian market, and unsafe factory working conditions (Khan et al.). In contrast, according to LinkCxO, Coca-Cola has made various strides toward women's empowerment, from employing women throughout its supply chain to partnering with several organizations in developing countries to increase women's education and resources. Regarding employee wellness, Coca-Cola has implemented programs to improve employees' physical and mental health, such as employee assistance programs that offer access to mental health services. The company has also implemented many regulations and assessments for factory conditions to ensure workers' safety. In order to prevent prejudice in the workplace, Coca-Cola has implemented bias training for their workers. It supports several Employee

Resource Groups that create community and foster diversity and connection in the workplace (“CSR Unveiled”).

Finally, regarding stakeholder and customer relations, Khan et al. report that Coca-Cola has engaged in channel stuffing – the act of overselling products to sellers in order to maximize profit, knowing the distributors will be unable to sell the amount of product – throughout their supply chain. They also report that Coca-Cola concealed this from their shareholders, damaging the relationships and contributing to waste. In addition, the company has faced controversy due to a lack of disclosure regarding health effects and over-promising recyclability in its marketing. They suffered even more because they were not serious in their remediation efforts for these scandals (Khan et al.). While Khan et al. found Coca-Cola to have exhibited poor behavior in past disputes with shareholders and customers, LinkCxO reports that Coca-Cola has implemented programs for stakeholders to share their concerns and criticisms with the company and has established panels with members from the NGOs they have partnered with in order to receive input on their CSR efforts (“CSR Unveiled”)

Discussion

After considering the results of each company's CSR efforts, it can be determined that Lego's CSR initiatives represent sincere CSR efforts. In contrast, Volkswagen's and the garment industry's CSR initiatives represent insincere CSR efforts. Key differences between the cases stand clear: whether or not the companies follow through on their commitments, the extent of their follow-through, and the discrepancy between their legitimate actions and what they market to the public. One similarity between Lego and Volkswagen is that both of their CSR efforts involved the public announcement of their sustainability efforts; however, their cases diverge regarding the follow-through. Volkswagen failed to follow through with its CSR commitments, while Lego, on the other hand, produced tangible results showing the sincerity of its commitments (Figure 2).

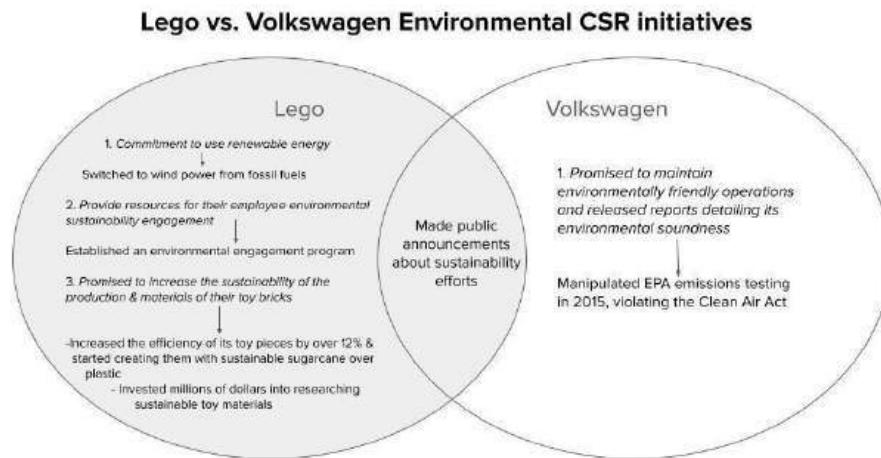


Fig 2: Comparison of Lego and Volkswagen's CSR Efforts (Bouzzine et al; Guess; "Lego's efforts"; Gavin; "In Partnership with WWF").

Like Volkswagen, the garment industry failed to follow its CSR commitments decently. The researchers analyzed multiple garment companies' follow-through on their commitments to pay their workers higher wages. They discovered that the companies were reluctant to change the core part of their business model that would allow for actual change. Unlike Lego, which changed the core parts of its operations to produce tangible environmental benefits, the garment MNCs did not redistribute resources through their supply chains to allocate more money for employee wages, resulting in no improved wages.

However, what constitutes an adequate follow-through of CSR initiatives? This quandary is exemplified in the Coca-Cola case study. The literature review examined two studies on Coca-Cola's CSR efforts. One listed Coca-Cola as pursuing exemplary CSR efforts ("CSR Unveiled"), while the other depicted Coca-Cola as being entirely socially irresponsible (Khan et al.). For example, LinkCxO mentions that Coca-Cola recycled 69% of its bottles and cans in 2021, but Khan et al. state that Coca-Cola releases 3 million tons of packaged waste annually. Similarly, regarding employee treatment, LinkCxO asserts that Coca-Cola's employee-based CSR efforts are successful because the company has taken many strides to further women's empowerment, such as hiring women throughout its supply chains. In contrast, Khan et al. imply that Coca-Cola is socially irresponsible because the company has several factories with unsafe working conditions and has been accused of racial discrimination. A limitation of the Coca-Cola analysis is that both studies could have been cherry-picking their data to fit a particular narrative, stemming from the subjectivity around CSR. Because the statistics presented by LinkCxO and Khan et al. are opposing but not mutually exclusive, they paint an inconclusive picture of Coca-Cola's social responsibility, which shows how a lack of standards for CSR measurement results in ambiguity when attempting to assess a company's success regarding CSR efforts. While both hold merit, the two studies take polar opposite stances on Coca-Cola's CSR, which poses the question: What exactly qualifies a company to be socially responsible?

To begin discussing this question, the lawsuit portion of the Coca-Cola case study can be referenced. As mentioned in the literature review, a lawsuit was taken against Coca-Cola for its environmental irresponsibility, specifically accusing it of over-representing the recyclability of its bottles to the public. This paper defines this type of action as socially irresponsible. However, the case was dismissed. Because Coca-Cola's announcement about their 100% recyclable bottles was legally regarded as an aspiration, they were not violating the CCPA. Hence, it was legal for Coca-Cola to make a statement about having their bottles being 100% recyclable but not recycling 100% of their bottles.

In order to eliminate the subjectivity behind CSR, higher legal standards should be established. While existing acts, such as the CCPA, are meant to protect against unfair trade practices, no laws enforce a substantial degree of CSR. The main factor driving companies to engage in CSR efforts is the increased importance that society has been placing on social responsibility over the last several decades. However, societal pressure is not a concrete enforcer of CSR; as proven by the Volkswagen, garment industry, and Coca-Cola case studies, unwritten social standards are insufficient to hold companies accountable for executing their CSR

commitments. Applying the institutional theory in this context, the requirement institutions place on companies to adhere to them to achieve legitimacy does not account for the idea that companies do not have to follow through with their commitments that align with institutions to achieve legitimacy, making institutions an insufficient source of pressure for producing sincere CSR initiatives.

If there were a legal benchmark that dictates a company's social responsibility, it would be unnecessary to debate the morality of a company to assess true CSR impact. For example, in the context of Coca-Cola, if the legal standard for beverage companies were to recycle at least 75% of their bottles and cans, Coca-Cola would have failed to meet that benchmark in 2021 because they only recycled 69%. That would show the company that they need to change parts of their business practices to increase the percentage of bottles recycled without the need for societal pressure. Currently, the only thing setting standards for CSR are societal norms, which are often rooted in bias and emotion rather than tangibility and practicality and are almost always heavily debated; this is exemplified by the difference in framing between the two Coca-Cola studies. As seen in the Volkswagen and garment MNC case studies, the pressure to be perceived as "good" often pushes companies to make commitments they have little to no intention of executing. By standardizing expectations for CSR efforts, implementing legal requirements takes the focus off subjective pressure, makes achieving CSR more straightforward, and forces companies to adhere to a higher benchmark of CSR initiatives. The core purpose of CSR should not be to evaluate the morality of companies to feel a higher sense of self-morality when endorsing them but rather to ensure that companies are not detrimental to the environment.

Conclusion

Over the last several decades, a company's engagement in social responsibility has been increasingly vital to its success. However, there has been subjectivity around what qualifies a company as socially responsible. This is mainly due to the lack of legal standardization and regulations regarding CSR; the main factors determining a company's legitimacy are unwritten societal norms and subjective perceptions, which have allowed companies to be insincere with their CSR initiatives. In the past few years, several companies, such as Volkswagen, garment MNCs, and Coca-Cola, have been found to have made commitments to better the environment or increase their employee welfare but have not followed through with their promises, as it impeded their business practices, and they were not legally obligated to do so. Furthermore, the lack of legal obligation to execute CSR initiatives increases the ambiguity around companies' morality, making CSR a debatable concept rather than an objective standard. To eliminate companies' ability to produce insincere CSR efforts and clarify the definition of adequate CSR, since it has been proven that unsaid social norms are insufficient, there need to be legal measures and regulations established that enforce higher standards of responsibility.

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The Impact of Features in Popular Music on Physiological and Psychological Stress

Responses By Ruhi Bhaskar and Mytien Le, M.A.

Abstract

Stress is a prevalent issue affecting about 75% of Americans in 2024 (Single Care, 2024), contributing to numerous physical and psychological health problems like obesity, endocrine disturbances, and sleep loss. Many popular stress interventions include face-to-face therapy and meditation (DrKumo, 2023), though effective, may not always be accessible or enjoyable. This review paper explores the potential of music therapy as an accessible and effective intervention for stress. This paper analyzes past research on the impact of various musical features and genres on stress responses. It was found that music with middle-range frequencies, medium tempo, legato articulation, major keys, and lyrics are the most beneficial in alleviating stress and the harm it causes. It was concluded that listening to specific types of music daily improves overall well-being and stress management. Further research includes exploring the direct effects of music on obesity and the fluctuation of endocrine levels, exploring studies on how specific genres could affect stress, obesity, and endocrine levels, and exploring updated results about the effects of different musical genres and features to satisfy new trends in music.

Introduction

Stress can be caused by feeling under pressure, facing big life changes such as worrying about something, losing control over the outcome of a situation, and being overwhelmed by responsibilities (Mind, 2022). Stress is not only a psychological phenomenon but also a physiological concern. For instance, problems like psychosocial and socioeconomic stressors are highly prevalent in society today and have been associated with the development of obesity (Tamashiro, Sakai, Shively, Karatsoreos, & Reagan, 2011). Additionally, stress can cause sleep loss, which further causes compromised cognitive performance, memory deficits, depressive mood, and involuntary sleep episodes during the day (Porkka-Heiskanen, Zitting, & Wigren, 2013). There are many stress interventions like face-to-face therapy, group therapy, meditation, etc. (DrKumo, 2023). However, listening to music has been shown to be a promising avenue of stress relief through enhancing well-being, reducing stress, and distracting patients from unpleasant symptoms (Kemper & Danhauer, 2005). Music therapy, regarded as expressive therapy, uses music and its physical, emotional, mental, social, aesthetic, and spiritual facets, to help patients improve and maintain their health (Center, Center, & Center, 2005). Cognitive function, motor skills, emotional and affective development, behavior and social skills, and quality of life are clinically proven to be improved through music therapy (Center, Center, & Center, 2005). This paper will include past studies and research about the impacts of different musical features and genres on stress responses and endocrine disruptions. Biological, psychological, and neuroscientific research findings will be analyzed to understand better the effect of music (including lyrics, genre, rhythm/tempo, instrumentation, etc.) on stress levels.

The findings offered will provide recommendations for potential future music-based stress-reduction interventions.

Stress

Stress, a prominent issue in modern-day society, is defined as a state of threatened homeostasis (Kyrou & Tsigos, 2009) and can be the cause of many physical and emotional problems like cardiovascular diseases, cancers, anxiety disorders, depression, and burnout (de Witte, Pinho, Stams, Moonen, Bos, & van Hooren, 2022). Additionally, stress interferes with cognitive processes such as executive function and self-regulation (Tomiyama, 2019). The ability to be stressed can start from the womb, and its effects can be carried out throughout adulthood or immediately after the stressful situation (Koenig, Walker, Romeo, & Lupien, 2011).

The impact of stress on key biological and behavioral functions

Endocrine system

The endocrine system is an important part of the body that produces hormones. Generally, hormones control growth, metabolism, electrolyte composition of bodily fluids, reproduction, and development of the body (Hiller-Sturmhöfel & Bartke, 1998). The endocrine system has beneficial regulatory effects on the human body, and it controls and maintains the appropriate functions within many physiological systems, such as homeostasis (Hackney & Lane, 2015). The hormones of the endocrine system affect every organ in the human body. Human physiological processes such as homeostasis, metabolic demand, development, and reproduction are all possible because of hormones and the processes mediated by their actions (Campbell & Jialal, 2019). The endocrine system of the HPA axis, a major system that is closely involved in stress, prompts the production of cortisol, which mobilizes the body's energy supply and increases the availability of energy (Baltazar, Västfjäll, Asutay, Koppel, & Saarikallio, 2019). Hair cortisol is an objective biomarker for analyzing and measuring cortisol exposure for clinical, diagnostic, and research purposes (Greff, Levine, Abuzgaaia, Elzagallaai, Rieder, & van Uum, 2019). Additionally, salivary cortisol is routinely used as a biomarker of psychological stress and related mental or physical diseases; it is also a reliable measure of the hypothalamus–pituitary–adrenal axis (HPAA) adaptation to stress (Hellhammer, Wüst, & Kudielka, 2009).

Obesity

In many circumstances, body weight can be affected by stress. Stress has been shown to influence human eating behavior, appearing to alter overall food intake in two ways: under-eating or overeating (Torres & Nowson, 2007). In terms of overeating, many start consuming food high in calories, fat, or sugar and decrease physical activity (Tomiyama, 2019). Chronic stress can harm the whole body's metabolism, especially glucose homeostasis (Kyrou & Tsigos, 2009). Both being overweight and underweight are detrimental to health (Golubnitschaja,

Liskova, Koklesova, Samec, Biringer, Büsselberg, & Kubatka, 2021). Additionally, America's average weight is associated with an increased risk of heart disease (Wickelgren, 1998). Obesity rates have increased in all demographics, even though the obesity rates are generally higher in older people and women (Chooi, Ding & Magkos, 2019). Emotional Eating (EE) is understood as a maladaptive self-regulation strategy to satisfy emotional needs instead of hunger, and it has been identified with negative health consequences. Enjoyment of food and music share similar neural activations in the brain, and both are used for regulation. Associations were also made between music listening and EE in people with low and high (non-clinical) levels of disordered mood (depression, anxiety, and stress) (van den Tol, Coulthard, & Hanser, 2020).

Sleep

It is critical to get good sleep because it improves brain performance, mood, and health (News in Health, 2021). However, stress can contribute to fragmented and unstable sleeping in aging and dysfunction of neuroendocrine regulation, causing severe sleep disturbances (Van Reeth, Weibel, Spiegel, Leproult, Dugovic, & Maccari, 2000). Sleep loss leads to increased sleepiness, fatigue, and reaction time which were associated with the selection of less difficult tasks (Engle-Friedman, Riela, Golan, Ventuneac, Davis, Jefferson & Major, 2003); in addition, sleep deficiency affects alertness, cognition, productivity, safety, learning, and mood (Mansfield, Hillman, Antic, McEvoy & Rajaratnam, 2013).

The Healing Power of Music

Historically, music has been used as a form of therapy for stress and is still used to this day. Music therapy, using the specific qualities of music in a therapeutic relationship with a music therapist (de Witte, et al., 2022), is based on ancient cross-cultural beliefs that music can have a “healing” effect on the mind and body (Thaut, 2015). Modernly, music is still used widely to reduce negative emotions and feelings, such as subjective worry, state anxiety, restlessness, or nervousness (de Witte, et al., 2022). Additionally, everyone has their music preference, which cannot be categorized by music genre but rather by how engaged the listener is to the music they are listening to (Greasley & Lamont, 2006). Musical therapists typically go through certain steps like selecting a song based on group needs, describing the purpose and process of song discussion for the clients, playing the song with careful attention to the client’s responses, and facilitating a discussion about the client’s responses to the song. Clients are called upon to actively respond to what they hear, in overt responses (responses that are external and observable) and covert responses (responses that are internal and largely unobservable) (Gardstrom, Sorel, & Wheeler, 2015). Depression and anxiety can be managed using music therapy, preventing harmful stress responses to mental changes, improving mood, increasing physical energy or leading to relaxation, and even offering cathartic or positive messages in lyrics (Pandora Cloudcover Music, NA). Music does not imply an obvious physiological satisfaction, but neuroimaging studies show activation of emotion, reward, motivation, and arousal networks during music listening. Music has been implicated as a versatile and effective

tool to regulate emotions in a variety of studies. People also use music and lyrics for cognitive effects, including cognitive reappraisal, search for meaning, and diversion from boredom, intrusive thoughts, and emotions (van den Tol, Coulthard, & Hanser, 2020). In regards to musical features, rhythm is defined as the ordered characteristic, either conceived or perceived, of succession. Under rhythm's perceptual aspects is tempo (Fraisse, 1982). Tempo can be either fast or slow, and it typically relates to the number of perceived elements per unit time (Fraisse, 1982). Additionally, pitch is the scale going from low to high, and it usually depends on the frequency of a sound stimulus, the sound pressure, and the waveform of the stimulus (Stainsby, & Cross, 2009). Legato, another musical feature, is a smooth and continuous flow of notes (Palmer, 1989). In sum, music therapy incorporates different musical features in order to help with prevention of harmful physical and psychological stress responses.

Hypothesis

The following hypotheses are:

- 1) If the music used for intervention from stress has a slower tempo, lower pitch, and more legato, the amount of sleep a person gets would be increased.
- 2) If the music used for intervention from stress has a slower tempo, lower pitch, and more legato, then there would be less fluctuation of endocrine levels after a stressful situation.
- 3) If the music used for intervention from stress has a slower tempo, lower pitch, and more legato, the amount of weight a person gains would be decreased.

This first hypothesis about sleep originates from research suggesting that slower, lower-pitched music can allow for relaxation, reduce anxiety, and promote better sleep quality. Slow tempos and low pitches are typically associated with creating a calmer effect, aiding in sleep. The second hypothesis about endocrine levels is based on findings that music with these characteristics may help stabilize physiological responses to stress, like the regulation of hormones like cortisol. The smoother, slower, and lower-pitched music might lower the body's stress response, leading to more stable endocrine levels after a stressful situation. The last hypothesis about weight gain comes from the understanding that stress can lead to weight gain through causes like increased cortisol production, emotional eating, and disrupted metabolism. By listening to calming music to reduce stress and stabilize endocrine function, the hypothesis suggests that there would then be a decrease in stress-induced weight gain.

Literature Review Results

To begin, a systematic search of academic databases was conducted using Google Scholar, to identify studies and articles that demonstrate the impact of music on stress, the endocrine system, amount of sleep, and obesity. The search involved using specific keywords and phrases such as "music therapy," "stress reduction," "tempo and stress," "pitch in music therapy," "endocrine response to music," "music and sleep," and "music and weight management." By combining these keywords, the aim was to capture a broad range of studies

that prove the relationship between musical features (tempo, pitch, legato) and physiological as well as psychological outcomes. The initial search included around 10 articles. Then more research was conducted in relevance to the hypothesis, and publications within a recent time frame were also found to ensure the review includes current research that is relevant to modern society. After reading through the articles that were selected, the most directly relevant information to the hypotheses was included in the review.

In a study about how background music affected students' stress levels during the dissection of cadavers, stress was reduced by about 33% for students dissecting with music in the background compared to students dissecting without background music. In addition, students listening to background music had higher scores in 2 or 3 test sections (Anyanwu, 2015). This shows that background music plays a huge role in reducing stress and therefore helps with reducing the side effects of having stress.

Next, regarding endocrine levels, a study found that cortisol levels were higher after high-stress scenarios compared to low-stress situations (Harvey, Bandiera, Nathens & LeBlanc, 2012). Cortisol has a role in mediating the stress response (McEwen, 2019). Additionally, various hormonal changes occur in the body in response to stress, which enhances the secretion of different hormones (Khanam, 2017). Several experimental studies in which participants were subjected to a stress induction and then listened to self-selected music have shown decreased state anxiety, improved negative mood, and reduced stress compared to a non-music control group (van den Tol, Coulthard, & Hanser, 2020). In addition, data shows that in the presence of music, the salivary cortisol level did not increase after the stressor; contrastingly, in silence, it continued to increase for 30 minutes (Khalfa, Bella, Roy, Peretz, & Lupien, 2003). Studies show that music reduces stress by lowering cortisol levels, preventing the increase of cortisol levels after high-stress scenarios, and improving mood and anxiety compared to silence.

Regarding sleep, a study shows how certain types of music improve sleep (Dickson & Schubert, 2022). The most helpful musical features with a 78% success rate were middle-range frequencies, medium tempo, legato articulation, major music, and included lyrics. On the other hand, the unsuccessful musical features included lower frequency, legato articulation, and high rhythm. These results prove that sedative music does not always aid sleep (Dickson & Schubert, 2022). Another study talks about the effects of popular, everyday music on the amount of sleep received, showing that the following are the most useful genres for sleep on Spotify: sleep, k-pop, lullaby, lo-fi beats, pop/UK pop, chill hop, electro-pop, and piano cover; these genres were being played right before it was time to sleep to see how much they facilitated (Scarratt, Heggli, Vuust & Jespersen, 2021). Techno music was also tested on its effects on psychological responses: it worsened healthy people's mental states. However, classical music bettered their mental states; each type of music was played for 30 minutes for each subject (Gerra, Zaimovic, Franchini, Palladino, Giucastro, Reali, & Brambilla, 1998). The studies show that specific musical features and genres, such as middle-range frequencies and classical music, can improve sleep quality and mental states, while genres like techno may have the opposite effect, demonstrating the importance of selecting the right music to improve sleep.

Changes in endocrine function, for example, cortisol levels, can cause obesity (Álvarez-Castro, et al., 2011). Music listening, however, can help regulate stress responses by decreasing cortisol levels (Baltazar, Västfjäll, Asutay, Koppel, & Saarikallio, 2019). A study shows that hormone levels were higher in patients with obesity compared to “normal-weight” individuals of the same age and gender (Poddar, Chetty & Chetty, 2017). Stress secretes glucocorticoids, increasing motivation for food, and insulin, increasing food intake and obesity. While around 20% of people have normal feeding habits under stress, around 40% or more increase caloric intake when stressed. Normal-weight women showing ‘dietary restraint’ to stay thin can also be found stress-eating (Dallman, 2010). Music listening could be a healthy alternative to Emotional Eating (EE) in terms of physical health. In this research, it was found that both EE and discharge (releasing anger or sadness through music that expresses these same emotions) were associated with depression, anxiety, and stress. EE was higher when there was a high level of disordered mood, regardless of music listening. EE was lowest when people scored low on using music as a strategy and low on disordered mood (van den Tol, Coulthard, & Hanser, 2020). The increase of stress-induced cortisol can lead to obesity, but music listening can help regulate stress and serve as a healthier alternative to emotional eating.

Further Research

More research could be done on the direct effects of music on obesity and the fluctuation of endocrine levels. Specifically, concerning obesity, none of the studies explored the impact of musical features on obesity, making it harder for people to find effective music for their stress. For example, the source addressing how music listening can help regulate stress responses by decreasing cortisol levels (Baltazar, Västfjäll, Asutay, Koppel, & Saarikallio, 2019) lacks information about how specific musical features (pitch, tempo, and legato) can affect how the music affects obesity. Another example includes the source addressing how music listening could be a healthy alternative to Emotional Eating (EE) in terms of physical health (van den Tol, Coulthard, & Hanser, 2020). This source did not include information on what types of musical features would be most helpful when listening to music as an EE alternative.

Additionally, more studies should be on how specific genres could affect stress, obesity, and endocrine levels. While there were many studies on specific musical features, they are harder to apply when trying to find everyday music to listen to. By identifying specific genres or songs to listen to, people could find it easier to soothe their stress. For example, the source that found that both EE and discharge (releasing anger or sadness through music that expresses these same emotions) were associated with depression, anxiety, and stress (van den Tol, Coulthard, & Hanser, 2020), shows no information about which specific genres would tend to influence people’s feelings of sadness. Additionally, the study about how background music affected students’ stress levels during the dissection of cadavers (Anyawu, 2015) did not mention what type of musical genres were being played to soothe the students’ stress. Another example is the study about how the presence of music did not increase the salivary cortisol level after the stressor. This source also did not mention what genres of music were used when testing for the

fluctuation of the salivary cortisol level. While studies have not shown the direct effects music has on obesity and endocrine levels, based on the results of previously shown sources, middle-range frequencies, medium tempo, legato articulation, major music, and lyrics (Dickson & Schubert, 2022), would improve endocrine levels, weight gain, amount of sleep, and overall stress response.

Additionally, some articles did talk about the effects of different musical genres and features; however, as time passes, this data should be updated to satisfy new trends in music. While most of the population may have liked a certain type of music in 2021, opinions may have changed with time. For example, the study about the effects of popular, everyday music on the amount of sleep received (Scarratt, Heggli, Vuust & Jespersen, 2021) only gives results about the popular music of 2021. Sleep, k-pop, lullaby, lo-fi beats, pop/UK pop, chill hop, electro-pop, and piano covers are genres that may not be as popular or preferred anymore.

Conclusion

The hypotheses were partially supported as the criteria of the musical features were not completely accurate. While it was hypothesized that a slower tempo, lower pitch, and more legato would be more effective in relieving stress, it has been shown that the music intervention should be of middle-range frequencies, medium tempo, legato articulation, major music, and lyrics to have the best results of alleviation. Ultimately, people of all ages who are under any stress should use music as an intervention to alleviate themselves from problems like stress, sleep loss, obesity, and endocrine level fluctuation.

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Research Report on the Educational Issues of Children of Migrant Workers in Xiaogan, Hubei Province, China By Cody Wu

Introduction

As China's cities rapidly develop, large numbers of migrant workers move to these urban areas. These workers have not only contributed to infrastructure and economic development but have also become an essential part of the city's growth. Despite the benefits they bring, the accessibility of education for their children has always been a concern. This report, based on extensive empirical research—including surveys and in-depth interviews on the educational challenges faced by children of migrant workers—provides a comprehensive analysis of the current situation, challenges, and feasible improvement measures in the education sector for this group.

Background and Goal

Migrant workers play a crucial role in the development of Chinese cities, yet the educational issues faced by their children have frequently been ignored. These issues include a lack of educational resources and unequal access to educational opportunities. This study aims to further understand the current situation of migrant worker families through surveys, interviews, and case studies. It seeks to identify existing problems and propose effective solutions to address the issue of unequal education.

Although the government and society have made some efforts to improve the educational conditions for the children of migrant workers, the current level of changes made remains insufficient to successfully fix the complex challenges faced by this group. Due to the mobility of migrant families and the unequal distribution of urban educational resources, migrant workers' children often struggle to access stable educational support. Therefore, the core objective of this study is to systematically analyze and reveal the status of migrant workers' children within the urban education system, identify gaps in resource distribution, policy support, and social-cultural integration, and propose more targeted policy and practical recommendations.

Research Method

This study employs a variety of research methods to ensure the comprehensiveness and reliability of the data, including:

1. Surveys: Educational information was collected from migrant workers and their children across China Hubei Xiaogan. A questionnaire was sent to migrant workers that works at a local company, with 129 valid responses returned. The survey covered various aspects, such as access to educational resources, family support for education, and the school environment. The goal was to systematically understand the current educational situation of migrant workers' children in urban areas.

2. In-depth Interviews: In-depth interviews were conducted with a group of migrant workers to gain a deeper understanding of their concerns regarding their children's education and the challenges they face. The interviewees included migrant workers from different age groups and regions, aiming to gather more in-depth qualitative data that would help explore the role of families in education, the practical issues they encounter, and their expectations for education.
3. Case Studies: Five typical case studies were selected to conduct an in-depth analysis of the educational conditions of migrant workers' children. These cases involved students from different types of schools and migrant worker families facing unique challenges in various cities. The analysis focused on the impacts of educational resources, social support, and cultural integration on the education of their children from multiple perspectives.

Results

1. Educational resources are unevenly distributed

- Differences between urban and rural areas and within cities: The data show that the children of migrant laborers tend to concentrate in schools in rural areas or small towns (49.12 per cent) and in third-tier cities (40.35 per cent), while the proportion studying in first-tier cities is only 3.51 per cent. This shows that there are significant differences in the distribution of educational resources between urban and rural areas and within cities, with high-quality educational resources concentrated in economically developed areas. This imbalance in educational resources results in a significant disadvantage for children of migrant laborers in receiving quality education.

- Gaps in School Facilities and Teachers: Many parents in the survey said that the teaching facilities and teachers in schools are unable to meet their children's learning needs. Especially in rural areas and third-tier cities, schools lack modern educational equipment and qualified teachers, limiting the development potential of students.

2. Public schools predominate, but resources are still insufficient

- 78.95% of children of migrant laborers attend public schools, but surveys show that only 9.65% of parents believe that their children's schools provide their children with proficient education. Although public schools are the main place of education, there are obvious deficiencies in their allocation of resources to adequately meet the learning needs of students. Public schools often lack the capacity to provide individualized educational support due to limited funding, resulting in gaps in academic tutoring and psychological support for students.

3. Uneven family participation

- Due to working hours and economic pressures, it is difficult for migrant laborers to participate fully in their children's education. 35.09% of families are very actively involved in

their children's education, while 44.74% are occasionally involved, but 18.42% are rarely involved. This reflects the inadequacy of family support for education, especially the significant gap in participation in academic counseling and school activities. As most migrant laborers work long hours and lack flexibility, they are unable to actively participate in their children's academic activities and school activities as much as local urban residents, leading to a weakening of the family's educational function.

4. Insufficient policy support

- Although the government has introduced a number of policies, such as the “double-decrease” policy, to reduce the burden on students, the specific support provided by these policies to children of migrant laborers is still insufficient, and the needs of migrant laborer families are not effectively met, particularly in terms of access to quality educational resources and fair schooling opportunities. Most policies lack specificity at the implementation level, resulting in children of migrant laborers remaining marginalized in the education system.

5. Difficulties of social integration:

- Children of migrant laborers face difficulties in social integration in cities, such as language and cultural differences that make it difficult for them to fully integrate into city life, resulting in a lack of a sense of belonging and identity in the education system. Some of the students interviewed said that they were ostracized and discriminated against by their peers at school, making it difficult for them to participate in collective activities and leading to a sense of psychological inferiority. This sense of social exclusion further exacerbated their academic stress and negative feelings towards the school environment.

Analysis and Potential Solutions

1. Optimizing the allocation of educational resources

- Potential problem: Focusing investment on under-resourced schools may lead to weakening of resources for other schools.
- Suggested Measures: It is recommended that a needs-based funding allocation model be adopted, along with the establishment of a minimum resource standard for all schools to ensure that no school is left with fewer resources as a result of the new policy.
- Monitoring and Evaluation: It is recommended that an inter-departmental monitoring group be set up to monitor the equity and effectiveness of resource allocation.

2. Strengthening Family-School Interaction

- Potential Problems: Enhancing educational support for migrant families may result in other families feeling neglected.

- Family education support: Conduct education support programs for all families, while paying special attention to those most in need of help to ensure the universality and fairness of the policy.
 - Community Resource Centers: Resource centers serve all community members while providing specific support to more marginalized groups, such as migrant families.
3. Specific and Flexible Policy Support
- Potential Problems: Flexible education support measures may lead to inconsistent and inequitable implementation.
 - Transparent policy implementation: Establish clear guidelines and criteria to ensure policy consistency and fairness across districts and schools.
 - Policy evaluation and adjustment: Regularly collect feedback and adjust the details of the policy accordingly to meet the actual needs of different groups.
4. Promoting social integration
- Potential problems: The promotion of multiculturalism may give rise to exclusion or cultural conflicts among certain groups.
 - Community exchange activities: Consider diversity and inclusiveness when designing exchange activities to ensure that they promote both understanding and respect for the cultural backgrounds of all participants.
 - Cultural education programs: Train teachers and community leaders to effectively manage conflicts that may arise in multicultural environments and to promote positive cultural exchanges.

Conclusion

The education of children of migrant laborers is a complex social issue that involves the distribution of educational resources, family education support, policy support and social and cultural integration. By increasing the government's balanced investment in education resources, strengthening family education support in schools and communities, and improving the policy system, the education status of children of migrant laborers can be effectively improved, the quality of their education upgraded, and the fair and harmonious development of society promoted.

Educational equity is not only an important cornerstone of social stability and harmony, but also an important way for individuals to realize their self-worth. By adopting comprehensive measures in the distribution of educational resources, participation in family education, policy support and social and cultural integration, we can provide children of migrant laborers with a better educational environment and help them gain more opportunities in society, thus enhancing the fairness and inclusiveness of the whole society.

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1 **Bone Tissue Engineering: An Insight into the Viability of its Components**

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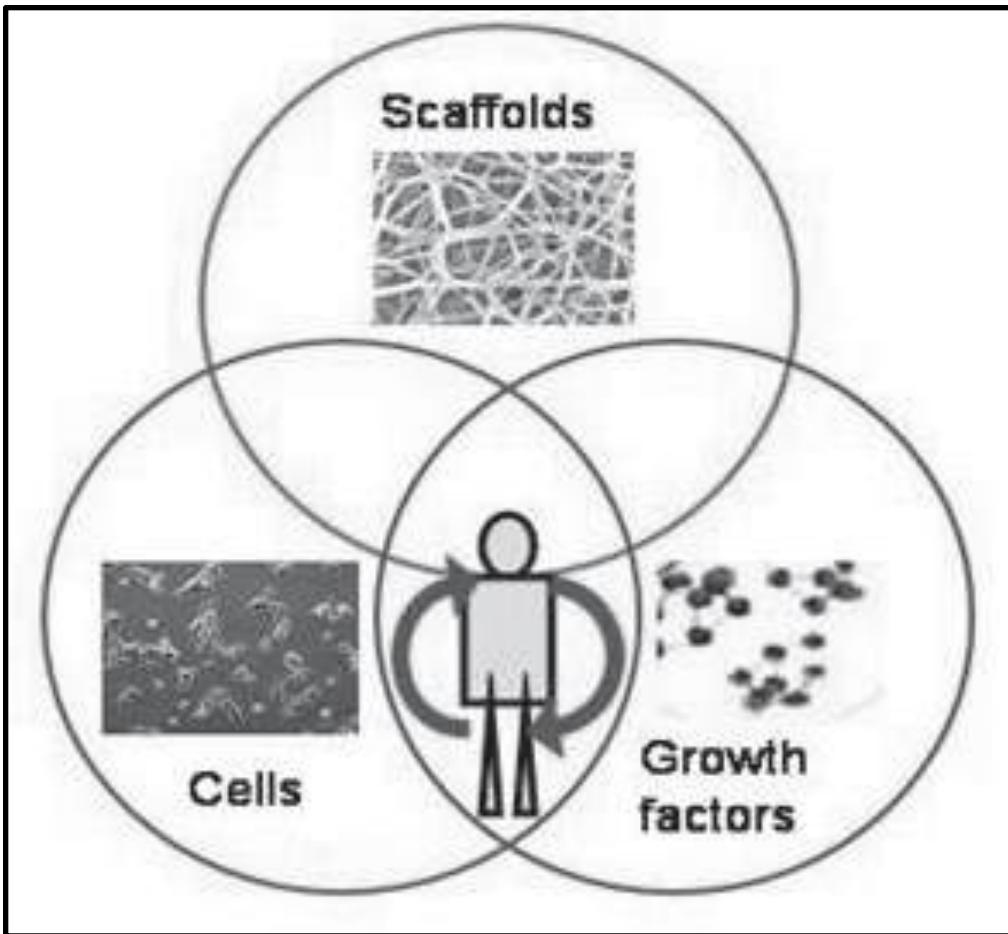
7 **Abstract**

8 Bone tissue engineering is the process by which bone is regenerated by means of bone substitutes, as the bone has a
9 critical sized defect that prevents it from healing. It is most efficient when made up of 3 factors, the scaffold
10 (biomaterial), the growth factor, and the mesenchymal stem cell (MSC). The scaffold is the supporting structure in
11 the bone fracture when the gap is too wide for blood vessels to connect and grow. The scaffold is then injected with
12 mesenchymal stem cells, which then grow and replicate the surrounding bone. To accelerate the process of bone
13 regeneration, growth factors are used. Once healing is over, the newly regenerated bone tissue completely replaces
14 the scaffold. In order for the proliferative and differentiative capacity of the stem cells to be maximized, the three
15 components of bone tissue engineering need to be identified with their various benefits and detriments. The
16 knowledge of these three factors is essential to the health of the patient.

19 *Keywords: Bone tissue engineering, Scaffold, Growth factor, Stem cell*

20 **1. Introduction**

21 Bone tissue engineering has risen in popularity over the last years due to its viability over its alternatives, autogenic
22 and allogenic bone transplantation. Autografts result in significant donor site morbidity and surgical risks such as
23 infection, bleeding, and pain, on top of requiring large volumes of bone. Allografts have lower osteogenic capability
24 than autografts due to being inactive “dead” materials and have higher risk for immune reactions and infection
25 transmission. Overall, both procedures are high cost and demands for materials are rarely met. But even bone tissue
26 engineering has its drawbacks, specifically with its components of scaffolds, growth factors, and mesenchymal stem
27 cells (MSCs). Fig.(1) This paper intends to assess the advantages and disadvantages of specific components
28 individually to determine which components are appropriate for particular patients.



30
31 **Figure 1:** The typical three components of bone tissue engineering, the scaffolds being the support structure,
32 the cells being the mesenchymal stem cells that differentiate into corresponding cells needed for regeneration,
33 and the growth factors being the signaling cells that promote enhanced cell differentiation and proliferation (S. Honsawek.
34 V. Parkpian, 2007).

35
36 **2. Materials and Methods**

37
38 A review of the three aspects of bone tissue engineering conducted using PubMed and Google Scholar. Papers that
39 pertained to scaffolding, growth factors, and stem cells were used to write this report. Keywords and phrases that
40 were searched for include, "bone tissue engineering," "inorganic biomaterials," "natural polymers," "synthetic
41 polymers," "composite biomaterials," "growth factors," "Bone morphogenetic protein," "mesenchymal stem cells,"
42 "Bone marrow," "Adipose tissue," and "Umbilical cord." After an overview of 51 sources, 16 sources were chosen
43 to write the report. The majority of sources date from 2018 to 2021, while a choice few date back to 2010.

44 Figures 2 and 3 are based on work observed at the Lee group laboratory at UCLA. In figure 2, a compression
45 machine is used to calculate the stress and strain of PLGA scaffold through Young's Modulus. In figure 3,
46 microscopes are used on PLGA scaffolds to observe its porous nature. These two figures represent various beneficial
47 elements of PLGA scaffolding that are conducive to stem cell efficacy and proliferation.

48
49 **3. Scaffolds**

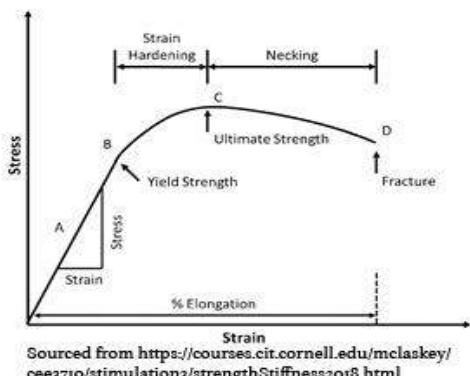
50
51 The scaffold is a vital component to bone tissue engineering. Therefore, its requirements are imperative for effective
52 bone tissue regeneration. These include cytocompatibility (products of the scaffolds should be non-inflammatory

53 and non-toxic), biodegradability (the scaffold should have a controlled degradation, safe for the environment),
54 tunable properties (the scaffold should be able to be fine-tuned to the designer's liking), mechanical features (the
55 scaffold should replicate the elasticity and strength of the bone tissue site), suitable porosity (the scaffold should
56 have micro porosity in order to have enough surface area. Macro porosity is required for cell growth and migration),
57 bioactivity (the scaffold should interact with the tissue in accordance to normal patterns of osteoinduction and
58 osteoconduction), and easy manufacturing (the scaffold should be easy to fabricate and sterilize). The main scaffold
59 types include inorganic biomaterials, natural polymers, synthetic polymers, inorganic-organic composite
60 biomaterials.
61
62

The Compressive Strength of Scaffolds



By utilizing compressions machines (and tensile machines) the stress and strain on the object can be computed. In regards to scaffolds, this determines the Young's modulus, which relates to the durability of the scaffold.



$$\text{Stress} = F / A_{\text{crossoverction}} \quad \text{Strain} = \Delta l / l_0$$

Young's Modulus = Stress / Strain

The larger the modulus the stiffer the tested material is, and vice versa, the lower the modulus is the more elastic the tested material is.

63
64 **Figure 2:** The compressive strength of PLGA scaffold computed through Young's modulus.
65

66 3.1 Inorganic Biomaterials

67
68 Inorganic biomaterials, which are mainly utilized for periodontal repair, orthopedic load-bearing coatings, and bone
69 grafts and cements, include metals and bioceramics; the metals include titanium and its alloys and the bioceramics
70 include HAp, β -TCP, Bioactive glasses, Alumina, and Zirconia. The metal, titanium has high strength, is bioinert
71 (having minimal interaction with its surrounding tissue), and has low density but is not biodegradable and has a low
72 modulus of elasticity. The traits of the bioceramics are as follows: HAp is biocompatible and
73 osteoinductive/osteconductive (osteoinductive meaning recruiting of cells which eventually develop into
74 preosteoblasts that contribute a large part into bone healing; osteoconductive meaning bone growing on the surface),

75 but it is brittle, has low mechanical strength, and has slow resorption rate (the breakdown of minerals which releases
76 calcium and phosphorus into the bloodstream); β -TCP is biocompatible, highly resorbable,
77 osteoinductive/osteocductive, but it is brittle; bioactive glass is bioactive, has high strength, has an elastic
78 modulus, and has wear resistance, but it has fast degradation rates; alumina has high hardness, high abrasion
79 resistance, is bioinert, and has great biocompatibility, but has low fracture toughness and is brittle; zirconia is
80 bioinert, has great fracture toughness, high strength, elastic modulus, wear resistance, and good thermal shock
81 resistance, but its friction against the tooth root has been of concern in crowns. These two ceramics are typically
82 used for hip or knee arthroplasty. Overall, metals are optimized for high strength but lack flexibility and density,
83 while bioceramics have better biocompatibility and osteoconductivity.

84

85 3.2 Natural Polymers

86

87 The natural polymers include collagen, (which has enzymatic biodegradability, cytocompatibility and cell-binding
88 properties, versatility in being processed in different physical forms, possible injectability, and is FDA approved but
89 has low mechanical strength, is difficult to disinfect, and is difficult to handle) gelatin (which is cytocompatible,
90 biodegradable, has porosity tunability, and osteoconductivity, but has poor mechanical properties and low stability
91 in physiological conditions), chitosan (which is cytocompatible, biodegradable, has cell binding, has differentiation
92 and migration properties, has antibacterial properties, has mucoadhesivity, and has tunable properties, but has poor
93 mechanical strength and stability while also having rapid in vivo degradation rate), hyaluronic acid (which is
94 cytocompatible, enzymatically biodegradable, viscoelastic, easily manipulable, and has easy chemical
95 functionalization but has poor mechanical strength and very rapid degradation) alginate, (which is cytocompatible,
96 tuneable, and is easy to gel, but it is difficult to sterilize and has low cell adhesion), cellulose (which is hydrophilic,
97 cytocompatible, bioactive, optically transparent, and has low cell adhesion, but is not biodegradable and has poor
98 osseointegration [the integration of bone with an artificial implant]), silk fibroin (which is cytocompatible,
99 immunogenic, flexibly processable, has limited biological adhesion, high mechanical strength, thermal stability, and
100 easily chemically modifiable but has low mechanical parameters [which include modulus of elasticity, hardness,
101 resistance, and ductility] and high enzymatic degradation rate.) Altogether, natural biopolymers are a viable option
102 due to their biocompatibility and biodegradability.

103

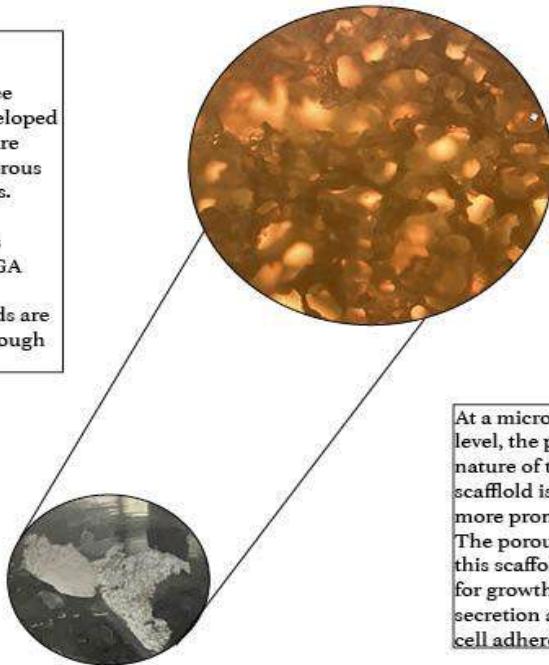
104 3.3 Synthetic Polymers

105

106 The synthetic polymers include PCL or Polycaprolactone (which is cytocompatible, biodegradable, and has a slow
107 degradation rate, but hydrophobic and has low bioactivity), PLA or polylactic acid (which is cytocompatible,
108 thermally stable, has tunable properties but does not have suitable cell adhesion), PLGA or polylacticcoglycolic acid
109 (which has a wide range of degradation rate and tunability but has suboptimal mechanical properties and poor
110 osteoconductivity), PU or polyurethane (which is biocompatible, biodegradable, and has good mechanical properties
111 but has toxic degradation products and has slow degradation). Although synthetic polymers have high strength and
112 stiffness, they can undergo a bulk erosion process causing failure of scaffold, which can lead to release of acidic
113 product and thus an inflammatory process.

Scaffolds at a Microscopic Level

Through the utilization of sucrose, the Lee group has developed a new procedure for creating porous PLGA scaffolds. By creating a heterogeneous mixture of PLGA and sucrose, porous scaffolds are obtainable through solvation.



At a microscopic level, the porous nature of the scaffold is even more prominent. The porous nature of this scaffold allows for growth factor secretion and stem cell adhesiveness.

114

115 **Figure 3:** PLGA scaffolds at a microscopic level.

116

117 3.4 Inorganic-Organic Composite Biomaterials

118

119 The inorganic-organic composite biomaterials consist of SF/ β -TCP or starfish-derived β -tricalcium phosphate,
120 SF/HAp or silk fibroin hydroxyapatite, and collagen/BCP or Bioactive Collagen Peptides. All of these have
121 enhanced mechanical properties, high cell attachment and proliferation, and increased in vivo responses. Despite
122 this, SF/ β -TCP degrades before full bone regeneration, and it has low mechanical strength; SF/HAp is non-
123 biodegradable. The inorganic-organic composite biomaterial is an optimal combination that can induce bone
124 formation, maintain porosity, and keep mechanical strength.

125

126 **4. Growth Factors**

127

128 Actions of adult mesenchymal stem cells (MSCs) include the creation of a regenerative environment via production
129 of trophic growth factors. One strategy in augmenting the impaired bone regeneration process of bones is using
130 growth factors. Combining both scaffolding and growth factors have great potential in being effective in bone
131 regeneration. Growth factors are signaling molecules that assist mesenchymal stem cells with proliferation,
132 migration, and differentiation. These growth factors include FGF or Fibroblast Growth Factor (which is angiogenic,
133 osteogenic, and can proliferate; it is sourced from mesenchymal osteoblast chondrocyte inflammatory cell
134 endothelial; its purpose is to undergo angiogenesis, proliferation, and osteogenic differentiation), IGF or Insulin-
135 Like Growth Factors (which have an anabolic and catabolic effect on osteogenesis; it is sourced from osteoblast
136 chondrocyte hepatocyte endothelial; its purpose is to undergo osteogenic differentiation), PDGF or Platelet-Derived
137 Growth Factor (which is osteoinductive, angiogenic, and can under tissue cell proliferation; it is sourced from

138 platelet osteoblast inflammatory cells endothelial; its purpose is to undergo cell proliferation and vascularization),
139 and TGF-B or Transforming Growth Factor Beta (which is osteoinductive, angiogenic, has immunosuppression, and
140 can undergo cell differentiation and growth; it is sourced from platelet osteoblast chondrocyte endothelial
141 inflammatory cells fibroblast; its purpose is to undergo osteogenic and chondrogenic differentiation).

142

143 4.1 Bone Morphogenetic Protein

144

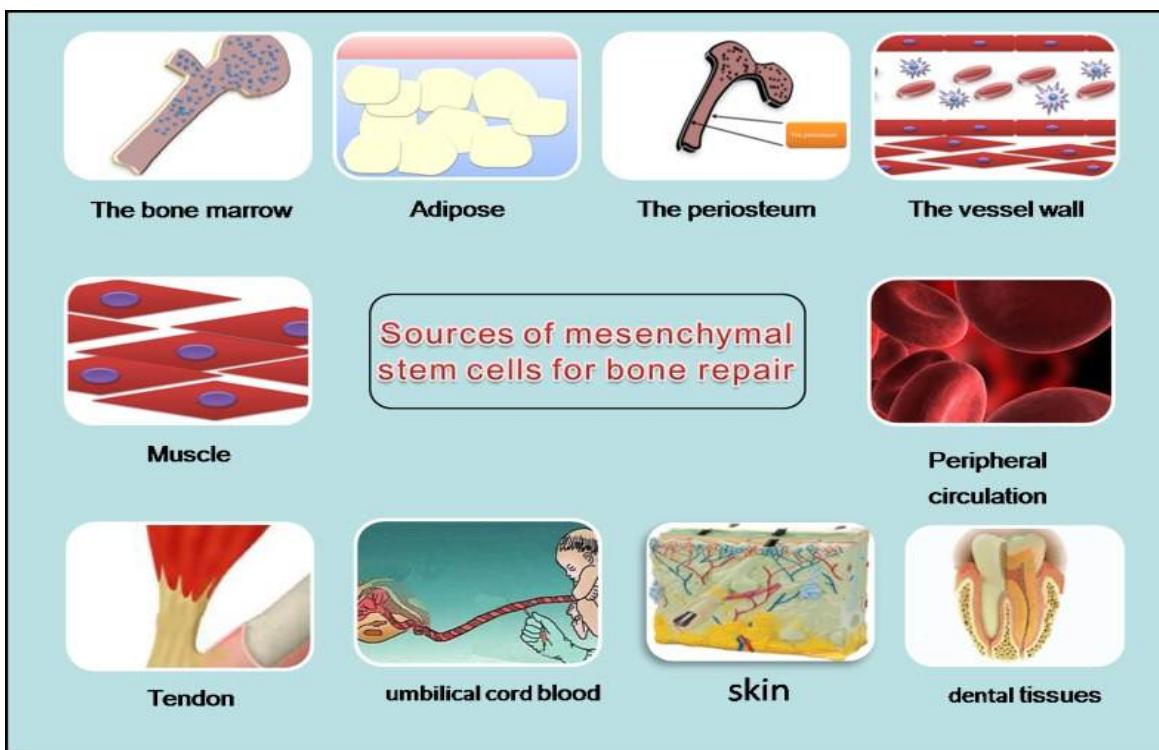
145 BMP or Bone Morphogenetic Protein is chondrogenic, osteogenic, and osteoinductive; it is sourced from
146 mesenchymal osteoblast endothelial chondrocyte; its purpose is to carry out bone induction.⁴ BMP-2 or Bone
147 Morphogenetic Protein-2 is the only Food and Drug Administration (FDA)-approved osteoinductive growth factor
148 used in bone graft substitution.

149

150 5. Stem Cells

151

152 Stem cells act as the most vital component in bone tissue regeneration. The main subsection of stem cells that are
153 primarily used in bone tissue engineering are mesenchymal stem cells. Though mesenchymal stem cells are
154 sometimes identified as only coming from bone marrow, there are actually three most commonly used mesenchymal
155 stem cells. These being: The aforementioned bone marrow stem cells, adipose tissue stem cells, and umbilical cord
156 stem cells. There are distinct differences between each of these three stem cells that should be highlighted.
157 Therefore, it is instrumental to distinguish the traits of each stem cell type in order to accommodate for the situation
158 of any patient.



159 **Figure 4:** An overview of different types of mesenchymal stem cells (X. Wang, et. al., 2013).

160

161 5.1 Bone Marrow Derived Stem Cells

162

163

164 BMSCs are widely regarded as the optimum derivation of stem cells for clinical use. This is because of some key
165 factors: they are immune-modulatory, anti-inflammatory, plastic adherent, and multipotent. The fact that BMSCs are
166 immune-modulatory and anti-inflammatory assists with patient health and comfortability, plastic adherence is
167 beneficial due to the fact that this allows BMSCs to adhere to the inorganic aspects of scaffolding, and multipotency
168 allows BMSCs to be utilized in a diverse manner. In regards to BMSCs' multipotency, they can differentiate into
169 chondroblasts, osteoblasts, and adipocytes; this means BMSCs have tri-lineage differentiation potential, or the
170 ability to differentiate into bone, cartilage, and adipose cells. Additionally, BMSCs can support both hematopoiesis
171 and angiogenesis, which assist in the creation of new blood cells and vessels for regeneration. Furthermore, BMSCs
172 release paracrine factors, promoting the health of surrounding tissue and creating a highly osteogenic cell
173 environment. However, the overall efficacy of BMSCs are dependent on a multitude of factors: whether the source is
174 autologous or allogeneic, cell configuration, the state of the microenvironment around the cell, how the BMSC is
175 transplanted to the area of interest, (whether it be direct, or indirect through migration) the vascularity of the
176 environment, the timing of administration of the BMSC, and how mechanical stress or strain is applied to the
177 BMSC. Along with these variations of the traits of BMSCs, there are certain downsides in all BMSCs. It has been
178 shown that BMSCs may not engraft with high efficiency after transplantation, meaning that the creation of blood
179 cells might not be as rapid as other stem cells. In addition, BMSCs are extremely rare, making up only around 0.01
180 percent of mononucleated cells in bone marrow, and this percent decreases even further as donor age increases, due
181 to a decreased self-renewal capacity and proliferation efficacy.

182

183 5.2 Adipose Tissue Derived Stem Cells

184

185 In 2001, the ATSC was added to the roster of already established stem cells that already included the BMSC.
186 Sharing these traits with BMSCS, ATSCs are also plastic adherent, multipotent, anti-inflammatory, and
187 immunosuppressive. In addition, they have the capacity for self renewal and tri-lineage differentiation. Additionally,
188 due to the fact that ATSCs are derived from autologous fat, they are very easy to obtain and culture. This is possible
189 through minimally invasive procedures such as subcutaneous lipoaspiration and liposuction. Furthermore, adipose
190 tissue is one of the most abundant stem cell sources in the body. Similar to the aforementioned BMSCs, ATSCs also
191 release paracrine factors, including cytokine, transcriptional factors, and growth factors. As a result, ATSCs interact
192 with the nervous system, endocrine system, and cardiovascular system. ATSCs also have variable factors that affect
193 their efficacy. One main example is the difference between white adipose tissue and brown adipose tissue; white
194 adipose tissue stem cells are more common, have a higher proliferation capacity, and differentiation potential. In
195 addition, there are some negative factors that are common in ATSCs. Alike to BMSCs, ATSCs' proliferative
196 efficacy and self-renewal capability decrease heavily as donor age increases. However, due to the fact that ATSCs
197 are derived from adipose tissue, new components must be considered. These include traits that inherently affect the
198 adipose tissue, such as Body-Mass Index (BMI) and gender, but also external traits such as regular smoking. For
199 example, it has been shown that obesity of a donor leads to cancerous cells acting as niche cells, leading to
200 tumorigenesis. Additionally, cigarette smoking has been shown to express lower immunomodulatory and angiogenic
201 capabilities.

202

203 5.3 Umbilical Cord Derived Stem Cells

204

205 The main advantages of UCSCs are multipotency, the utilization of paracrine factors through the secretion of
206 cytokines and interleukins, plastic adherence, self-renewal capacity, and a minimally invasive collection procedure.
207 Adding on, UCSCs are also beneficial in clinical practices due to their immunosuppressive and anti-inflammatory
208 capabilities, and antifibrotic nature. UCSCs are immunomodulatory because their surface antigens are not
209 prominent, allowing for a fewer number of transplanted cell rejections; this allows for allografts to be a viable
210 option. However, there is also a possibility for excessive immunosuppression to occur in UCSCs, causing a higher
211 risk for infection and tumorigenicity. UCSCs are antiinflammatory due to their paracrine effect (production of
212 interleukin-10 and interleukin-4 and the suppression of interleukin-8). Regarding UCSCs' proliferative ability, The

French Academy of Medicine has found that a mm³ Wharton's jelly is able to provide as many as a billion UCSCs in 30 days. This proliferative efficacy does change depending on what area of the umbilical cord is used to harvest the UCSCs. UCSCs are procured from various parts of the umbilical cord, including the aforementioned Wharton's jelly, blood from the umbilical vessels, and the walls of tissue surrounding these walls. In a study comparing the umbilical arteries, umbilical vein, and Wharton's jelly as areas of procurement, it was shown that the umbilical vein is the optimum site for obtaining the UCSCs with the highest proliferative capability.

5.4 Final Comparisons

We have now characterized each of the 3 main derivations of stem cells used in bone tissue engineering, and have seen the common traits of multipotency, self-renewal capacity, plastic adherence, immunomodulatory nature, and anti-inflammatory capabilities. However, within these commonalities, comparisons can be drawn that can infer the efficacy of each stem cell situationally. Firstly, BMSCs and ATSCs demonstrate tri-lineage differentiation potential, while UCSCs do not. This is due to the fact that UCSCs exhibit a very low osteogenic potential. UCSCs are also less immunosuppressive than both BMSCs and ATSCs. However, commonality and proliferation efficacy is also crucial to the quality of stem cells. According to a study, UCSCs proliferate at a higher rate and for a longer period of time than both BMSCs and ATSCs. In addition, when taking into account the procedure of harvesting and donor dependencies, only BMSCs and ATSCs vary greatly due to these factors. BMSCs and ATSCs are dependent on donor age, while ATSCs are also dependent on BMI, gender, and external factors such as smoking. Furthermore, BMSCs are extremely rare within bone marrow and have an invasive harvesting procedure. ATSCs and UCSCs, on the other hand, both have non-invasive procedures, and are abundant from their sources. A study has shown that the yield of BMSCs compared to ATSCs is about 2000 times lower. So, to summarize, ATSCs and UCSCs have the least invasive procedures and are the most common in their donors, BMSCs and ATSCs are the most immunomodulatory and multipotent, UCSCs have the highest proliferative capacity, and ATSCs vary the most due to donor factors. In conclusion, each stem cell has its own positives and negatives that will vary in importance in each clinical use. Thus, these three mesenchymal stem cells act as the pinnacles of stem cell usage in bone tissue engineering.

6. Component Interactions

Now that the three components of bone tissue engineering have been summarized and distinguished, the final discussion of importance is how these three components interact with each other. The synergy between the three components is conducive to an optimized proliferative capacity and differentiation potential of all of three major stem cell derivatives. As mentioned in the prior sections, stem cells can secrete growth factors through the paracrine effect or growth factors can also be added externally. To optimize the utilization of these growth factors, scaffolds are needed to regulate the secretion of growth factors to the stem cells. Extracellular matrices assist in this, as growth factors bind to them, which by extension regulate their secretion. The regulation of growth factor secretion, and thus stem cell proliferation, is vital due to the fact that the niche of the stem cell could cause unwanted differentiation. This is because only stem cells have the ability to differentiate, while the terminally differentiated cells do not. As a general example of this phenomena, if the surrounding cells of the stem cells are tumorigenic, these cells will act as niche cells. If growth factors are not regulated these stem cells will differentiate into tumorigenic cells at an even higher rate. Finally, the interactions between stem cells and scaffolds are vital due to their effect on stem cell development. Stem cells can not develop in suspension, therefore scaffolding must interact with stem cells to help support stem cell development.

7. Conclusion/Summary

262
263 To conclude, we have found that the three factors of bone tissue engineering are extremely variable, whether it be
264 biocompatibility for scaffolds, proliferative efficacy of stem cells, or regenerative capacity of growth factors. Thus,
265 it is important to classify these variations in each component to better understand the optimum usages of all three to
266 better adhere to the patient's needs. Bone tissue engineering and regenerative medicine in general is an innovative
267 and dynamic space right now. Therefore, the general knowledge of already precedent practices is essential to further
268 these innovations to the utmost capacity.
269

270 **Acknowledgment**

271

272 We would like to thank Dr. Min Lee for his help on this paper.

273

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A Perfect Match: Partner Compatibility in the *Pride and Prejudice* Literature By Luran (Amy) Yu

Abstract

Speaking of Pride and Prejudice, an inevitable theme to address is marriage. However, it often intertwines with other themes. Under the original setting, marriage is an indication of socioeconomic status and power as the notion of monetary values permeates throughout the novel, dictating the “material” nature of romance. Mr. Collins intends to arrive in Longbourn to marry a Bennet daughter. His desire for marriage is merely an expression of gratitude for his inheritance. When he later marries Charlotte Lucas, their compatibility does not result from their desire for love but from the mutual benefit of their social reputations. This explicit expression of intention, albeit in different ways, also applies to other Pride and Prejudice remixes. In Pride, Zuri Benitez’s dream for independence aligns with Darius Darcy’s respectful manner, resulting in a successful relationship. In Bridget Jones’s Diary, when encountering two partners from different backgrounds, Bridget’s choice indicates her desire for an endurable relationship. In this close analysis, I unravel the marriage value through various Pride and Prejudice literature to highlight the truth of a successful romance. In general, one would assume that material wealth and socioeconomic status indicate the compatibility of marriage, but it is the intention for marriage that determines the success and longevity of this romance.

Introduction

It is a truth universally acknowledged that marriage within comparable socioeconomic backgrounds is compatible. Partner compatibility, measuring the success of romantic relationships, symbolizes one’s sincere desire to prolong their romance. Though lacking a unanimous definition in society, the metrics of romance implicitly appear in existing literature, confirming society’s long assumption of the importance of equal socioeconomic status (SES) in partner compatibility. In *Pride and Prejudice* by Jane Austen, the concept of marriage intertwines with the themes of material wealth and permeates the novel. Austen thoroughly presents this central inclination of equal or superior social standing, including educational background and other material proof of one’s prosperity, in pursuing a sustainable romance. The seemingly sound formula of partner compatibility unveils:

$$\text{Partner 1 SES} \geq \text{Partner 2 SES}$$

This simplified formula morphs to adapt to realistic social circumstances. In 18th-century patriarchal England, the rigid social structure regulated expressions of love and courtship, limiting the tangible practices of romance. Therefore, marriage became the only clear expression of love. Nonetheless, this cultural practice deviated from its original purpose, gradually evolving into a means for exchanging resources and forming social connections, benefitting primarily the middle class, as the prohibition of female inheritance hinders a family’s advancement on the social ladder. Therefore, an ideal marriage in *Pride and Prejudice* is as follows:

$$\text{Male partner SES} > \text{Female partner SES}$$

Apart from the social definition of marriage and love, the ultimate goal of romance ought to be emotional satisfaction. The perceptual end of a relationship signifies heart-pounding experiences of falling in love. In this way, a romance is incomplete without an emotional spark, as partners sense the biological attraction that strengthens their connection. However, the quality of a romance does not invalidate the rational factors sustaining its longevity. When both partners pursue goals other than affection in marriage, this partnership enhances the relationship despite shifting away from a traditionally recognized love. In essence, a loveless relationship does not indicate a meaningless one, though not conforming to the general expectations of romance, can become a successful match as partners possess complementary motivations.

In general, one would assume that material wealth and SES indicate marriage compatibility, as material possessions indicate one's life experiences and values. However, this explanation fails to provide a holistic understanding of the rationale behind successful marriages; that is, genuine partner compatibility depends on the intention of marriage, regardless of one's upbringing and SES. Therefore, this paper examines the effect of the matching intention in determining the viability of a romantic relationship through *Pride and Prejudice* and its remixes created over time with similar romantic plots but under various social settings.

Marriage in the Regency Era

In the Regency Era in England, the limitations of social structure and technology restricted communications. The progression of social relationships marked a tedious process of conformity to the social order—people, especially women, lacked the freedom to socialize. In *Pride and Prejudice*, social norms dictate the development of a courtship, with the envisioned goal of a lasting marriage. The opportunities to seek relationships often occur through private invitations to semi-public spaces such as ballrooms, where individuals of similar social status mingle. Therefore, in order to achieve status change through romantic relationships, one must seize the opportunity for upward networking. During such occasions, besides verbal interactions stimulated by matchmakers, gentlemen invite ladies for dances as a manifestation of their fondness and an indication of courtesy. As one gradually develops a match on social occasions, partners would continue their communications through letters until the settling of engagement. In such an era of reservedness, one could interpret affections through actions instead of outright statements; the only tangible evidence of love occurred through matrimony. Consequently, historical restrictions on courtship contributed to the formation of false conceptions about romance.

As social structures regulated the procedure of forming romantic relationships, established practices gradually erased human emotion from the picture. When Mr. Bennet notifies his wife of the arrival of Mr. Bingley, her astonishment with this affluent gentleman's making of “four or five thousand a year” (Austen, 2) indicates the weight of income in her criteria in judging a son-in-law. The initial encounter with Mr. Darcy highlights the wide acceptance of this criteria when Darcy’s income of “ten thousand a year” (Austen, 7) and his luxurious estate at Pemberly captivate the public and even diverts their attention from Mr.

Bingley, who appears more amiable but inferior in economic status. Therefore, in seeking a partner, one's wealth plays a significant role in the first impression.

Furthermore, with the presence of patriarchy, families fretted about the future—the husband—of their daughters. Their primary solution aimed at arranging an upward marriage. Mr. Collins, initially an irrelevant relative, reveals his legal inheritance of “an estate away from a family of five daughters” (Austen, 52) due to the lack of a male inheritor in the Bennet family for their Longbourn estate. Despite the grudges from Mrs. Bennet, the only viable solution to accept is marriage. Even so, this choice would primarily ensure the prosperity of her daughters instead of regaining control over the estate. Nevertheless, Mrs. Bennet, a reflection of public opinion, readily regards this gracious man with “her good graces” (Austen, 61), for she retains a steady future for her daughters through such unequal exchange.

Under the constraints of existing social orders, people uphold the inherently unjust norms for a temporary material benefit, forsaking their rights and continuing a legacy of oppression. In specific, marriage loses its original romantic connotation but evolves into a practical method to build social connections and elevate socioeconomic status. With the increasing practice of this notion, a biased definition of relationship and marriage continues to prevail among people, forming a false impression of these romantic customs. Therefore, this inaccurate assumption that material wealth and SES predict the compatibility of marriage misleads people with a flawed concept of love.

Marriage compatibility in *Pride and Prejudice* and remixes

To unravel a genuine criterion of partner compatibility, marriage examples in *Pride and Prejudice* and remixes present a valuable case study, for the couples connect in an asymmetrical way but collectively possess a promising future.

As protagonists in the original plot, the relationship between Elizabeth Bennet and Mr. Darcy symbolizes a unity of shared unique characteristics. Despite their disparate upbringings, both characters express a firm arrogance through pride and prejudices from their first impression, which repels the two personalities. Elizabeth's tenacity originates from her independence, while Mr. Darcy's social standing shapes his dignity—both individuals steadfastly maintain their beliefs. Elizabeth is a courageous lady who refuses to obey social conventions. She unreservedly refuses Mr. Darcy's initial dance invitation and adamantly rejects Mr. Collins's proposal. In the ballroom, Mr. Darcy receives his first sarcasm from Elizabeth due to his indifference toward unoccupied ladies at the ball. Similarly, Mr. Darcy views others critically, demonstrating his confidence in public while disdaining unnecessary flattery, as shown in his attitude towards Mr. Collins.

When they encounter misunderstandings, both sides are willing to yield and recognize their bias. After his unsuccessful proposal, Mr. Darcy humbly reflects his pride and acknowledges his mistakes through a lengthy, thoughtful letter in which he exposes the stigma of his family. From Elizabeth's perspective, she critically evaluates Darcy's offense to her family. In spite of the protectiveness of her family, Elizabeth recognizes the honesty within Darcy's

uncensored proposal and his letter. Since then, both sides have reevaluated each other through an altered lens, and such similarity in personality leads to their eventual union. Overall, the formation of the Elizabeth and Darcy romance develops with little emphasis on economic status but instead on personalities. Considering that both matrimonial intentions seek attraction of inner beauty, this match appears compatible, as indicated through this equation:

$$\text{Darcy's Personality} = \text{Elizabeth's Personality}$$

Compared with Elizabeth's romance, Charlotte's marriage with Mr. Collins has more practical benefits to both ends. The specific intention of marrying Charlotte differs from that of Mr. Collins. When persuading Elizabeth of her intention, Charlotte emphasizes that she wishes for "a comfortable home [and] Mr. Collin's character, connections, and situation in life" (Austen, 109). As a nonromantic person, Charlotte does not long for an emotional attraction from her partner. Her goal is simple: conform to the societal expectation of a woman's marriage and sustain a decent life. Therefore, Charlotte seizes the valuable opportunity as she recognizes Mr. Collins's need for a wife and accomplishes her mission.

Regarding Mr. Collins, his arrival at Longbourn primarily aims to marry one of the Bennet sisters. However, as a single man with a high sense of superiority, he willingly accepts any pursuer, for the inheritance law already ensures his future advancement. Since one is in search of a husband and the other lacks a wife, despite the difference in individual goals the two possess, this loveless yet complementary partnership presents a balanced equation:

$$\text{Charlotte's urgent need for marriage} + \text{Collins's lack of a wife} \rightarrow \text{compatible partnership}$$

An outlying example of an incompatible marriage in *Pride and Prejudice* is the relationship between Lydia and Wickham. As a naive, ignorant teenage girl, Lydia fiddles much of her life, flirting with men and looking for a romantic partner to gain respect among her sisters. Though she is not mature enough to envision an ideal relationship, her random participation in social occasions leads to her encountering Mr. Wickham and crushing on this seemingly educated, attractive militia. Likewise, Wickham's decision to form a romance with Lydia does not originate from true love—he flees from the regiment as a result of his debt. Consequently, the idea of eloping with Lydia emerges as it poses no harm to his escape. Moreover, when Mr. Darcy approaches Wickham with enough money but asks for an orthodox marriage, he readily agrees to the condition. Therefore, as the intention of marrying Lydia aims for Darcy's money, a short-term gain, while Lydia's vanity indicates her temporary attachment to Wickham, one can easily anticipate the end of their short-lived marriage.

Despite such disparities, social conventions force the formation of such a marriage in avoidance of family stigma. Since their elopement was the result of lust instead of an authentic romance, the decision to marry is not a spontaneous plan but an enforcement of the social norms. Therefore, the motive of this couple's partnership does not entail an eventual marriage; hence, the metrics of marriage compatibility inherently fail in their case:

$$\text{Lydia's crush on Wickham} \neq \text{Wickham's paying for debt through the means of marrying Lydia using Darcy's money}$$

The formula of partner compatibility also applies to the contemporary world and other cultural backgrounds, with slight modifications to its format. In *Pride* by Ibi Zoboi, the original Anglo-centric setting shifts to Bushwick, New York. The additional racial theme highlights the emphasis on socioeconomic status in society. The two protagonists, Zuri and Darius, inherit the original characteristics of Elizabeth and Darcy and experience a hate-to-love transition. In this modern society, a more understanding culture often accepts explicit actions of affection, but the exact expectations for socioeconomic status remain unchallenged.

Moreover, the young age of the two protagonists creates a more nuanced relationship, inevitably encountering conflicts. Nevertheless, the two demonstrate their partner compatibility through conflict resolutions: inputs from Zuri and processing by Darius that yield a harmonious output. Zuri's pride and independence (at a higher level than Elizabeth Bennet's) are balanced by Darius's understanding. Thus, this input/output system resembling their relationship determines the successful romance:

$$Zuri's\ independence + pride \rightarrow Darius's\ understanding \rightarrow compatible\ partnership$$

In front of two pursuers with similar socioeconomic status, one's choice would indicate their romantic ideals. In the movie *Bridget Jones's Diary [2001]*, Bridget flirts with her handsome boss, Daniel, when she encounters the son of her family friend, Mark Darcy. Suddenly, two options lay in front of this "spinster." As an awkward personality, Bridget needs understanding and support from her partner. When Bridget embarrasses herself at the workplace, Daniel reassures her and invites her to a date night. When Bridget struggles to cook for her friends, the sudden arrival of Mark brings her encouragement and assistance. Bridget also seeks a loyal partner. Despite Daniel's physical attractiveness, she despises his disloyalty in a relationship and his untrue telling of Mark's marriage. Similarly, Mark seeks a loyal, respectful partner; he is unafraid to retrieve his pursuit when he misinterprets Bridge's diary. As a result, Bridget adamantly rejects Daniel due to his infidelity and pursues Mark by resolving their misunderstanding once she recognizes Mark's desirable characteristics. Consequently, when one has a defined qualities goal in a partner, the discovery of a compatible match yields easy success:

$$Bridget's\ ideal\ partner\ characteristics = Mark's\ ideal\ partner\ characteristics$$

The process of forming romantic intentions

The formation of diverse marriages and couples in the *Pride and Prejudice* literature proves the determinant role of romantic intentions on partner compatibility. Regardless of specific motivations, the matching of such goals ensures a sustainable relationship. Moreover, *Pride and Prejudice* and its remixes discuss the societal influences on the formation of such expectations.

In the original context, a conservative society that restricts female social roles, the primary intention for marriage is the obligation from social norms. A rigid patriarchal society regulates the activities of females in different life stages. As adolescent girls mature into young adults, they ought to seek single men to complete their transitions in societal roles from daughters to wives. Those with little freedom thus conceptualize marriage as a cultural obligation

rather than a romantic pursuit. There is essentially little love in a monitored— even arranged— marriage. In the *Pride and Prejudice* world, however, Charlotte's mundane decisions become the outlier from Elizabeth's perspective, while Elizabeth's marriage values reflect the longing for a fairy tale love as a result of social constraints. Therefore, the peculiarity of the Elizabeth and Darcy romance, the presence of love, finds its only expression through literature as a collective hope in reality.

The surmounting attention of *Pride and Prejudice* aligns with the emergence of genuine romance in reality that breaks away from the shackles of archaic traditions. Thus, as modernization renews society, the motivations for a relationship alter, as indicated through other *Pride and Prejudice* literature. The increasing female autonomy allows Zuri Benitez to pursue education and to dream beyond marriage. Additionally, Bridget Jones receives understanding from her family despite being single in her thirties. The rise in female awakening in literature reflects the change in norms in society, which provides a greater freedom of romance. In this way, the intentions of love become more diverse and personal, as one is thus able to envision a relationship of their own without tailoring to adhere to social expectations.

Conclusion

Society dictates one's role in public spheres, which often influences one's decisions within private spheres. From the 18th century in England to the current global society, people's romantic ideals represented an interconnection with their competence and societal roles. This causal relationship between their experiences and romantic views shapes their individual marriage values. Consequently, as a result of the legacy of traditional societies, a widespread misconception regarding marriage compatibility denotes the importance of socioeconomic status. From a holistic perspective, however, the encompassing metric measuring partner compatibility relies on the marriage intention. Through the revelation in *Pride and Prejudice* literature and its adaptations to the modern world, the matching of this intention proves its enduring validity in determining the eventual success of a marriage. The formula reflecting compatibility in the *Pride and Prejudice* context, despite nuance alterations in adaptation to specific settings, proves its paramount significance in maintaining a balanced, lasting relationship. Therefore, regardless of the distinctiveness of individual marital preferences, one can always ensure a longevous relationship via compatible intentions.

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Applications of the Riemann Zeta Function in Cryptography

Ryan Doraiswamy

1.1 Abstract

Understanding the Riemann hypothesis is integral for the continuation of math into the future and potentially the security of cyberspace. The Riemann hypothesis is one of the Millennium Problems, a set of 7 famous unsolved problems in mathematics. It is a hypothesis that scientists and mathematicians alike have tried to prove for decades, but have not yet been successful. It is hypothesized that it may have applications in various mathematics and scientific fields, such as quantum mechanics. Beyond that, the applications of the Zeta function and Riemann hypothesis are relatively unknown.

One way the hypothesis can potentially be used is in cryptography. Using the implications of the hypothesis and the distribution of prime numbers, algorithms can be created through the primes to send and receive messages with dependable security. In this project, the hypothesis was used to create an algorithm that can generate long alphabetical phrases to relay classified information in a unique way that might be difficult to identify for an adversary. These results indicate that there are applications of the hypothesis in cryptography and that one could algorithmically create prime number sequences that could be used for encryption and decryption. This finding is significant as it provides supplemental evidence for the Riemann hypothesis, while also opening a pathway to explore unfamiliar connections between number theory and cryptography.

1.2 Introduction

Riemann Zeta function:

The Riemann Zeta function belongs to a class of functions known as Zeta functions, and can be written in series notation as denoted below:

$$\zeta(n) = \sum_{k=1}^{\infty} \frac{1}{k^n}$$

The Riemann zeta function is a mathematical tool used to understand the distribution of prime numbers. It was introduced by the mathematician Bernhard Riemann in 1859. The function itself has roots going back to earlier work by Leonhard Euler in the 18th century. The primary purpose of the Riemann zeta function is to explore the properties and distribution of prime numbers.

Unlike simpler functions that deal with whole numbers or real numbers, the Riemann zeta function deals with complex numbers (numbers that have both a real part and an imaginary part).

Of all the zeta functions, the Riemann Zeta function is arguably the most well-known, although the extent of its applicability is not as well-known and has not been fully explored. More specifically, The Riemann Hypothesis is a hypothesis about the zeros of the Riemann Zeta function, stating that the non-trivial zeros of the function all lie on the *Critical line* $\text{Re}[s] = \frac{1}{2}$, where $\text{Re}[s]$ denotes the real part of a complex number s . The non trivial zeros are the zeros that contain an imaginary as well as real component. The hypothesis is of great interest in number theory due to its theorized connections with the distribution of prime numbers.

Chebyshev PSI function:

The Chebyshev PSI function is a function that can help calculate prime density. The function is defined as the sum of the logarithms of the prime numbers with powers less than or equal to a given value. It is often denoted by $\Psi(x)$, and is given as

$$\psi(x) = \sum_{k=1}^{\infty} \sum_{p^k \leq x} \log p$$

The function, rather than focusing on the exact values of prime numbers, focuses on their distribution, and it can be incredibly useful as it is simple to evaluate and connections can be drawn to the Riemann hypothesis through the Prime Counting function described in the following section. This is through various studies and proofs dating back to the work of Euler.

Prime Counting Function

The Prime Counting function is a function that is given to us by the proofs of the Riemann hypothesis. Although incomplete, the parts of the proof that exist allow us to draw connections between the two functions, as many famous mathematicians have done before. It allows for us to know the exact number of primes less than or equal to some number x .

$$\pi(x) = |\{p \leq x : p \text{ is prime}\}|$$

The explicit formula for $\pi(x)$ involves a sum over the non-trivial zeros of the Riemann zeta function. Assuming the Riemann Hypothesis, the explicit formula for $\pi(x)$ can be written as:

$$\pi(x) = Li(x) - \sum_p Li(x^p) + c$$

Where $Li(x)$ is the logarithmic integral, given by

$$Li(x) = \int_2^x \frac{dt}{\log t}$$

And p runs over the non-trivial zeros of the Riemann Zeta function. c denotes small correction terms negligible for large x .

Because it gives the exact number of primes less than or equal to a target, it can also be used in the context of prime density. For example, $\pi(10)$ would refer to the amount of primes between 0 and 10, which would evaluate to 4. This can also be thought of as 4 prime numbers out of 10, meaning a 40% density of prime numbers over the interval $[0,10]$. It is important to note, with respect to the Prime Counting function and the Chebyshev PSI function, that as intervals (the argument to the Prime Counting function and related prime density estimate) get larger, the accuracy of the density estimate will decrease. However, the function serves as a strong estimate.

Sieve of Eratosthenes and RSA algorithm

The Sieve is a simple algorithm used to find all prime numbers up to a specified integer n . This is significant to this research as the Prime Counting and Chebyshev PSI functions allow us to know the amount of prime numbers within specified intervals and the density of them within those intervals, respectively.

The RSA algorithm is an algorithm that utilizes prime numbers to encrypt and decrypt data, e.g., words like “Rainbow” “GOOD DAY” or “Stick”. The RSA algorithm utilizes large prime numbers to create a *public key* that encrypts data (convert plaintext into ciphertext), and a *private key* that decrypts that data (convert ciphertext back into plaintext), ensuring that only authorized parties can access the information. Such mathematical cryptography is the practice of securing information through the use of mathematical techniques. Cryptography relies heavily on mathematical theories and computational algorithms to protect data and communications.

Research Question

The theorized research question is “Can we find an application of the Riemann Zeta function in cryptography?” If the Riemann hypothesis lends itself to accurately computing the Prime Counting function, then there may be plausible applications of the Riemann Zeta function in cryptography, due to its relation to the Prime Counting function. In order to find an application of the Riemann Zeta function in cryptography, one can look to employ the Prime Counting function, Chebyshev PSI function and the Sieve of Eratosthenes, utilizing their properties and information they relay regarding prime numbers.. Initially, tests need to be run to ensure the agreement of the Prime Counting function and Chebyshev PSI function to ensure their estimates for prime density are sufficiently close (in order to justify using the PSI function over the Prime Counting function as it is computationally simpler). In the case that they are sufficiently similar, one can develop algorithms to check for prime density on larger and larger intervals. One can use the PSI function in order to estimate the density on those intervals and use the Sieve to find the prime numbers on the interval. Then, the large prime numbers can be used within the RSA algorithm for secure encryption and decryption.

1.3 Methods

A: Review of Cryptographic Algorithms:

To develop a new cryptographic algorithm, one should start by studying existing algorithms for inspiration. Begin with the Advanced Encryption Standard (AES), which was created to secure sensitive information and became a standard due to its robustness and efficiency. Understanding AES's purpose and development process will provide valuable insights into designing a strong algorithm. Next, explore algorithms that utilize prime numbers, such as the RSA algorithm, to understand how prime numbers are employed in encryption and decryption processes. This analysis will help identify the role of prime numbers and their potential application in the new algorithm.

B: Creating Connections

In the research, the Chebyshev PSI function was tested to find connections between it and the Prime Counting function suitable for algorithm design. In the code, the Chebyshev PSI and the Prime Counting function were tested together on 10 different intervals: (0, 100), (0, 200), (0, 300), and onwards, and the results showed that the answers differed by approximately 0.06, allowing for them to be used interchangeably in this research due to their small difference. It was found that as the amount of primes increased over intervals on number line, prime density also increased.

C: Testing

An algorithm was created and then tested to check the efficiency of the Prime Counting function in comparison to the Chebyshev PSI function via a simple brute-force method. Then, an algorithm was written to take interval values and extract prime numbers, substituting them into the RSA algorithm to determine the results.

The code for the Sieve and Chebyshev PSI functions are written below:

```
function sieveOfEratosthenes(limit) {  
    var sieve = [];  
  
    for (var i = 0; i <= limit; i++) {  
  
        sieve.push(true); // Initialize all elements to true  
    }  
  
    for (var p = 2; p * p <= limit; p++) {  
  
        if (sieve[p]) {  
  
            for (var i = p * p; i <= limit; i += p) {  
  
                sieve[i] = false;  
            }  
        }  
    }  
  
    var primes = [];  
  
    for (var i = 2; i <= limit; i++) {  
  
        if (sieve[i]) {  
    }
```

```

        primes.push(i);

    }

}

return primes;

}

// Function to calculate Chebyshev psi function

function chebyshevPsi(x) {

    var primes = sieveOfEratosthenes(x);

    var psi = 0;

    for (var i = 0; i < primes.length; i++) {

        psi += Math.log(primes[i]);

    }

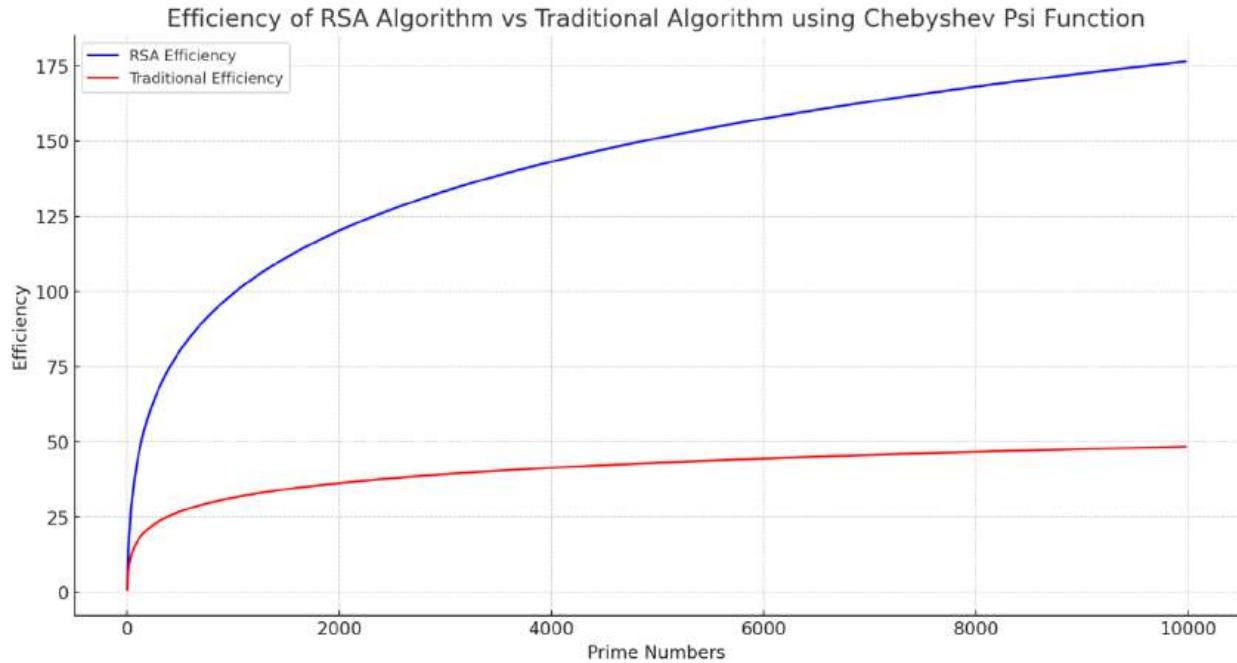
    return psi;

}

```

D: Analysis

In the post-experimental analysis, the algorithm's effectiveness and its benefits and detriments were analyzed in comparison to similar algorithms that perform similar functions, such as the ones mentioned previously in the paper. This allowed for conclusions to be drawn about the potential effectiveness of the Riemann Zeta Function within the context of cryptographic algorithms.



This graph shows the comparative efficiency of the modified RSA algorithm described in this research against a traditional algorithm over larger and larger intervals, where efficiency is defined as

. It shows that the algorithm proposed in this research has a much greater efficiency.

$(p) = (\log_2(p))^2$ This function was used to create an efficiency scale, where p is the amount of prime numbers. The function takes into account the seconds taken, and improves that by using a simple algorithm.

1.4 Results

When exploring the application of the Riemann Zeta function in cryptography, several key findings arose. The findings were that there was a connection between the Chebyshev PSI

function and the Prime Counting function and that they could be utilized to create a cryptographic algorithm that evaluated prime density. Because of the way RSA utilizes primes, using large prime numbers on an interval can help create longer encryptions of words that can be harder to decipher due to their size, since the difficulty of factoring large primes is the theoretical basis of RSA. The Chebyshev PSI function was used to find intervals with high prime density. Then the Sieve of Eratosthenes was used to find the specific prime numbers on those intervals. These primes were then used within the RSA algorithm in order to generate the encryptions, which would then be decrypted by the receiver of the message. This was an application of the Riemann Zeta function as it utilized conclusions of the Riemann hypothesis and the Prime counting function and drew similarities to the Chebyshev PSI function, which was then used to create a cryptographic algorithm to generate prime numbers over an interval.

```
Prime Interval with High Density: [1009, 1013, 1019, 1021, 1031, 1033, 1039, 1043]

Public Key: (317, 155779)
Private Key: (79373, 155779)

Original Message: This is a message encrypted using the Riemann Zeta function.

Encrypted Message: [131810, 128279, 141977, 138613, 142882, 102719, 140996, 135951]

Decrypted Message: This is a message encrypted using the Riemann Zeta function.
```

Figure 1: Example usage of the RSA algorithm in tandem with the Zeta function

This is an example of the running of code over the interval [1000, 1500]. The function takes all of the prime numbers over the interval and uses them to encrypt a message. Once encrypted, it is decrypted using the private key of the receiver, displaying the original message.

1.5 Discussion

Based on the results section, this application of the Riemann Zeta function lends itself to encrypting messages and sending them to others who can decrypt them using their own generated private key. As compared to other prominent algorithms for encryption and decryption, this algorithm may offer unique benefits due to the advanced security through its complexity. The algorithm primarily serves to be supplemental evidence for the Riemann hypothesis and demonstrates that the hypothesis can be applied with similar efficacy to traditional algorithms in cryptography.

1.6 Summary and Conclusions

The original goal of the project was to explore potential applications of the Riemann Zeta function within cryptography, a mathematical function that has not been extensively studied in this context. The project successfully identified a novel application of the Riemann Zeta function in enhancing cybersecurity protocols. Specifically, the function was utilized to develop a new encryption algorithm that significantly improves the security of digital communications by using the complex properties of the Zeta function to create better cryptographic keys. This breakthrough not only demonstrates the utility of advanced mathematical concepts in cybersecurity but also paves the way for further research and exploration in the field of cryptography. The findings suggest that incorporating the Riemann Zeta function into cryptographic frameworks can offer new methods for securing data, protecting against cyber threats, and ensuring the integrity and protection of sensitive information. This approach has the

potential to revolutionize current cryptographic practices and inspire future advancements in the discipline.

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Stem Cell Therapeutics for Crohn's Disease

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Abstract

Inflammatory bowel diseases (IBD), which include Crohn's disease (CD) and ulcerative colitis (UC), are a group of chronic, relapsing-remitting, inflammatory conditions of unknown etiology, affecting the gut. The CD is a chronic inflammatory disease of the gastrointestinal tract that might lead to progressive bowel damage and disability. The disease is believed to arise from an uncontrolled immune response against intestinal microbes or microbial components that are transmitted by the intestinal mucosa. According to the most recent data from the CDC, there were over three million adults living with CD or UC in the United States. Approximately 38% and 70% of patients with CD undergo surgery in the first 10 and 20 years after diagnosis, respectively. Current treatments including biologics work by inhibiting inflammatory response but cannot achieve durable remission periods. An effective and safe treatment is urgently required. Stem cell studies and clinical trials have proven the potential to modulate immunity and achieve efficacy in treating CD. This review provides an overview of the regenerative capabilities of stem cells in repairing gut intestinal tissues and promoting immune system regulation in the gut. Additionally, the paper will highlight current limitations and future perspectives of stem cell-related therapy for CD/IBD.

Keywords

Crohn's Disease, Inflammatory bowel diseases, Ulcerative Colitis, fistulization, CRISPR, Colorectal Cancer, Anemia, Biologics, Stem Cells, Regenerative Medicine, Mesenchymal Stem Cells, ESCs, HSCs, ASCs, iPSC, Organoids, Transplantation, Immune Suppression, Tumor Necrosis Factor, Immunology, Human Intestinal Organoid, HIO, Stem Cell Studies, IBD

Introduction

Inflammatory Bowel Disease (IBD) includes Crohn's Disease (CD) and Ulcerative Colitis (UC), conditions that are characterized by chronic inflammation of the gastrointestinal tract. CD may affect any part of the GI tract, is patchy in distribution, and has full-thickness inflammation, whereas UC is limited to the colon and rectum, with continuous and superficial inflammation. CD is a debilitating and incurable chronic IBD affecting more than 2.5 million individuals in the Western world and has an increasing incidence in the developing world². CD can affect any part of the gastrointestinal tract. It can progress from initially mild to moderate inflammatory conditions to severe penetrating (fistulization) or stricturing disease. If left untreated, the disease becomes more severe and may also lead to potentially serious complications, including stricture formation, which can lead to intestinal obstructions, anemia, osteoporosis, kidney stones, and colorectal cancer.

There is no single treatment that works for everyone, the goal of current medical treatments is to reduce inflammation. With recent advances in molecular biology and understanding of immunologic pathways in IBD, therapies include new biologics and stem cell therapies. Multiple specific drug targets within the inflammatory pathways, via the use of monoclonal antibodies (e.g., Tumor Necrosis Factor α [TNF α], IL-23, IL-17) and, more recently, small molecules (e.g., JAK inhibitors), have been developed⁶. However, inhibiting the

inflammatory response (anti-TNF- α antibodies) alone is insufficient to completely cure CD and achieve long-term remission and mucosal healing. Therefore, there is an unmet need for the development of highly effective and safer therapeutics that can advance the management field in CD and provide better clinical, endoscopic, and histologic outcomes.

Stem cells (SCs) have emerged as innovative and effective therapeutics for CD, given their anti-inflammatory and regenerative properties. SCs have the potential to modulate immunity, suppress inflammation, and have anti-apoptotic and pro-angiogenic effects, making them an ideal therapeutic strategy to target chronic inflammation and intestinal damage in IBD¹. The therapeutic potential of SCs is primarily attributed to their roles in pro-angiogenesis, cellular homing, and immune regulation. Intestinal resident SCs, mainly intestinal stem cells (ISCs) and resident mesenchymal stem cells (MSCs) maintain the structure and function of intestinal structural and immune cells, preserving intestinal mucosal integrity and immune homeostasis. Transplantation of SCs can regulate or rebuild immune cells, repair or supplement structural cells, such as intestinal epithelial cells (IECs), and potentially lead to a complete cure of CD.

This review summarizes the current research progress on the safety and efficacy of SC-based therapy for IBD in both preclinical models and clinical trials. We discuss potential mechanisms of SC therapy, including tissue repair, paracrine effects, and the promotion of angiogenesis, immune regulation, and anti-inflammatory effects. The current SC engineering strategies aimed at enhancing the immunosuppressive and regenerative capabilities of SCs for treating intestinal diseases are also highlighted.

Results

This review focused on whether SC therapy can improve CD. It is evident after reviewing SC clinical studies conducted so far that SC transplantation reduces gut inflammation and improves the quality of life. However, more high-quality randomized controlled clinical trials and basic research are required.

Discussion

Disease Pathogenesis & Progression

CD pathogenesis involves a complex interplay over time between genetic, epigenetic, immunological, and microbiological mechanisms affected by exposure to triggering factors. Some of the environmental factors are smoking, drug use, diet habits, mental stress, and many other external factors are related to the occurrence of IBDs. Distinguishing features of CD include discontinuous, transmural inflammation involving the whole thickness of the bowel wall, and an inflammatory response associated with lymphoid aggregates and granulomas. The most widely accepted hypothesis purports CD as an immune-mediated condition in genetically susceptible individuals, where disease onset is triggered by environmental factors that perturb the mucosal barrier, alter the healthy balance of the gut microbiota, and abnormally stimulate gut immune responses². In addition, CD has a strong genetic tendency, especially in the first-degree relatives of patients who are at higher risk for IBDs.

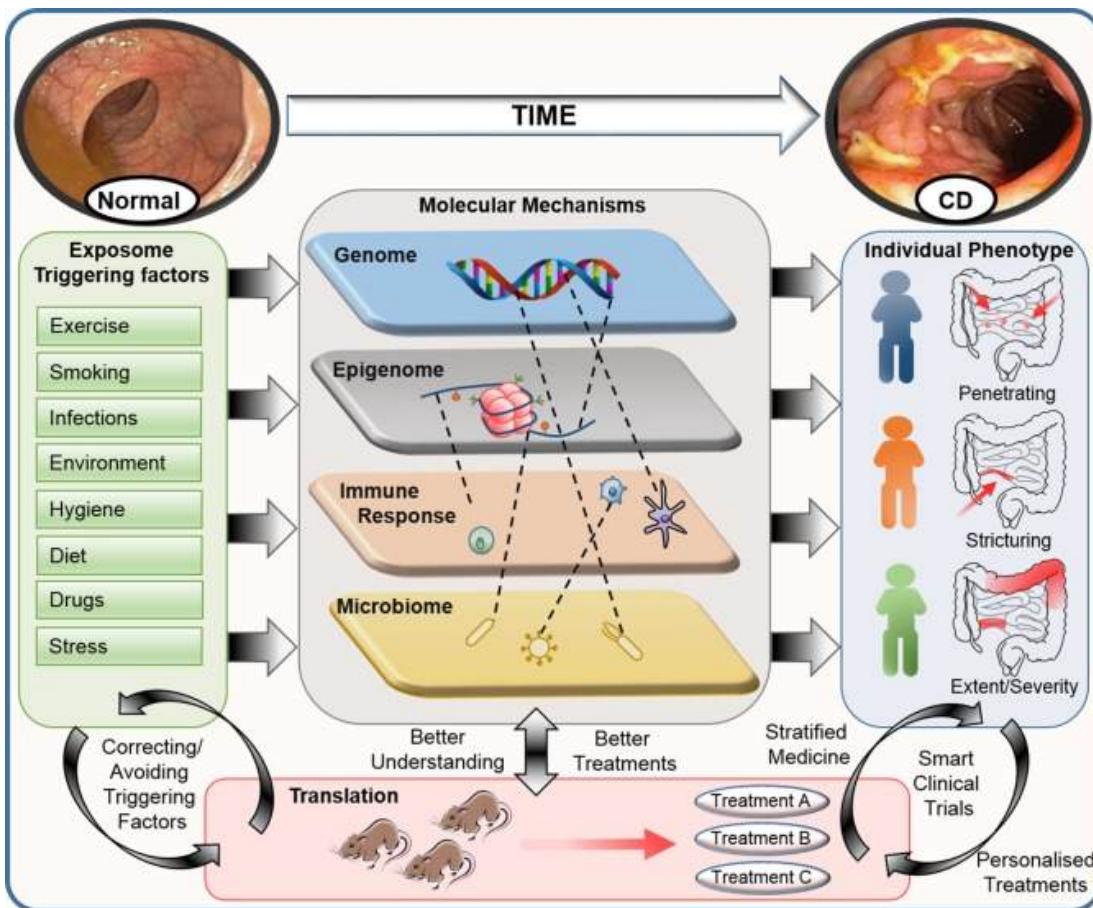


Figure 1. Crohn's disease (CD): multi-layer interactions in pathogenesis and clinical translation².

The most fundamental pathogenetic pattern of CD/IBDs is the dysregulation of innate and adaptive immunity. CD is mainly characterized by Th1 cell-mediated immune response. CD4+ T cells are involved in CD initiation and development, and Th1 or Th2 cells are involved in inflammation³. The levels of mucosal CD4+ T helper (Th) cells that secrete effector cytokines such as TNF- α and IFN- γ are abnormally high in the guts of CD patients. In response to different types of pathologic factors and inflammatory cytokines, naive CD4+ T cells can differentiate into distinct subsets of CD4+ Th cells, such as Th1, Th2, Th17, and CD4+FoxP3+ T regulatory cells (Tregs). Th1 and Th17 cells can secrete a variety of inflammatory cytokines that trigger the infiltration of inflammatory cells into the intestinal epithelium, leading to acute or chronic enteritis.

In the CD mucosa, macrophage-derived IL-12, IL-18, and TNF- α are overexpressed, driving the Th1 immune response to increase the production of IL-2 and IFN- γ . This response is thought to cause intestinal inflammation¹². Th17 cells are induced by IL-6 and TGF- β and produce IL-17A, IL-21, and IL-22, and those soluble factors will cause inflammation in CD mucosa. Also, deficiency or aberrant activation of intestinal MSCs may lead to disturbance in mucosal and immune homeostasis, thus contributing to the pathogenesis of IBD.

CD progression can vary from patient to patient, but the most common progression starts with moderate inflammation and then advances to more severe forms of inflammation such as a stricturing disease. Early-stage CD is often characterized by mucosal inflammation compared to advanced stages involving transmural inflammation. This can lead to injuries such as fistulas, strictures, and abscesses. The disease's erratic nature is a hallmark of CD, complicating diagnosis and treatment. Over time, chronic inflammation can cause irreversible tissue damage, raising the risk of colorectal cancer and other serious complications.

The course of CD is very erratic and unique with periods of both relapse and continued remission. Some factors that may influence the disease progression include environmental triggers, changes in diet, and the patient's immune response. Thoroughly understanding the clinical progression of CD is vital to developing new and improved therapies that may be able to stop or even reverse the damage caused by CD. Stem cell

treatment, immunomodulatory treatment, and biologics are steppingstones to finding the ultimate therapy for CD.

Stem Cells

Stem cells are undifferentiated cells that can differentiate into specific cells of tissues or organs. SC therapy is a novel therapeutic approach in immune-mediated conditions, and, because of their peculiar biological properties, stem cells represent a promising tool for regenerative medicine and chronic inflammatory diseases²⁹. The goal of stem cell-based therapy is to rejuvenate or replace dysfunctional tissues and organs through stem cell pluripotency, self-renewal, and regenerative cytokine secretion. As expectations rise for regenerative treatment through the application of stem cell therapies, the number of applications of various types and stem cell sources has increased, and stem cell therapies have diversified from autologous (isolated from the same individual, i.e. the patient himself) to allogenic (isolated from a donor, ideally human leukocyte antigen [HLA]-matched) to induced pluripotent stem cells (iPSCs))³⁰.

The SC treatments can vary in risk, depending on the cell manufacturing process and clinical experience, and among other factors, the strengths and weaknesses of each type of stem cell should be identified in order to determine the maximum therapeutic effect of stem cells in various diseases. As stem cells derived from various sources have different characteristics, capabilities, potential, and efficiency, selecting the right source of stem cells that is appropriate for the target can be effective in assuring treatment efficiency³⁰.

Key characteristics and differences of various stem cells with an emphasis on therapeutic treatments for CD is summarized below.

Stem Cells	Classification	Preclinical/Clinical Use?	Advantages	Disadvantages
MSCs	Multipotent	Clinical	<ul style="list-style-type: none"> Potent immunomodulatory and anti-inflammatory Repair damaged tissues Tumor homing Attenuate immune responses 	<ul style="list-style-type: none"> Adverse immune reactions Tumor formation Transmit viral infections and are vulnerable to many microorganisms More affected by donor age A limited number of cells
BM-MSCs	Multipotent	Clinical	<ul style="list-style-type: none"> Immune regulation and immunosuppression Ease of extraction and culturing Bone and cartilage reparatory cells Support angiogenesis Autologous BM-MSCs are used for such regenerative therapies Lower risk immune rejection Increased anti-inflammatory expression Homing features 	<ul style="list-style-type: none"> Require younger donors Invasive harvesting procedure Differentiation potential of BM-MSCs decrease with aging
ESCs	Pluripotent	Preclinical	<ul style="list-style-type: none"> Better differentiation potential Longer lasting proliferation capacity Immune-privilege and immunomodulatory in transplantation as allogeneic cells A high degree of inherent plasticity, which assists in the adoption of ESCs by the recipient tissue 	<ul style="list-style-type: none"> Derived from human embryos leading to ethical and FDA concerns Tumorigenic potential Difficulty in vitro work Difficulty in controlling differentiation
HSCs	Multipotent	Clinical	<ul style="list-style-type: none"> Better differentiation potential Ultimate source of blood and immune cells Responsible for the generation of all the lineages of the blood 	<ul style="list-style-type: none"> Sensitive to inflammation Extensive inflammation may cause HSC exhaustion/ senescence and malignant transformation Long-term exposure to inflammation can impair HSC self-renewal activity and accelerate aging
hUC-MSC	Multipotent	Clinical	<ul style="list-style-type: none"> Control inflammatory response Promote granulation angiogenesis Inhibit scar formation Derived from discarded umbilical cord tissue, with the advantages of easy obtaining Immunomodulatory, and anti-inflammatory properties Stronger proliferation, differentiation, and immune regulation abilities 	<ul style="list-style-type: none"> Uncontrollable immune regulation Abnormal accumulation Nontherapeutic differentiation Low survival of transplanted cells
ISCs	Pluripotent	Clinical	<ul style="list-style-type: none"> Differentiate into the mature cell types required for normal gut function High self-renewal rate as well as remarkable regenerative properties ISCs are a valuable cell source to grow organoids ISCs/Intestinal organoids are human-derived and nearly physiological, and can simulate multiple types of organ-specific disease states in vitro 	<ul style="list-style-type: none"> Fixed differentiation lineages High Heterogeneity high manufacturing costs, limited scalability, and risk of pathogen contamination Low reproducibility
IPSCs	Pluripotent	Clinical	<ul style="list-style-type: none"> Not derived from human embryos Creation of cell lines that are genetically tailored to a specific patient eliminating immune rejection Reverse injury or disease 	<ul style="list-style-type: none"> Production of iPSCs using retroviruses is associated with cancer Retroviruses can insert DNA anywhere within a cell's genome, allowing for potential activation of cancer-causing oncogenes C-Myc, which is one of the genes commonly used in iPSC reprogramming, is a known oncogene whose over-expression could also cause cancer
pESCs	Totipotent	Preclinical	<ul style="list-style-type: none"> Allogeneic Immunomatching Less tumorigenic 	<ul style="list-style-type: none"> Loss of heterozygosity abnormal imprinting and high levels of homozygosity may complicate applications of pESCs
ADSCs	Multipotent	Clinical	<ul style="list-style-type: none"> Participate in immune regulation Inhibit of scar formation Rich source Regulate metabolism and the immune system Easy accessibility 	<ul style="list-style-type: none"> May increase the risk of tumor growth and metastasis Uncertainty about the clinical efficacy of ADSC-based therapies

Table 1. The properties of different stem cells with an emphasis on therapeutic treatments for CD cell therapies.

Stem Cells and CD

The use of stem cells in CD/IBD treatment is expected to achieve sustained remission and mucosal healing. Preclinical studies in IBD models are increasing, and various types of stem cells, such as embryonic stem cells (ESCs), MSCs, hematopoietic stem cells (HSCs), iSCs, and iPSCs, have demonstrated positive efficacy and stable safety in IBD animal models. These cells have the potential to directly improve chronic inflammation in the intestine by modulating immune cells and repairing the intestinal mucosal barrier. In addition to addressing inflammation, they can play a beneficial role in enhancing intestinal microecology, resolving microcirculation disorders, and preventing fibrosis and cancerization, among other benefits.

The CD is usually described as a Th1/17-associated disorder since the main inflammatory cytokines in this condition are the Th1/17-related molecules like IL-12, IL-17, IFN- γ , and TNF- α ¹¹. The gastrointestinal tract is protected from adverse substances in the gut environment by a single layer of epithelial cells that are known to have great regenerative ability in response to injuries and normal cell turnover. The gastrointestinal tract is highly vulnerable to damage, tissue inflammation, and diseases once the degradation of the mucosal lining layer occurs.

In recent years, HSCs and adult MSCs have shown efficacy in treating IBD. In addition, numerous clinical trials have evaluated the efficiency of MSCs in treating the disease.

Inflammation and Immune Suppression Properties of Stem Cells

Inflammation is generally present in damaged tissues, without which the initiation and completion of the repair process cannot occur. However, excessive inflammation impairs tissue regeneration.

MSCs also modulate the cytokine milieu generated by different T cell subsets by decreasing the pro-inflammatory cytokine production and increasing the anti-inflammatory cytokine production. Some cytokines like IFN- γ , TNF- α , and IL-17 are usually reported to be downregulated and IL-10, IL-4 upregulated, thereby indicating a possible MSC-mediated alteration in Th1/Th2/Th17 subset balance¹⁴. MSCs mediate their immunomodulation via the release of soluble factors or by cell-cell contact manner (Figure 2). Some key soluble factors are: transforming growth factor (TGF)- β , hepatocyte growth factor (HGF), IL-6, indolamine dioxygenase (IDO), prostaglandin E2 (PGE2), human leukocyte antigen (HLA)-G5, TNF-stimulated gene-6 (TSG-6), IL-1 receptor antagonist (IL-1Ra) and IL-10. IDO causes reduced proliferation and cytotoxicity of natural killer (NK) cells and decreases the Th17 differentiation with induction of Tregs.

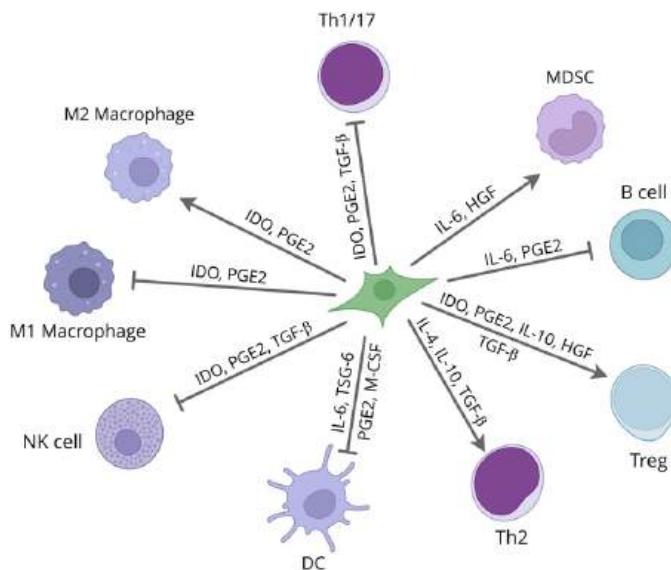


Figure 2. Underlying mechanisms behind the immunomodulatory attributes of MSCs¹¹.

Higher levels of pro-inflammatory factors, such as IL-1 β , IFN- γ , and TNF- α , stimulate MSCs to reduce inflammation and avoid autoimmune reactions by releasing, for example, TGF- β , IL-10, IDO resulting in an inhibition of the migration, maturation, and antigen presentation of dendritic cells (DC), and of T-cell function and proliferation, along with the proliferation of Tregs. Therefore, the TGF- β , IL-10, and IDO levels have been proposed as the switcher between the pro- and anti-inflammatory effects of MSCs¹⁰.

Mucosal Healing and Regeneration Properties of Stem Cells

The intestinal barrier makes a separation between the body and the contents of the intestine. It consists of various sections, including a mucus layer comprising antibacterial peptides lining the luminal surface of the epithelium, the epithelial cell monolayer, junctional proteins, intraepithelial lymphocytes (IELs), and also a subepithelial layer of extracellular matrix (ECM) and mesenchymal cells like myofibroblasts and fibroblasts (Figure 3). The intestinal barrier provides a shield against potentially damaging molecules and also pathogenic bacteria, thus supporting intestine immune homeostasis. Mucosal healing is associated with a more favorable prognosis for patients with IBD, including lower relapse and hospitalization rates, as well as a diminished risk for surgery.

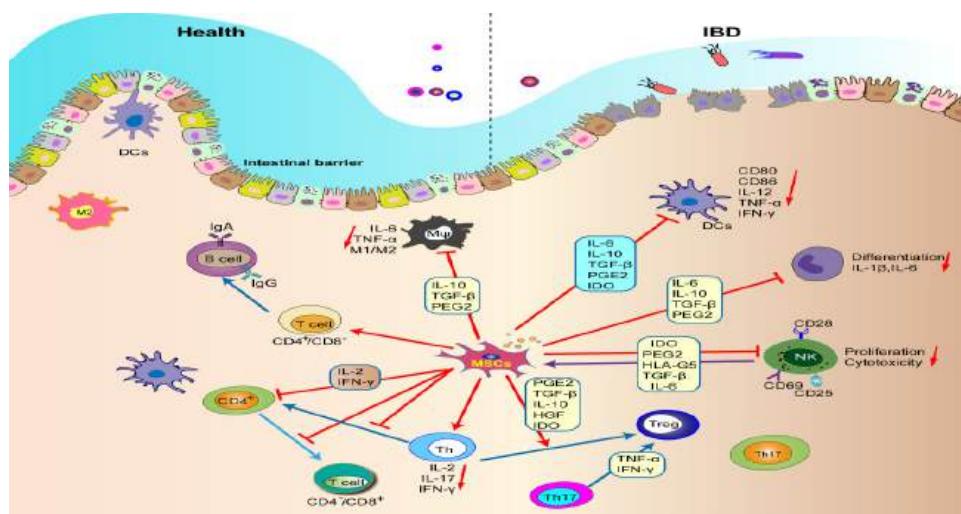


Figure 3. Gastrointestinal Trac - MSC can secrete PEG2, IL-10, TGF- β , inducible, IDO and IL-6 to inhibit the proliferation of T cells and NK cells, thus reduce the production of inflammatory cytokines in Th1 and Th17, and inhibit immune response and inflammation¹.

In CD, evidence points to a dysfunctional epithelium (innate and acquired) as a pathogenic factor leading to a breakdown in gut homeostasis and loss of barrier function⁶. In addition, specific damage to the ISC results in further de-regulation and the loss of the capacity to regenerate a functional epithelium with a full complement differentiated cells. More importantly, there is accumulating evidence to show that ISC function is affected in IBD/CD. In human CD, a reduction in the ISC population is observed within active disease compared with nonaffected gut mucosa. This is shown by correlating pathological assessment of activity with ISC frequency using *in situ* hybridization of the LGR5 stem cell marker¹⁵. The perturbation of ISC function or potential may contribute to the failure of IBD mucosa to heal or return to normal homeostasis. It is of interest that a low ISC population appears to predict future clinical recurrence in CD.

The gastrointestinal tract is lined by a single layer of columnar intestinal epithelial cells—a sophisticated multifaceted barrier that comprises several specialized cell types, each with a distinct function. Intestinal epithelial cells (IECs) play a critical role in maintaining the barrier's integrity given their anatomical and functional location. MSCs promote the expression of TJs proteins in IECs, thereby reducing inflammation-stimulated permeability. In addition, induced pluripotent stem cells (iPSC)-derived MSCs could boost IECs proliferation to ameliorate mucosal healing in a mice colitis model by TSG-6 secretion³⁵. In vitro, TSG-6 could

promote Akt phosphorylation in mice colonoids (primary cultures derived from intestinal crypts), reflecting the key role of Akt activation in the TSG-6-mediated proliferation of IECs. Similarly, the administration of iPSC-MSCs promoted IECs proliferation, raised the Lgr5 + ISCs frequencies, and potentiated intestinal angiogenesis in colitis rodents. Positive regulation of Lgr5 + ISCs proliferation and differentiation, as shown by exogenous PGE2 injection, may augment intestinal integrity and promote mucosal healing in IBD patients¹¹.

Thus, these early studies provide the premise for an intervention that is targeted toward the correction of ISCs in the IBD gut (either by replacement with healthy ISCs or, augmentation, or restoration of ISC function).

Overview of SCs for IBD Treatment

Mesenchymal Stem Cells (MSCs)

Human mesenchymal stem cells (MSCs), also known as mesenchymal stromal cells or medicinal signaling cells, are important adult stem cells for regenerative medicine, largely due to their regenerative characteristics such as self-renewal, secretion of trophic factors, and the capability of inducing mesenchymal cell lineages. MSCs also possess homing and trophic properties modulating the immune system, influencing the microenvironment around damaged tissues, and enhancing tissue repair, thus offering a broad perspective in cell-based therapies⁷. MSCs secrete bioactive factors that favor tissue remodeling and repair, as well as immunoregulatory properties. MSCs are present in the umbilical cord blood, placenta, muscle, and other tissues, with bone marrow and adipose tissue being the most important sources¹⁷.

Recent studies have also implicated the importance of intestinal MSCs in digestive organ development, mucosal tissue, and immune homeostasis, which can provide multiple niche signals to support the functional integration of mucosal epithelial cells, immune cells, and gut microbiota¹². Most recently, the emerging studies using scRNA-seq have significantly improved our understanding of the heterogeneity and the distinct role of diverse subsets of intestinal MSCs in regulating mucosal homeostasis and immunity by providing different niche signals under both physiological and inflammatory conditions. For instance, recently identified distinct subpopulations of stromal fibroblasts with gene signatures that are differentially regulated by chronic inflammation through scRNA-seq analysis of colon-derived mesenchymal stromal cells provide mechanistic insight into how inflammation affects the function and behavior of intestinal MSCs and their crucial role in orchestrating mucosal tissue remodeling and healing.

Besides MSCs, cytokines and extracellular vehicles (EVs) which are released by MSC also have a therapeutic effect on CD. Because of the low immunogenic profile, which decreases the potential for cell rejection and graft-versus-host-disease, more and more studies begin to focus on the paracrine action of MSC. MSC secrete growth factors, exosomes, cytokines, and metabolites that inhibit inflammation, restore the intestinal mucosal barrier, and are protective.

MSCs regulate immune responses by releasing various modulatory factors including PGE2, IL-6, TSG-6, and IDO. The constant interaction between MSCs and the immune system is key to balancing inflammatory responses and maintaining tissue homeostasis. There is increasing evidence that MSCs play an important role in both innate and adaptive immunity. For instance, MSCs can inhibit CD4+ (helper) and CD8+ (cytotoxic) T cell, affect B cell functions through cell-to-cell contact, suppress the proliferation and cytotoxicity of NK cells, as well as increase Tregs generation via cell communication and soluble factors both in vitro and in vivo⁷.

MSCs transplantation also decreased the expression of IL-6, TNF- α , and IFN- γ and concurrently increased the levels of IL-10, TGF- β , and forkhead box protein P3 (Foxp3), a crucial regulator of Tregs, in colon tissues. MSCs could decrease CD4 + T cell proliferation, inhibit Th1/Th17 cell activation, while inducing Th2 cell's function. These events finally diminish pro-inflammatory IL-17 and IFN- γ , and improve TGF- β , IL-10 levels in colon tissue of MSCs-treated IBD models. Regardless of the pro-inflammatory cytokines, systemic administration of MSCs could affect T-box expressed in T cells (T-bet) and retinoid-related orphan receptor

gamma(t) (ROR γ t) expression in T cells. T-bet and ROR γ t, as a central regulator of Th1 and Th17 cells, respectively, act as causative factors in IBD progress. Thus, their inhibition by MSCs-secreted mediators could lead to the suppression of Th1/Th17-related pathological events in IBD patients¹¹.

An increasing number of studies show that many of the therapeutic effects of MSCs may be the result of the paracrine factors secretion of EVs, rather than cellular engraftment and response to the site of injury³¹. MSC-EVs cannot self-replicate, thereby becoming attractive cell-free and safer therapeutic sources because uncontrolled cell division and risks of contamination with other cells are prevented. Moreover, allogenic MSCs have good safety profiles for patients with inflammatory bowel disease for up to 1 year⁶.

BM-MSCs

Bone marrow-derived mesenchymal stem cells (BM-MSCs) are a potential treatment for CD. Studies have demonstrated that local administration of autologous or allogeneic BM-MSCs achieved obvious clinical efficacy in patients with fistulizing CD by downregulating local immune responses and initiating wound healing. BM-MSCs can restore intestinal epithelial cell by differentiating into epithelial cells through “cell fusion” in vitro under certain culture conditions that include HGF, EGF, KGF, and IGF-II. BM-MSCs were involved in the repair of intestinal epithelial cell injury through the cell fusion mechanism after transplantation¹².

BM-MSCs have been shown to reverse the epithelial-mesenchymal transition (EMT) of TGF- β 1-treated IEC-6 cells by carrying miR-200b, resulting in a significant reversal of intestinal fibrosis. Trials using bm-MSC were also performed in CD complicated by complex perianal fistula. Local administration of autologous BM-MSC was well tolerated and feasible in a study involving 10 patients with CD and actively draining complex perianal (n=9) and enterocutaneous (n=1) fistulas. Local injections were scheduled at 4-week intervals; all patients showed either complete (n=7) or partial (n=3) fistula closure at 1 year, with no adverse effects. All patients improved their disease activity, especially after the second administration. Endoscopic healing was also observed in 7 out of 9 patients with perianal disease and endoscopic rectal activity. However, in the long-term follow-up, the probability of fistula relapse-free survival decreased over time was 88% at 1 year, 50% at 2 years, and 37% during the following 4 years¹³.

Hematopoietic Stem Cells (HSCs)

Hematopoietic stem cells (HSCs) may be used in autologous or allogeneic transplantations for the treatment of patients with diverse hematopoietic disorders and several inherited immune-deficient and autoimmune diseases and to reconstitute the hematopoietic cell lineages and immune system defense. The use of hematopoietic stem cells transplantation (HSCT) in IBD is restricted to severe CD with few therapeutic options. These are patients who do not respond to standard treatment for whom surgery is not an option due to the extent of the disease.

The first phase I trial using autologous HCST was conducted in Chicago and recruited 12 patients with active moderate to severe CD refractory to conventional therapies. Eleven of 12 patients demonstrated sustained remission after a median follow-up of 18.5 months, and one patient developed a recurrence of active CD⁹.

The rates of clinical remission induced by HSCT seem to be the highest ever reported in CD, when compared to steroids or any biological agent, even in the difficult clinical scenario of refractory disease. In some reports, objective deep remission has been reported, in terms of not only clinical but also endoscopic response, in higher percentages than any conventional treatment. However, some impressive long-term remissions, maintained continuously for more than 10 years without any other treatment, suggest the need to better understand the mechanisms of action of HSCT and, therefore, to better select the best responders among CD patients and how to protect them from disease relapse. As stated in the EBMT guidelines, autologous HSCT should be considered as a therapeutic option at second line or beyond for patients with severe autoimmune diseases progressing despite standard established and/or approved therapy¹³.

Human Umbilical Cord -Mesenchymal Stem Cells (hUC-MSCs)

hUC-MSCs are intended to treat multiple immune diseases (for instance, psoriasis, liver failure, and lupus nephritis) by intravenous infusion. Compared with human bone marrow and adipose-derived mesenchymal stem cells, they are easier to obtain, have demonstrated strong proliferation and differentiation capability and strong plasticity, with less ethical controversy, and have less cell loss after cryopreservation⁴.

In a recent study on a TNBS-induced colitis mice model, hUC-MSCs transplantation protected against experimental colitis by promoting CD5 + B cells and IL-10-secreting CD5 + regulatory B cells (Bregs). It has previously been evinced that deficiency or reduction of Bregs function intensifies intestinal inflammation in mice models and is in association with CD/IBD pathogenesis. In addition to the enhanced Bregs population, hUC-MSCs therapy led to improved Tregs while decreasing Th1/Th17 cell populations in colon tissue of treated mice¹¹.

Embryonic Stem Cells (ESCs)

ESCs are pluripotent cells derived from the inner cell mass of blastocysts and have the potential to induce cell types of all three germ layers. ESCs have established cell lines that can be maintained through *in vitro* culture. They are pluripotent cells that can be differentiated into almost any type of cell present in the body. In a study aimed to evaluate the differentiation and repair potential of murine ESCs in a murine model of CD, histopathological analysis showed improved colon tissue and immune studies indicated a shift from TH1 to TH2 response, suggesting immune recovery. Overall, the findings suggest that the differentiation and repair capabilities of embryonic stem cells could offer new therapeutic options for treating and preventing inflammatory bowel disease³³.

However, the use of ESCs in clinical practice has a major limitation related to ethical concerns as the generation of ESCs is linked to the use of germ cells and the destruction of human embryos.

Intestinal Stem Cells (ISCs)

Mucosal healing is associated with a more favorable prognosis for patients with CD, including lower relapse and hospitalization rates, as well as a diminished risk for surgery. Successful transplantation of intestinal stem cells (ISCs), which are responsible for tissue homeostasis and injury response in murine models of experimental colitis demonstrated that they adhere to and become an integrated part of the epithelium, thereby improving mucosal healing. Hence, ISC transplantation might constitute an appealing therapeutic approach to re-establish the epithelial barrier in CD/IBD. However, if the patient's ISC cells were to contain genetic mutations that predispose to malignancy, then transplantation might lead to risk of malignant transformation in a greater area of the intestine after engraftment.

ISCs are located at the base of the intestinal crypts where they renew the epithelium through differentiation to multiple epithelial progenies and drive mucosal regeneration. ISCs can be cultured *in vitro*, giving rise to three-dimensional self-organizing structures called organoids. An intestinal organoid is a three-dimensional organlike structure grown *in vitro*, consisting of intestinal epithelial cells. The nomenclature varies and is also referred to as a mini gut.

In studies investigating organoid therapy to restore the epithelial barrier function, the engrafted organoids successfully healed areas of epithelium and retained a human phenotype both in terms of shape and size of villi. In a model more representative of IBD, after exposure to DSS colitis, organoid transplant recipient mice were found to have areas of healed mucosa, with a full complement of differentiated cell types⁶.

Induced Pluripotent Stem Cells (iPSCs)

iPSCs are artificially created stem cells. These cells are made by reprogramming adult somatic cells such as fibroblast cells. They share many of the characteristics of ESCs, including self-renewability, pluripotent

differentiation, and malformed species performance. Unfortunately, these cells have little scientific evidence regarding changes in cell-specific regulatory pathways, gene expression, and epigenetic regulation. In murine models of IBD, transplantation of iPSC-derived intestinal cells led to significant histological improvements, including reduced inflammation and tissue damage³⁴.

In a separate study on mouse models of IBD, the regenerative effects of iPSC-MSCs were explored and the mechanisms by which iPSC-MSCs promote mucosal healing via tumor necrosis factor- α -stimulated gene 6 (TSG-6)³⁵. The iPSC-MSC treatment promoted mucosal healing in colitis mice, accompanied by increased epithelial cell proliferation, CD44-positive cells, and Lgr5-positive cells. Organoids co-cultured with iPSC-MSCs showed increased epithelial cell proliferation, CD44-positive cells, and Lgr5-positive cells, which was abolished by TSG-6 knockdown. The study concluded that iPSC-MSCs promoted epithelial cell proliferation to accelerate mucosal healing in a murine colitis model via TSG-6 through hyaluronan–CD44 interactions in an Akt-dependent manner, demonstrating a patient-specific “off-the-shelf” format for IBD/CD treatment.

However, the use of iPSCs for cell therapy also has concerns and challenges. The potential of tumorigenicity caused by the non-complete differentiation, accumulation of genetic mutations, epigenetic abnormalities, and expression of the reprogramming factors are considered as the major challenges.

Adipose Derived Stem Cells (ADSCs)

ADSCs appear to be the most advantageous cell type for regenerative therapies owing to their easy accessibility, multipotency, and active paracrine activity. The great advantage of ADSCs is that they can be harvested through a less invasive method and in larger quantities without any ethical concerns. ADSCs repopulate damaged tissues via adhesion, proliferation, and differentiation. ADSCs have paracrine activity and secrete a broad spectrum of bioactive molecules, such as cytokines, antioxidant factors, chemokines, and growth factors.

ADSCs have stronger proliferation ability and immunomodulatory function compared with BM-MSCs. ADSCs can suppress dendritic cell differentiation, immunoglobulin synthesis, CD8+ and CD4+ T lymphocytes , natural killer cell proliferation and promote M2 macrophage polarization and Treg proliferation. ADSCs can alleviate excessive inflammation and regulate the immune system through direct cell–cell contact or indirect paracrine activity. ADSC-exo-based treatment can reproduce ADSCs' immunomodulatory function and overcome the limitations of traditional cell therapy.

The data referring to the clinical efficacy of AD-MSC transplantation in the treatment of complex perianal fistulas in CD are also promising and darvadstrocel (allogeneic AD-MSCs) has recently become commercially available in Europe in adult patients with non-active/mildly active luminal CD, when fistulas have shown an inadequate response to ≥ 1 conventional or biologic therapy¹³.

ADSCs can be recruited to tumors and integrated into the tumor stroma, after which some ADSCs are converted to cancer-associated fibroblasts, while others remain as ADSCs¹⁶. Meanwhile, undifferentiated ADSCs in tumors exhibit active paracrine activity and secrete various cytokines that facilitate tissue regeneration, including growth factors and VEGF¹⁷. These bioactive molecules secreted into the tumor microenvironment may enhance tumor vascularization, promote the survival and proliferation of tumor cells, and accelerate tumor progression.

MSC Mechanisms Summary

MSCs possess biological and regenerative effects mostly due to their secreted trophic (regenerative) factors that mediate cell-to-cell communications, regulate cell proliferation/differentiation, and have anti-inflammatory properties. By producing extracellular vesicles (EVs), cytokines, and growth factors, MSCs have demonstrated excellent potential to modulate both adaptive and innate immune system responses. These

findings are supported by *in vitro*, and *in vivo* experiments, as well as by clinical data that shows a complex network of interactions between immune cells and MSCs⁷.

The immune modulating functions of MSCs are via secreted paracrine factors such as the beta fibroblast growth factor (bFGF), the insulin-like growth factor-1 (IGF-1), the vascular endothelial growth factor (VEGF), the epidermal growth factor (EGF), the tissue inhibitor of metalloproteinase-1 (TIMP-1), progranulin, and the brain-derived neurotrophic factor (BDNF), or by direct cell-to-cell communications with various immune cells such as T cells, B cells, natural killer (NK) cells, macrophages, monocytes, dendritic cells (DCs), and neutrophils, stimulating or suppressing the immune responses.

Stem Cell Delivery

Dosage, dose frequency, intervals, and suspensions are important parameters for MSC administration. The dosages reported in many clinical trials are heterogeneous depending on the route of injections. The MSC dosages are usually decided by the patient's condition and therapeutic properties. In MSC clinical trials, dose frequency, interval, and dosage vary significantly. The dosages are typically described in cells/kg body weight ($0.5\text{--}12 \times 10^6$ cells/kg as a single dose). Allogeneic MSCs doses might go up to 1×10^8 level⁷.

In conclusion, it is essential to evaluate in preclinical studies and thoroughly evaluate the condition of patients, progression of diseases, treatment regimens, and the potential route risks before choosing the optimal MSC transplantation dose and administration method.

Methods

Stem Cell Studies for CD/IBD Treatment

The International Society for Cellular Therapy (ISCT) established unique criteria that apply for all MSCs isolated from different sources. Based on the ISCT criteria for MSCs, authentic human MSC-like cells must express certain MSC positive surface markers 5'-nucleotidase (CD73), Thy-1 (CD90), and Endoglin (CD105) and they must lack the expression of macrophage marker CD14, HSC marker CD34, lymphocyte marker CD45, B cell marker CD19, B-cell antigen receptor complex-associated protein alpha chain CD79a and MHC class II cell surface receptor HLA-DR⁷.

Clinical trials based on MSCs therapy in IBD conditions registered on <https://clinicaltrials.gov> (June 2022) were demonstrated in Figure 4. The promising results from animal studies have encouraged researchers to design and conduct a variety of clinical trials. Meanwhile, both autologous and allogeneic MSCs transplantation have been accomplished given their immune-suppressive and regenerative competencies with remarkable safety and acceptable efficacy.

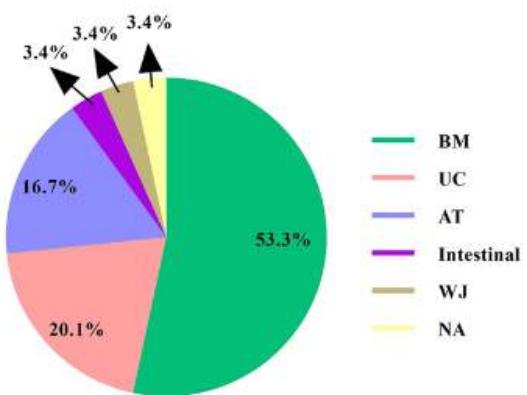
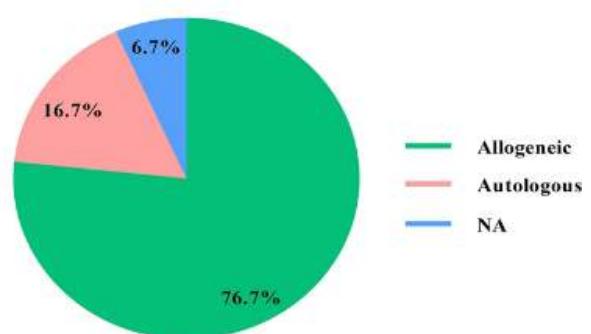
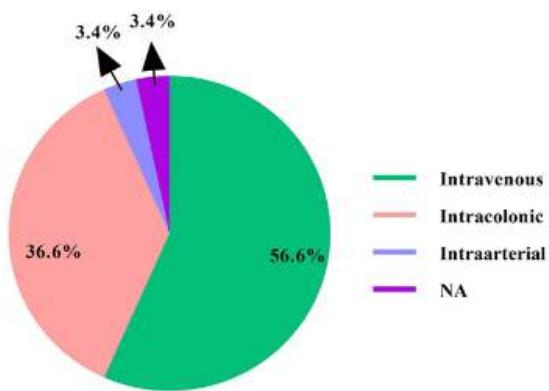
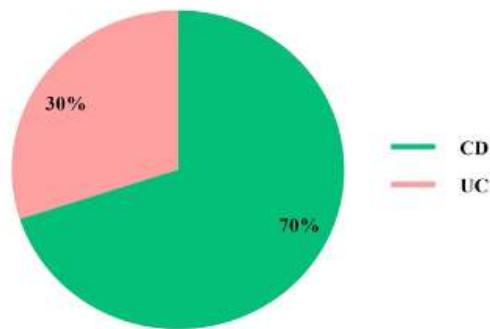
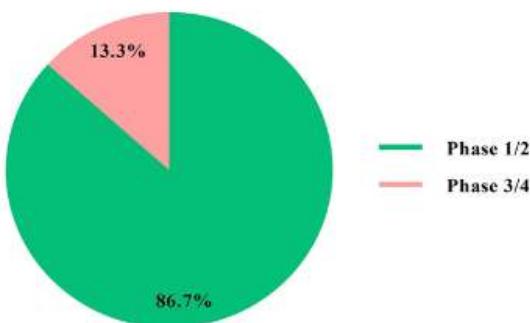
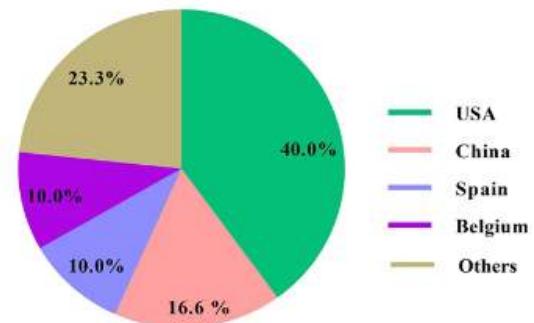
A**B****C****D****E****F**

Figure 4. -MSCs therapy-based clinical trials in IBD conditions registered on <https://clinicaltrials.gov> (June 2022)¹¹. The schematics illustrate clinical studies based on cell source (A), cell type (B), administration route (C), condition (D), study phase (E), and study location (F). Inflammatory bowel diseases (IBD), mesenchymal stem/stromal cell (MSC), bone marrow (BM), umbilical cord (UC), adipose tissue (AT), Wharton's jelly (WJ), Crohn's disease (CD), ulcerative colitis (UC), not applicable (NA).

Autologous Studies

Recent studies involving autologous stem cell treatments for Crohn's disease have shown promising results. In one trial, five patients with refractory Crohn's fistulas received intracolonics administration of autologous AT-MSCs at a dose of 35×10^6 cells per patient. This treatment had no severe side effects and led to the complete cessation of drainage in three of the patients over a six-week follow-up period¹⁸. Another phase 1 trial with twelve patients demonstrated that intracolonics administration of AT-MSCs was both safe and effective, with complete fistula healing achieved in 57% of the patients¹⁹. The primary adverse effect observed

was proctalgia, which lasted a few days; additionally, two patients developed small abscesses, one experienced urinary retention, and another had minor bleeding during liposuction. A different phase 1 trial showed that injecting $1\text{--}2 \times 10^7$ cells of AT-MSCs per patient was safe and feasible in Crohn's disease patients²⁰. Autologous BM-MSCs administered intravenously at a dose of $1\text{--}2 \times 10^6$ cells/kg also did not cause serious side effects in ten patients with refractory Crohn's fistulas²¹. This intervention led to a reduction in the Disease Activity Index (DAI) in three patients over six weeks, although three others required surgery due to disease worsening. Additionally, another study reported that systemic injection of autologous BM-MSCs at a dose of 1×10^7 cells/kg was modestly safe and feasible in twelve patients with Crohn's disease²².

Allogeneic Studies

A trial involving 82 patients, with 41 in each control and intervention group, demonstrated that systemic injection of allogeneic UC-MSCs at a dose of 1×10^6 cells/kg could reduce the DAI, Harvey–Bradshaw Index (HBI), and corticosteroid dosage without causing serious side effects²³. Additionally, local administration of 3×10^7 allogeneic MSCs/ patient improved the healing of perianal fistulas²⁴. Intracolonic injections of $3\text{--}9 \times 10^7$ allogeneic BM-MSCs /patient resulted in smaller fistula tracts after four years, with no long-term side effects observed in CD patients²⁵. In a phase 1/2 clinical trial, local administration of allogeneic AT-MSCs at a dose of 20×10^6 cells/patient in 24 CD patients led to a reduction in the number of draining fistulas for 69.2% of patients, complete closure of the treated fistula in 56.3% of patients, and closure of all existing fistula tracts in 30% of patients²⁶. These results indicated the safety, feasibility, and efficacy of allogeneic AT-MSCs in treating CD. Forbes and colleagues conducted a phase 2 trial, showing that weekly transplantation of 2×10^6 allogeneic MSCs/kilogram for four weeks reduced both DAI and the Crohn's Disease Endoscopic Index of Severity (CDEIS) scores in patients with luminal CD who were refractory to biologic therapy²⁷. Furthermore, a phase 3 randomized, double-blind controlled trial, conducted across 49 hospitals in eight countries from July 6, 2012, to July 27, 2015, evaluated the safety and efficacy of local administration of expanded allogeneic AT-MSCs (Cx601)⁸. Intralesional injection of 120×10^6 Cx601 cells per patient in 107 CD patients demonstrated an acceptable safety profile and significant efficacy, particularly in those who did not respond to conventional or biological treatments. MSC therapy was well tolerated, and clinical remission post-treatment was sustained for up to 104 weeks in patients with perianal fistulizing CD²⁸.

According to researcher-initiated registered data from the US National Institutes of Health, there has been a rapid development of cellular therapy during the last decade using MSCs in clinical trials. The number of MSC-based clinical trials has doubled over the last five years. As of July 14th, 2021, 1014 MSCs-based clinical trials have been registered in the ClinicalTrials.gov database either as completed or in process.

Also, there is a double-blind study (NCT01541579) conducted at nearly 50 hospitals in Europe and Israel, which investigated the treatment of 212 CD and perianal fistula patients with allogeneic AD-MSCs (Cx601)⁸. After one year, the follow-up study showed that Cx601 was safe and effective compared to a placebo. The trial enrolled patients with CD who had complex perianal fistulas that had not adequately responded to standard treatments. Cx601 treatment led to a significantly higher rate of complete closure of perianal fistulas compared to the placebo group. The study concluded that expanded allogeneic AD-MSCs are a safe and effective treatment for complex perianal fistulas in CD.

Future Perspectives of Stem Cell-Based CD Therapies

Pre-treated (Primed) MSCs

AD-MSCs induced with IFN- γ and kynurenic acid substantially upregulated the expression and secretion of IDO-1, finally alleviating CD pathology-like colitis injury and fibrosis *in vivo*. Likewise, systemic injection of MSCs upon exposure with IL-25 decreased infiltrating inflammatory cell frequencies and enhanced Tregs in serum and colonic mucosa of the IBD rat model, leading to inhibited intestinal inflammation and decreased DAI score. In addition, animal models exhibited that IFN- γ increases the efficacy of human UCB-MSCs transplantation by improving PGE2 release and IDO activity¹¹. PGE2 in association with IDO inhibits Th1

cell differentiation and enhances Tregs differentiation, suggesting that a combination of PGE2 and IDO may be effective therapeutic mediators for potentiating the MSCs-induced immunosuppression.

Genetically Modified MSCs

Current reports exhibit that overexpression of various genes such as intercellular adhesion molecule (ICAM), CXCR4, and CXCR2 can improve MSCs homing to the injured area and thus enhance succeeding anti-inflammatory and pro-survival effects in IBD animal models. ICAM-1 overexpressing MSCs also reduced Th1 and Th17 subpopulation while enhancing Tregs frequency in the spleen of treated mice, ensuring down-regulated IFN- γ and IL-17A and upregulated Foxp3 levels. Other studies have focused on enriching the antioxidant potential of MSCs using genetic engineering. Nuclear factor erythroid 2-related factor (Nrf2) signaling adjusts multiple gene expressions by making interfaces with the antioxidant response element (ARE). Up-regulation of the Nrf2/ARE axis dampens numerous pathologic mechanisms correlating with the autoimmune response, and also IBD. Genetic modification of MSCs to overexpress HIF-1, IFN- γ , and IL-35 exhibited great potential to raise MSCs' anti-inflammatory and pro-regeneration capabilities.

Stem Cell Research Challenges

Stem cells are an evolving area of research that is riddled with multiple unknowns. The method of application (i.e., direct endoscopic injection), how to perform first-in-human testing, and in what IBD subgroup this will be relevant are key questions. Importantly, there is a question surrounding the potential immunogenicity of the transplant medium. Some research groups have transitioned transplant medium toward using substances such as fibrin, which is already licensed for human use, and hydrogel, which can be readily genetically altered and can adapt to mimic the gastrointestinal microenvironment⁶.

Immunological Rejection

A major challenge with stem cell transplants is rejection by the recipient's immune system. To evade tissue rejection, patients undergo immunosuppressive treatment, that makes them susceptible to microbial infections. Inducing pluripotent cells directly from the patient's cells to generate graft or tissue may resolve the problem associated with immunological rejection to an extent. However, low frequency of iPSCs is a major hurdle. It is clear that CD patients are at higher risk of infection compared to those who undergo transplantation to treat cancer or other diseases that do not involve the intestinal tract³. During SC mobilization, patient immunity is reduced, and the risk of infection is higher. Therefore, patients should be carefully nursed during mobilization and reasonable drug levels should be prescribed to reduce the development of adverse reactions.

Long term Safety and Efficacy

Stem cells being used in cell therapy or regenerative medicine could be exposed to microbes, which eventually could cause infectious diseases. The necessary preliminary diagnostic test must be developed before the treatment. In addition, retaining intended biological activity before treatment is crucial for the success of the therapy. Systematic protocols need to be developed for isolation, testing and transplantation of stem cells, to ensure patients' safety.

Hypothesis

Genetic modifications in human iPSCs using CRISPR-Cas9 gene editing technology

Synergistic advances in relevant scientific fields provide new directions for research toward (Human Intestinal Organoid (HIO)) clinical translation—namely CRISPR (clustered regularly interspaced short palindromic repeats) for gene editing and metabolic programming. In cystic fibrosis, the first successful CRISPR-based gene correction was reported in gut organoids from cystic fibrosis patients. In colorectal cancer, CRISPR/Cas9 is exploited to develop a closer human colorectal cancer model using HIOs. Both examples provide a scientific opportunity to modify the IBD ISC genetic susceptibility (for example, in NOD2 mutations in Paneth cell dysfunction in CD) and to develop a human IBD epithelial experimental model with the ability to perturb and interrogate function with gene editing⁶.

Gene editing technology with big-data analysis of transcriptome and proteome analysis is essential prior to undertaking clinical applications, in order to produce safe, reproducible, and cost-effective products that must be the goal for both standardized and optimized products.

We reason that one promising solution is to introduce desired genetic modifications in human iPSCs using i.e., the CRISPR-Cas9 gene editing technology, followed by differentiating the genetically edited iPSCs into MSCs. To develop cell therapeutics with gene-edited stem cell lines, it is vital to develop and maintain safety standards with criteria that include precise off-target checks, high efficiency, and reproducibility of data.

Human Intestinal Organoid (HIO)

How widely applicable HIOs are in the real-world clinic is unclear, given the present early stage of research⁶. We envisage several hypothetical clinical scenarios in which HIOs might be relevant: (1) in medically refractory IBD with significant gut damage; (2) in early postoperative recurrence of CD with localized inflammation in the operative anastomosis; (3) in fibrostenosing CD, in which animal studies have provided some data to suggest benefit. Organoid technology is a perceptible advance in translational science and the vision of using HIOs as a tissue repair approach in IBD.

Conclusion

Inflammatory Bowel Disease (IBD), including Crohn's Disease (CD) definitely needs more effective treatments as current therapies are only aimed at controlling inflammation. Stem cell therapies are promising for regenerative and immunomodulatory properties with potential in tissue repair and immune regulation in CD. SCs inhibit pro-inflammatory cytokines, including IFN-γ, TNF-α, and IL-17, while enhancing anti-inflammatory cytokines such as IL-10 and IL-4. This shifts the balance towards Th1/Th2/Th17. These immunomodulatory effects can be mediated through soluble factors like TGF-β, IL-10, and IDO, which could inhibit dendritic cell activity and T-cell function, thus inducing Treg proliferation. They contribute to mucosal healing and intestinal regeneration through increased proliferation of epithelial cells and improved intestinal barrier, particularly by promoting ISCs activity that is very crucial in mucosal regeneration.

Preclinical models have looked into several types of stem cells, including MSCs and HSCs, and showed positive results in targeting chronic inflammation and promoting repair of the intestinal barrier. Clinical trials for both autologous and allogeneic stem cell treatments for CD have been promising. Autologous stem cell therapies, including AT-MSCs and BM-MSCs, proved to be safe and effective in reducing disease activity, healing fistulas, and inducing remission with minimal side effects. Allogeneic stem cell treatments, including expanded AT-MSCs and UC-MSCs, were also effective in reducing disease activity, improving fistula healing, and providing long-term clinical remission. Overall, these studies highlight the potential of stem cell therapies in treating refractory CD and related complications.

Clinical trials have provided valuable insights into the potential applications and efficacy of SC therapy for CD/IBD. However, it is important to acknowledge the limitations of current SC therapy, including its efficacy, technology, and safety. Obtaining a large number of high-quality, homogeneous SC preparations remains technically challenging. Safety concerns associated with SC therapy include microcirculatory and coagulation dysfunction, immune rejection, and the risk of tumor formation.

Several modifications have been proposed to enhance the use of SC therapy, such as changes to the culture conditions and cultivation methods for SCs, modification of SC contents and genetic genes, and extraction of SC derivatives. These strategies can potentially optimize SC therapy and improve its efficacy and safety in treating CD/IBD. These next-generation SCs are being used as 'Trojan horses' to improve the delivery of drugs and oncolytic viruses to target tissues and are also being engineered with angiogenic, neurotrophic, and anti-inflammatory molecules to accelerate the repair of injured or diseased tissues.

Here we reviewed whether SC therapy can improve CD. It is evident that SC transplantation reduces gut inflammation and improves the quality of life. However, more high-quality randomized controlled clinical trials and basic research are required.

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Title: AI in Classrooms: A Cost-Based Analysis for Policy Makers

Abstract

The primary goal of the study is to address fiscal and policy challenges that could become a hurdle in the widespread adoption of AIED. Moreover, it aims to develop an understanding of the technical landscape, identify fiscal burdens, and highlight the current limitations. With the help of a cost-benefit analysis, the study proposes a framework to evaluate the feasibility and desirability of AIED. Employing a hypothetical case study, it attempts to present a logical argument for implementing AIED when faced with budget constraints. Based on the analysis, the study concludes that for AIED to benefit society, its ethical and legal costs must be minimized, and future returns must be strategically maximized. Furthermore, the study highlights current and potential policy challenges and argues that intentional and unintentional biases must be addressed at the policy level. Moreover, environmental costs should not be ignored, nor should sustainability be disregarded. It is concluded that public policies can not only play a pivotal role in overcoming these challenges but also help mitigate the economic, social, and ethical inequalities that might arise. The study might face limitations due to the unavailability of certain crucial data sets, but it is a positive step toward understanding the economic, social, and legal cost of AIED and opens debate for future research.

Key Words: *AIED, Artificial Intelligence, Intelligent Tutoring System, K-12 Education, Public Policy, Economics of AIED.*

Introduction

Although the term *artificial intelligence* (AI) was initially coined by John McCarthy, the father of AI, in 1956 (Andresen) to describe the "science and engineering of making intelligent machines, especially intelligent computers," (McCarthy et al.) recent disruptive advancements have sparked global interest and debate (Miao). The definition of AI has evolved beyond its original scope, becoming a technology with applications in numerous industries, if not all (Delipetrev et al.). AI has brought about significant transformations and innovations in education (Simhadri and Swamy). However, the **integration of AI into the US education system also brings multiple challenges**. AI's pervasive presence in education in the USA has revolutionized various aspects, from curriculum design to personalized tutoring (Holmes et al.). The study by (Zhang & Aslan, 2021) (Zhang and Aslan) Lists many applications of AI in Education (AIED), including expert systems, personalized learning systems or environments, visualizations, and intelligent tutoring systems (ITS). In addition to these applications, other applications include intelligent assistance for collaborative learning, the implementation of intelligent virtual reality (Kim et al.), monitoring of student forums to understand their problems and address queries, continuous assessment for personalized learning, the utilization of teaching and teachable AI agents, Chatbots for support (Fryer et al.), automated assessment marking, and few other applications implementing Machine Learning (ML) models to understand the determinants affecting students' adoption of wearable

technologies. (Al-Emran et al.). However, significant challenges persist, including privacy and data security concerns as well as potential biases in AI algorithms, which can reinforce existing inequalities in education (Chima Abimbola Eden et al.). These challenges highlight the need for careful oversight and ethical considerations as AI continues to expand within educational settings (Baker and Hawn).

While AI offers a wide array of uses in the education sector, the associated risks and challenges are substantial and cannot be overlooked (Chan). Effective data governance (Owoc et al.) has become a significant concern in the context of AIED because the students' data includes sensitive information, including their grades, attendance, and behavioral patterns, which should be protected against unauthorized access by implementing appropriate policies and protocols around it. Similarly, the other ethical challenges of data privacy and security (Huang), data ownership (Pedro et al.), and overall data management (et al.) in the end-to-end data lifecycle in the AIED context also need to be addressed. On a technical level, challenges such as model bias and discrimination (Ferrer et al.) are now more critical than ever. These risks can not only perpetuate the existing inequalities but also make these inequalities more challenging to combat if not taken care of in the early stages of the development of AI systems. User perception is a determining factor in understanding whether or not the adoption of technology results in the desired outcomes (Ni and Cheung). In addition to the functional aspects, such as the accuracy and correctness of the insights generated by the system, perceived fairness (Hauer et al.), perceived ease of use, and perceived usefulness are some of the non-functional aspects that are all significant considerations for AIED. Achieving projected benefits can quickly become impossible if the technology is challenging to learn and educators and/or students are unwilling to put in the effort to adopt the technology. Technology anxiety and insufficient interest might also pose additional challenges. Moreover, these challenges, in turn, raise other technical, fiscal, and policy challenges. Another perspective argues that the AIED "remains largely underutilized due to a lack of understanding among educators and policymakers" (Rizvi). Among other hurdles, effective and practical implementation of AIED faces infrastructure (Kayembe and Nel), investment (Rizvi), and fiscal challenges. All these challenges are common to any application of AIED. These challenges can be categorized at the macro level into fiscal, technical, and policy risks. The co-existence of these challenges and the indifference to these challenges can result in the failure of apparently well-planned and high-budget projects.

To ensure that AI in education has a net benefit for the country, it is important to facilitate the adoption of effective AI technologies at the federal, state, and district levels. Therefore, addressing the key policy challenges and concerns is crucial (Thomas). Currently, very limited laws and regulations deal with the specificities of AI, and even fewer regarding AIED.¹ Due to the nascent nature of the field, policymakers face the challenge of understanding the underlying technology because designing AI laws and policies is a complex task. Although ample literature is available

¹ For more information, see (Mittelsteadt), (Schiff)

that discusses the ethical concerns and policy challenges of AIED, there is a lack of awareness among decision-makers. AI has a wide range of potential impacts, and each possibility must be given due consideration before designing such laws and policies.²

Amidst the prevailing economic crisis, the existing gap between public spending on education and the cost of education can be bridged by private investment, especially in AI education technology that can reshape how teachers and students engage and increase productivity (Wong). However, in conjunction with federal expenditures, private investment in AI education technology has decreased in the USA from 2017 to 2022. In 2017, the AI-related private investment in education technology was 1.18% of the total private investment in AI, whereas, in 2022, it was only 0.25%. Where the total private investment in AI technology has grown at the average annual rate of 1.82% since 2017, the investment in AI education technology has decreased at the annual average rate of 0.39%.³ Conversely, education costs have increased dramatically over the past few decades.⁴ Therefore, policies, such as R&D subsidies, public-private partnerships, investment screening, sanctions, and export controls,⁵ that can play a crucial role in attracting private investors and encourage the continuation of private investment in AI technology in education are need of the hour.

The increasing inequalities that are associated with the use of AIED remain another major concern for policymakers. The school choices, the general perception of parents and teachers, and the diversity of the population have the potential to increase inequality in the implementation of AIED across schools (Mennle and Seuken). Successful and equitable implementation of AI in schools would require uniform distribution of investment in information technology (IT) and reliable internet access to bridge the gap between students from poor socioeconomic backgrounds. Furthermore, AI's long-term sustainability in education should be an important consideration for policymakers. The schools must carefully assess their budgets, costs, and return to investment to justify continuing funding in AI systems. They must also consider any added cost because of the legal repercussions of data privacy issues, as well as any funding that might be required for communication and advocacy efforts to change public perception and acceptance of AI-based learning and teaching tools.

The benefits of AIED are undeniable. Though its implementation in the USA leans toward automating administrative tasks, AI technologies can be adopted for broader scales. It has the potential to make education universal by fostering life-long learning through intelligent tutoring that focuses on the capabilities of the students and provides remedial learning appropriate for the student on an individual level (Stone et al.). AI systems that gauge the development of students and consider their interests and educational needs can prove to be an important milestone in

² Ibid

³ Calculated using the private investment in AI technology data. Dataset from Our World in Data.(Baraishuk)

⁴ For more information, see (DeAngelis)

⁵ For more detail, see (Arnold et al.)

improving the educational system (S. Plan). In addition to that, the demand for AIED is expected to increase in the coming years and has the potential to reshape the world. Unfortunately, the current economic slowdown has created the Solow paradox (Lu and Zhou). Therefore, addressing the challenges and concerns at the early stages of implementation is crucial. Only with the proactive adoption and implementation of policies at the state level can these challenges around the implementation of AIED be overcome.

To this effect, the objectives of the study are as follows.

1. Through literature, provide a comprehensive overview of the technical, ethical, and fiscal challenges of AIED in the USA.
2. To propose a cost-benefit analysis to weigh the pros and cons of implementing AIED in K-12 education in the USA.
3. Using a hypothetical CBA, outline a plausible approach that could mitigate various hurdles in the implementation of AIED in the USA.

Instead of a general discussion, the study focuses on a specific application of AIED, Intelligent Tutoring Systems. To that end, the study utilizes a hypothetical implementation of an intelligent tutoring system in K-12 education as an example to provide guidelines for policymakers. The framework considers the technical, economic, social, and environmental aspects of implementing AI-based technology in K-12 education.

Research Question:

1. What obstacles, both technical and policy-related, impede the effective implementation and operation of AIED, considering fiscal constraints?

The next section provides the literature review. In the preceding section, methodology, theoretical background, and data are discussed. Results and discussion are provided based on a hypothetical Cost Benefit Analysis. The study is concluded in the final section.

Literature Review:

AIED is revolutionizing the education sector, and Intelligent Tutoring Systems (ITS) are one of the most disruptive and transformative applications of Artificial Intelligence (AI) (Zawacki-Richter et al.). ITS corresponds to systems that comprise AI-based intelligent tutors who understand what, who, and how to teach (Nwana). According to the consensus reached in literature (Thomas), ITS has four major modules: "a domain or expert module that serves as the heart of the system by providing subject knowledge, a pedagogical module that identifies learners' knowledge deficiency, a student model that tracks learners' knowledge status, and a user interface module through which learners interact with the system" (Ni and Cheung). Another study (Wang et al.) call these modules *components* necessary to provide the features that ITS offers. Intelligent tutoring systems (ITSS) can perform a wide range of tasks. They can determine the optimal learning

path for each student, select and recommend relevant learning content, provide scaffolding and support, engage students in dialogue, and simulate one-to-one tutoring (Zawacki-Richter et al.). Additionally, ITSs can offer customized experiences to different students, teachers, and tutors (Churi et al.). Recommendation and Tutoring, Personalized Support, Exercise and Support, Personalization, Adaptive conversation, and Game-based learning are some of the applications of ITS (Wang et al.). The table below lists each application with its relevant ITS and key features (Wang et al.).

Application	ITS name	Main features
Recommendation and Tutoring	Cognitive Tutor (Bernacki and Walkington)	Capable of providing personalized problems and step-by-step instructions based on students' cognitive models.
Personalized Support	SARA (Mousavi et al.)	Capable of providing Automated and personalized feedback to students.
Exercise and Assessment	ASSISTments (Jiang et al.)	Capable of providing homework intervention in terms of adaptive assessment and feedback.
Personalization	HNTS (del Olmo-Muñoz et al.)	Capable of providing personalized learning path.
Adaptive Conversation	SKOPE-IT (Nye et al.)	Capable of talking to students to offer learning support.
Game-based Learning	GraphoGame Rime (Ahmed et al.)	Capable of teaching language learning through game-based learning.

Table 1: Applications of ITS (Wang et al.)

Technical Challenges:

In this section, a few significantly challenging technical risks of AI are discussed. While some of the challenges are specific to AIED, others encompass many other applications of AI. However, this study outlines these challenges from the perspectives of AIED and ITS.

ITSSs are prone to a technical challenge of **Algorithmic Divide** (Dieterle et al.) that occurs in the algorithms. In the context of this study and ITS, an algorithm can be defined as a piece of software code responsible for consuming data to train predictive models and generate data-driven insights useful for students, instructors, and administrators of educational institutions (G. Veletsianos). Ideally, a fair algorithm should not discriminate against anyone based on their category in the protected group. A protected group is often defined based on age, sex, color, race, religion, nationality, citizenship, veteran status, genetic information, physical disability, or mental disability (Office and Commission). However, pre-existing patterns of bias in historical data and the difference in trends in the system's utility can make the system discriminate against individuals. Unfairness, bias, and discrimination are issues raised by training these algorithms on such data. The bias does not have to be intentional. Sometimes, the mere unavailability or the abundance of certain types of data can cause this algorithmic divide. Identifying such unfairness is a challenging task that is usually overlooked, resulting in unintentional discrimination.

Different approaches can be employed to address this challenge. One solution to mitigate this effect is having more than one such algorithm trained on different data sets (Daniel). Oversampling is one technique applied to underrepresented groups to ensure ample data on underrepresented groups is available for AI models (Kizilcec and Lee). Additionally, it is the responsibility of the development team to test the algorithms and point out potential ethical issues to the stakeholders to avoid misrepresenting a particular class (Mitchell et al.). The validation team should comprise people from diverse backgrounds, including diversity in sexual orientations, disciplines, disabilities, life experiences, cultures, races, and religions. Moreover, diversity should be considered while formulating research questions for model training (Nielsen et al.). The incorporation of third-party data can impact the algorithm's validation since the development and validation team cannot control the data gathered by third-party vendors (Daniel). Nevertheless, to eradicate pre-existing bias in data, it is essential to clearly define the problem, properly analyze data to check for bias, and apply appropriate de-biasing techniques. Continuous monitoring of the performance of trained algorithms through audits of equity, quality, and education, as well as markets and policies, also plays a crucial role in keeping the bias in check (Shute et al.).

In its true sense, **educational equity** of AI-based educational systems referring to universal and equal access to resources among educators and learners without any influence of race, sexual orientation, gender, ethnicity, disability, family background, or family income has not been accomplished (CCSSO). As per the American Community Survey analysis carried out by Chandra and Colleagues, only 70% of K-12 public school students have access to the internet or a proper

device requisite for distance learning. In comparison, this proportion goes up to 90% as far as K-12 teachers are concerned (Chandra et al.). This scenario leads to the **big data paradox**, a case where a small sample size of a certain distribution in a big data set can render the sample a poor representation of a larger population (Parsons). According to another study, K-12 students with no access to the internet and digital devices have GPAs 0.4 lower than their counterparts, resulting in 4-6% lower expected income and annual GDP loss of \$22-33 billion (Nguyen et al.). Hence, sustainable access to digital resources, including hardware and high-speed internet, is the need of the hour to ensure equal and equitable representation of the masses in the big data context. Responsible AI is a term often tossed for accountability and responsibility.

The data generated through the utility of digital learning platforms can raise another ethical issue: the **interpretation divide**. The stakeholders, including the policymakers in an AIED context, tend to follow data-based decision-making (DBDM) that extends from classrooms to school level, from school level to district, state, and eventually country (Schildkamp et al.). The mere availability of data does not tell anything, i.e., the data itself does not provide any insights (Schildkamp et al.). Interpretation of the data is when the stakeholders try to make sense of it and its implications for future actions. Two challenges can surface through this DBDM. The first is the lack of interpretation of the data, and the second is the lack of knowledge of the application after interpretation (Perkins). **Confirmation bias** is another issue that can occur due to the interpretation of data by individuals or groups when they give greater weight to information that is in line with their experiences and preconceptions and trivialize information inconsistent with their perspectives (MacLean and Dror). Data interpretation education for teachers is very important to equip them to better understand the data. Additionally, the variation factors, including disability, language barriers, bullying, demographics, attendance, health, transportation, justice, and motivation, should be considered while analyzing student performance and behavior (Mandinach and Schildkamp).

Since AI is a highly technology-dependent and cross-disciplinary field (Kay and Kummerfeld), aligning with societal values is necessary for its sustainable development (Hwang et al.). The principles of AIED governance and stewardship of trustworthy AI (OECD) are of great significance in this regard. AIED governance and stewardship principles shed light on how AI should be utilized in education, the correlation between the technology being developed and deployed, and the purpose for which it was required in the first place. Inclusive growth, sustainable development and well-being, human-centered values and fairness, transparency and explainability, robustness, security, safety, and accountability come under the umbrella of principles of AIED governance and stewardship (OECD). These principles suggest that diversity from the stakeholders' view and ethical policies concerning multiple domains, including data analytics, learning analytics ethics, computational ethics, human rights, and inclusiveness, should be considered while formulating policies and frameworks. The data ownership, access, purpose of data usage, data collection process, and data reporting should be transparent, and the utility of the AI algorithm should be explainable and justifiable (Nguyen et al.). The deployment of AIED

should not derail the environment, economy, culture, or any socio-political aspect (Nguyen et al.). The system should ensure the consent of users as well as the confidentiality of users' information, either provided by users themselves or collected by the system (Nguyen et al.). The government and organizations related to the education sector should introduce skill development and learning opportunities related to AI literacy skills so that teachers and students can control the digital AI system and optimal human-machine collaboration can take place (Bryson and Theodorou). Several studies and initiatives by international institutes, including UNESCO Ethic AI 2020, UNESCO Education and AI, Beijing Consensus 2019, European Commission 2019, and European Parliament Report AI Education 2021 highlight some or all of the principles mentioned above in their respective ethical guidelines and reports (Nguyen et al.).

Fiscal Challenges and Considerations

This section outlines the fiscal challenges that the current economic outlook presents and how they might shape the future of AIED implementation. The United States is among the global leaders in research and development, with an average of 2.5% of GDP allocated to R&D (UNESCO). The percentage of GDP allocated to R&D has increased steadily since 2010, as depicted in Figure 1. Furthermore, the total allocation of R&D for AI technology also exhibits an increasing trend (Maslej). However, it is noteworthy that within the domain of federal R&D expenditures, the prioritization of investments in educational technology remains subdued. According to a federal budget report (2022), R&D spending allocated to education accounted for a mere 0.21% of total R&D spending; in 2023, it decreased to 0.17%. The future expectations suggest a further contraction, to 0.16% in 2024 (White House). Moreover, amidst the increasing demand for AIED (Miguel A. Cardona et al.), the education expenditure of the USA is on a downward trajectory, as shown in Figure 1. Combined with a decrease in GDP growth rate, it implies that adequately meeting the current fiscal needs of implementing AI-augmented learning might be challenging. Current fiscal challenges are rooted in record debt levels,⁶ the end of discretionary spending caps, predictable expirations, looming fiscal deadlines, and the depletion of major trust funds (Committee for a Responsible Federal Budget).

⁶ By the end of 2022, the U.S. debt level increased to \$31.42 trillion (U.S. Treasury). According to the Bureau of Economic Analysis statistics, the USA's national debt is 123% of its GDP (2022). For more information, see the Bureau of Economic Analysis. "Gross Domestic Product (Third Estimate), Corporate Profits (Revised Estimate), and GDP by Industry, (Third Quarter) 2021."

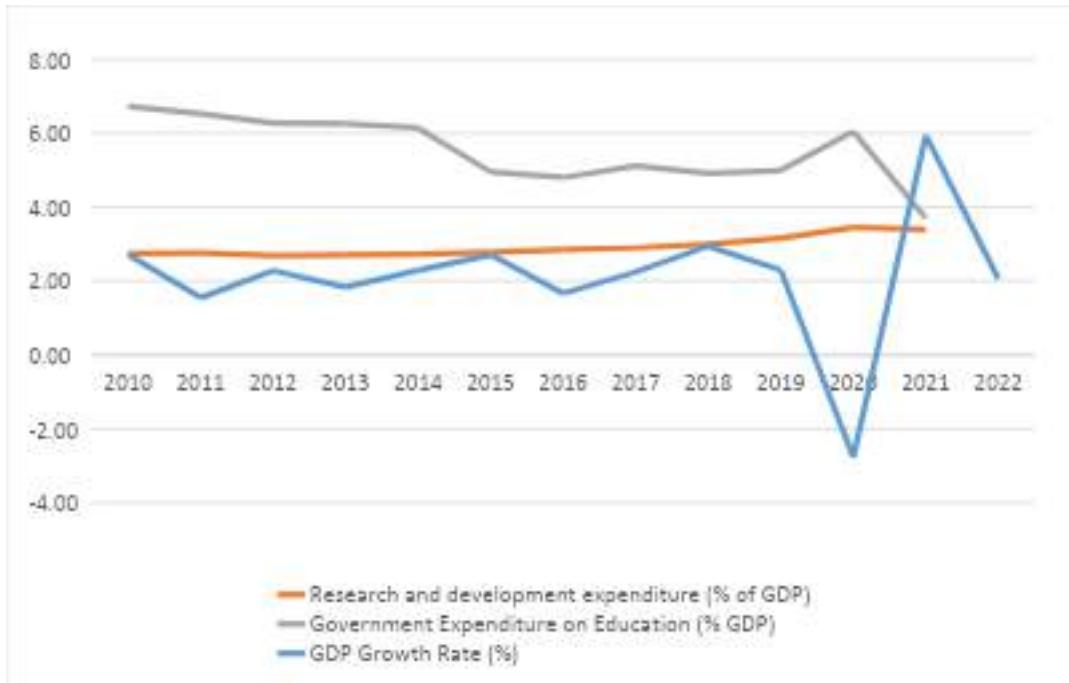


Figure 1: R&D and Government Education Expenditure (% of GDP) and GDP Growth Rate of USA (2010 to 2022)

Source: Constructed from the World Development Indicators Database (DataBank).

Implementing AI-augmented learning when schools face funding constraints is challenging because, aside from initial investments and implementation costs of AI tools and systems installation, its maintenance is also costly (Frackiewicz). Furthermore, there is a cost of training and professional development to ensure teachers and educators are well-equipped to use AI tools effectively (Akgun and Greenhow). Therefore, it is crucial to analyze the cost-effectiveness of AI-powered systems (Baraishuk). In addition to financial constraints, one of the significant challenges is the infrastructure for hardware installations and software. Specific requirements are necessary to meet hardware requirements and software capabilities (Owoc et al.), (Sellar and Gulson). Moreover, scalability is another significant challenge that persists in practice despite the available theoretical and conceptual research (Holstein et al.).

Policy Considerations for AIED Implementation in the USA

One of the most important concerns is algorithm bias (Baker and Hawn) because AI technology is developed using large datasets. However, if the dataset is non-inclusive and non-representative, it would result in AI technology that might be unfair in making automated decisions and detecting patterns (Miguel A. Cardona et al.), (Perry and Lee). Therefore, ensuring the quality of datasets used in the development of AI systems is important and remains one of the major concerns for policymakers. Otherwise, the issue might arise where all segments of society are not represented in an equitable manner (Hwang et al.). It also raises potential privacy and security concerns

regarding implementing AIED (Nguyen et al.). Therefore, transparency should be a priority focus for policymakers to ensure no security risks are involved in data collection and use (MacCarthy et al.). Any policy framework for AIED also needs to be fair and human-centered.⁷ In this regard, there is a need for a system-wide organizational structure that is capable of governing AIED.⁸ The governance of AIED alludes to establishing such policies that embody responsible management of the design and use of AIED (Ashok et al.), (Floridi).

Where state-level initiatives have been taken in recent years,⁹ there is a lack of federal-level policies and initiatives directly addressing AIED. (Lehot) In Table 2, federal-level policies are briefly summarized. These policies are not specific to AIED, but their scope of use is outlined. As the demand for AIED has increased, the regulatory framework that can adequately address the complexity of AI-based systems has become the need of the hour. The policies centered on AIED must take into account all the above-discussed challenges and concerns for the implementation of AIED to be beneficial for society as a whole. Another limitation of most federal policies is that they are not specific to AIED (Mittelsteadt), (Yandle).

		Scope
Every Student Succeeds Act (ESSA)	Passed in 2015	It is not specific to AIED, but it emphasizes the use of technology and innovation in education.
The National Education Technology Plan (NETP)	Updated periodically	It is a blueprint that outlines the government's strategies to use AIED effectively
The Education Innovation and Research (EIR) Program		It supports the implementation of innovative practices and technologies, including AIED, and is managed by the US Department of Education
Family Educational Rights and	Passed in 1974	It is not AI or AIED specific but governs the privacy and security of student educational records, and it is used to protect student data privacy when AI and AIED systems are used.

⁷ Also, see (Chan)

⁸ For more information on the issue of governance, see (Ashok et al.), (Miao et al.)

⁹ Some of the examples of state-level policies include but are not limited to, Statewide Data Privacy Laws, STEM Education Initiatives, Competency-Based Education (CBE) Programs, Digital Learning Initiatives, and Computer Science Education Policies.

Privacy Act (FERPA)		
National Artificial Intelligence Initiative Act	Passed in 2020	It relates to AI but does not cover explicit regulations.
Blueprint for an AI Bill of Rights	Policy Announcement of 2022	It defines broad guidelines of AI policy. However, it does not address AIED specifically.

Table 2: Existing AIED Policies in the USA

Considering the above discussion, a cost-benefit analysis (CBA) of AIED is proposed in the next section. The purpose of such an analysis is to provide a guideline for policymakers by providing an in-depth analysis of the costs and benefits of an AI system in K-12 education.

Methodology and Data:

The study utilizes a quantitative approach to evaluate the feasibility of implementing AI in Education (AIED), specifically intelligent tutoring systems (ITS) in K-12 education in the USA. Given the limited availability of real-world data on comparable AIED projects (Guo et al.), the study utilizes a hypothetical case study and employs hypothetical data for the CBA (Manning et al.), making the analysis exploratory in nature as it aims to provide a framework and guidelines for policymakers to understand the potential costs and benefits of AIED implementation.¹⁰

The choice of CBA as the evaluation methodology stems from its suitability for assessing projects with societal impacts. It facilitates a thorough analysis of both quantifiable and intangible costs and benefits, making it suitable for evaluating complex projects with broad societal implications, such as the implementation of AIED.¹¹ Moreover, CBA provides a framework for policymakers to make data-driven decisions by comparing the economic costs and benefits of implementing AIED. The study aims to address the fiscal and policy challenges of AIED adoption. In addition to that, it encourages the consideration of potential negative consequences, such as ethical issues and environmental impacts, which are crucial aspects of AIED implementation. Therefore, it is an

¹⁰ For example, Vagdatli T, Petroutsatou K. Modelling Approaches of Life Cycle Cost–Benefit Analysis of Road Infrastructure: A Critical Review and Future Directions. *Buildings*. 2023; 13(1):94. <https://doi.org/10.3390/buildings13010094>

¹¹ For further information see, Why Cost-Benefit Analysis is an Inefficient Decision-Making Process in Public Policy By Delaney Edge

appropriate tool for analyzing the feasibility and sustainability of AIED for the purpose of this study.¹²

Cost Benefit Analysis (CBA) of AIED

There is an array of research on both the gains and losses of AIED. While the proponents often highlight the gains in efficiency, scalability, and accessibility, the opponents focus on the alienation and ethical impacts that can potentially disrupt society. However, very few studies talk about the economic aspects of AIED (Yu et al.). AI can potentially improve, streamline, and facilitate both teaching and learning, as well as administrative services (Chaudhry and Kazim). On the other hand, it also has the potential to create various ethical, social, and legal problems (Holstein and Doroudi). Yet, it is equally important to analyze the potential economic gains of AIED (Schiff) to understand its desirability and sustainability better. Therefore, this study attempts to analyze the potential technical, social, and economic benefits and costs of implementing AIED. For this purpose, a cost-benefit analysis (CBA) is proposed, and policy implications are drawn based on the results.

CBA is an insightful policy tool that helps assess the viability, impact, and economic rationale of using AI in education. It provides a structured framework to balance the significant costs of implementing AI tools with the educational, administrative, and societal benefits they offer. By evaluating these factors, CBA helps stakeholders make informed decisions on whether AIED implementation is a sound investment in the future of education.

Theoretical Background of CBA:

The objective of a cost-benefit analysis (CBA) is to appraise the policies and/or projects aiming to improve services. It relies on data-driven decision-making and quantifiable information (Zolnowski and Anke), (Wilcox et al.). Hence, its primary goal is to determine in the most comprehensive way whether an economic decision is feasible and profitable (Robinson). It involves both measurable and intangible costs and benefits associated with a project and, therefore, provides an evaluation of projects that are of a social nature (Mishan and Quah).

The theoretical background of CBA is rooted in welfare economics. It aims to measure the utility or welfare improvements associated with a given decision. CBA is used to evaluate if a particular decision, investment, or policy increases societal welfare. In this case, welfare is assessed by examining the benefits to individuals relative to the costs. One of the core principles of welfare economics is Pareto Efficiency, where a change is considered beneficial if at least one person benefits without making anyone else worse off. While achieving pure Pareto improvements is rare,

¹² Also see, Boardman, A. E., Greenberg, D. H., Vining, A. R., & Weimer, D. L. (2018). *Cost-Benefit Analysis: Concepts and Practice* (5th ed.). Cambridge University Press.

CBA seeks to approach this ideal by maximizing total net benefits across society (James and Predo), (Pearce).

CBA is grounded in utilitarian philosophy, where the goal is to achieve the highest total utility or benefit. Decisions that maximize positive outcomes (benefits) and minimize negative ones (costs) align with this approach. It assumes all costs and benefits can be compared and aggregated, regardless of their nature (e.g., economic, social, environmental). In practice, this means monetizing non-financial outcomes to compare them on a common scale, typically money (Riley).

Moreover, the concepts of opportunity cost, diminishing returns, and discounting future costs and benefits are important considerations while maximizing net benefits. Thus, CBA is an appropriate analysis for this study. These theories help ensure that CBA balances benefits and costs in a way that maximizes overall utility, though they also highlight the method's limitations, particularly around monetizing intangible impacts and accounting for equity (Boardman et al.), (Florio and Pancotti).

Hypothetical Application of CBA in AIED

The first step of CBA is to identify the goals and objectives of the proposed projects. In other words, to clearly define what would make the project successful. In this context, the objectives of intelligent tutoring systems in K-12 education must be identified. Based on the literature review and prior discussion, we can conclude that the goals of implementing intelligent tutoring systems are as follows: (Gerard et al.), (Zafari et al.)

- To provide a personalized learning platform for guiding students individually to improve performance.
- To provide aid to teachers so that they may better analyze student performance and help them with automated assessment systems.
- And generate insights about student behavior with the help of facial recognition systems.

Based on these goals, the study attempts to perform a cost-benefit analysis of an AI-based system that is developed to meet the above-mentioned needs.

Identifying Costs and Benefits

The second step of performing CBA is to identify all costs and benefits of the project.¹³ This study focuses on ITS for K-12 education, and therefore, the study would identify the potential costs and benefits associated with adopting such technology.¹⁴

Direct and Indirect Costs:

These are fixed costs. In the case of the current analysis, the direct costs are infrastructure and hardware requirements, purchasing or licensing the software, and the cost of maintaining the system (Robinson et al.) . The indirect costs include the cost of training teachers and educators to use the systems and the cost of upgrading the system (Murphy).

Intangible Costs:

These include the current and future costs that might be difficult to quantify. The intangible costs of an intelligent tutoring system in K-12 education would include technical challenges and future costs associated with them, such as a decrease in performance or student grades, as well as social and economic inequalities because of algorithm bias or unintentional interpretation divide and discrimination.¹⁵ It also includes costs incurred due to ethical challenges and dilemmas, such as privacy and data breach issues, (Akgun and Greenhow) as well as the social cost of increased surveillance and any legal costs that might arise as a result (Miao et al.), (Ayoub), (Powers et al.). Moreover, environmental costs are also included in the intangible costs of adopting AIED in K-12 education. These costs stem from increased energy consumption¹⁶ and electronic waste¹⁷ generated by AI-powered devices and systems. A vast amount of energy is required for the widespread implementation of intelligent tutoring systems in K-12 schools, which would increase greenhouse gas emissions and the ecological footprint¹⁸ of the USA. Furthermore, implementing the ITS in schools would increase the demand for electronic devices, such as computers, tablets, and

¹³ For more information, see (Stobierski)

¹⁴ For ease of analysis, as well as, keeping the objective of the study under consideration, we assume that intelligent tutoring systems are available in the market. Therefore, the CBA would focus on the adoption and implementation costs and benefits.

¹⁵ For more information, see (Macgilchrist et al.)

¹⁶ The production of AI-enabled hardware requires raw materials, leading to resource depletion and environmental degradation. Data centers require significant cooling and maintenance, which further adds to their energy consumption. Additionally, cloud-based services that would be utilized to deliver AI applications in education would also require considerable energy. Thus, contributing to the overall environmental costs of the AIED.(Wu et al.)

¹⁷ According to the World Economic Forum, e-waste is the world's fastest-growing domestic waste stream, and only 20% of it is recycled in a certified process (Forti).

¹⁸ The ecological footprint of the USA is one of the highest in the world at 8.04 gha per capita (Ecological footprint).

smartphones. The waste of malfunctioning or outdated devices would result in electronic waste, increasing the environmental cost.

Opportunity Costs:

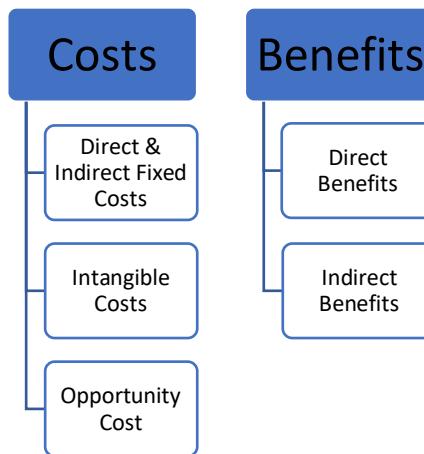
Opportunity cost refers to any cost forgone while allocating resources to AIED.¹⁹ The funding that schools use for AI technology could be used for other purposes, and depending on them, opportunity cost is measured in lost benefits.

Direct Benefits:

These are the benefits that are a direct result of implementing AIED. They include increased student performance because of immediate feedback on errors, adaptive instruction, minimizing working memory load, and personalized support and guidance (Ma et al.). Another direct benefit is the time saved for teachers.

Indirect Benefits:

The current and future benefits that might result from using AIED. From the perspective of the current analysis, these include better communication between students and teachers, increased efficiency of teachers by helping them and reducing their workload, reduction in education costs for the students, and improvement in the educational journey of the students by helping them achieve their goals through the right courses and better teaching techniques, and future job opportunities (FELDON), (Prest and Turvey), (APA).



¹⁹ For more information on opportunity cost, see (Pickering)

Figure 2: Overview of CBA Framework for ITS

Data Selection and Sources

This paper analyzes AI in education with specific attention to intelligent tutoring systems for K-12 education in the USA. Open-access data from various sources, including federal estimates, research papers, and secondary data from published case studies and surveys, are used for the purpose of the current analysis. All sources are cited appropriately. Where required data is unavailable, proxies are used, and proper justification is provided.

Results and Discussion

Cost Benefit Analysis is a useful tool for decision-making in public policy because it helps policymakers analyze the costs and benefits of any project in a meaningful way and understand the unintended consequences (Pearce), (Posner). Therefore, the study employs the CBA framework to study AIED to better understand the objectives of AIED projects, their costs, and expected benefits.

The real-world data and projects are ideal for performing CBA. However, it is beyond the scope of the current analysis. Moreover, data on comparable AIED projects is not available for CBA performance. Therefore, due to the practical limitations, the study uses a hypothetical project and utilizes hypothetical data for CBA by employing the framework established in the previous section. It allows for a controlled exploration of the CBA framework developed in the previous section. This approach, while hypothetical, ensures that the methodology remains robust, illustrating the utility and adaptability of the framework in the absence of empirical data.²⁰

Costs of Intelligent Tutoring Systems

For the analysis, we assume that schools want to implement an intelligent tutoring system for five years. Based on the available data and research, the study concludes that large-scale implementations can vary widely depending on factors such as the complexity of the system, the number of students, and the specific features included. On average, the cost can range from \$50 to \$4,300 per student per year. However, these figures can fluctuate based on the scope and scale of the implementation (Thomas et al.) (Ma et al.). To avoid overestimation as well as underestimation, the study assumes that the intelligent tutoring system costs \$2,175 per student per year.

²⁰ For details of hypothetical analysis and its importance, see, Manning, M., Johnson, S. D., Tilley, N., Wong, G. T., & Vorsina, M. (2016). *Economic analysis and efficiency in policing, criminal justice and crime reduction: What works?*. Springer. Also see, Ratnaweera, D., Heistad, A., & Navrud, S. (2021). The current use and potential of cost benefit analysis in water sector projects. *Water Supply*, 21(4), 1438-1449. More details can also be found here, Weimer, D. L., Vining, A. R., & Vining, A. R. (2009). *An agenda for promoting and improving the use of CBA in social policy* (pp. 249-272). Washington DC: Georgetown University Press.

Therefore, the five-year cost would be $\$2175 * 5 = \$10,875$ per student. Let us assume that it is the initial implementation cost of the system, which is the overall fixed cost.

The maintenance cost of the system depends on its complexity and scale and can vary significantly depending on various factors, including the complexity of the system, the technology used, the scale of deployment, the specific components being implemented, the region or environment in which the system operates, and the duration of maintenance. However, for simplicity, a conservative maintenance cost is assumed (Stobierski). Therefore, it is 15% of the implementation cost, i.e., 15% of $\$10,875 = \1631.25 . Maintenance costs include both fixed and variable costs; thus, they should be discounted to determine the present value of future costs. Assuming a discount rate of 3%,²¹ the maintenance cost is calculated employing the present value formula as follows:

$$PV = FV / (1 + r)^n$$

In this case, we have.

$$\text{Future Value} = \$1631.25 \quad r = 3\% \quad n = 5 \text{ years}$$

Therefore, the Present Value (PV) is;

$$PV = \$1631.25 / (1 + 0.03)^5 \approx \$1406.27$$

The complex interactions between technology, energy consumption, educational outcomes, and environmental impacts²² make it difficult to quantify the environmental costs of ITS accurately. However, proxies may be used while keeping in mind that they may not capture the real value of these costs. According to an estimate, schools in the USA emit 72 million metric tons of carbon dioxide annually. Assuming a 2% increase in carbon dioxide emission due to AI implementation,²³ we can assume that ITS results in an annual carbon dioxide emission of 1,440,000 metric tons. We then calculate the monetary value of carbon emission by using the social cost of carbon (SCC), which is \$51 per ton of carbon emitted (Giller). Thus, the environmental cost would be;

$$\text{Cost} = SCC \times 1,440,000 \text{ metric tons} = \$51 * 1,440,000 \text{ metric tons} = \$73,440,000$$

²¹ Determining an appropriate discount rate for AI in K-12 education involves considering various factors, including the time value of money, risk, opportunity costs, and the specific context of the investment. Discount rates are used to account for the time preference of money and to assess the present value of future costs or benefits. A lower discount rate of 3% is used to err on the side of caution and emphasize the near-term benefits.(National Archives), (Haacker et al.)

²² For more information, see (Dhar)

²³ A 2% increase in carbon dioxide emission is assumed as a thought experiment to highlight the importance of the potential environmental impacts of technology and to emphasize the need for responsible and sustainable AI development. For more information, see (Heikkilä), (Degot et al.)

Assuming a discount rate of 5%²⁴ and applying the Present Value formula, we have the following.

$$PV = \$73,440,000 / (1 + 0.05)^5 \approx \$57,472,066.18$$

Similarly, we can use the annual training and advisory services budget as a proxy to estimate the cost of training the teachers and educators.²⁵ The total budget is \$6575,000. Let us assume that 5% of it can be used to provide the necessary training to operate the system; then, the cost would be \$328,750. We also assume that teachers and educators would require training once every five years.

Ethical and legal costs that might result from implementing an intelligent tutoring system are difficult to quantify. It would depend on the specific nature of the system, society's acceptance, and various other factors. However, the potential ethical and legal costs of such a project cannot be ignored. A reliable CBA would analyze a data and risk framework tailored to AIED. However, it is beyond the scope of this analysis. However, the cost is expected to be non-zero, as discussed in the literature review. For the current analysis, a simplifying proxy may be utilized.²⁶

A conservative estimate may assume that 1% of the total education budget for a given year is allocated to legal and ethical costs. For 2023, the Department of Education budget allocated to K-12 education is \$42.6 billion.²⁷ Based on this figure, the study assumes that K-12 education incurs an ethical and legal cost of \$426 million per year, on average. However, not all this cost would be for the AI tutoring system. Keeping the analysis conservative, let's assume 1% of the legal and ethical cost is allocated to mitigate the effect of intelligent tutoring system implementation. Hence, the total ethical and legal cost of the system is estimated to be approximately \$4,260,000. Assuming this to be the legal and ethical cost over the five-year period, we may proceed with the analysis.

The opportunity cost of implementing an intelligent tutoring system would be allocating the funds for the next best alternate education program, such as hiring more teachers, offering specialized courses, spending on the extensive professional development of teachers, investing in improving the infrastructure of schools, upgrading existing technology, etc. The opportunity costs should be carefully analyzed to weigh the costs and benefits of the system.²⁸

²⁴ A slightly higher discount rate of 5% is used to estimate environmental costs to indicate that future costs might be less worth than present costs because AI technology has the potential to self-regulate.(Evans), (Sverdlik)

²⁵ The U.S. Department of Education budget for 2022.

²⁶ For more information on simplifying assumptions, see (Milgrom), (Denison)

²⁷ For details, see Fiscal 2022 K-12 spending explained in 6 charts: <https://www.k12dive.com/news/fiscal-2022-k-12-spending-explained-in-6-charts/620378/>

²⁸ For the purpose of the current analysis, opportunity cost is not calculated. The opportunity cost is not added to the total cost in CBA. The objective of calculating this cost is to better understand the next best alternative and benefits that would be forgone. Therefore, because the current analysis utilizes a hypothetical project, it is not necessary to calculate the opportunity cost.

Therefore, the total costs of implementing an intelligent tutoring system in K-12 education for five years would be;

$$\text{Total Cost} = \$10,875 + \$1406.27 + \$57,472,066.18 + \$328,750 + 4,260,000 = \$57,813,097.45$$

Benefits of Intelligent Tutoring Systems

The next step is to quantify the expected benefits of the project. The benefits of intelligent tutoring systems include increased student performance and the efficiency of teachers, as well as the effectiveness of education. Therefore, taken as a whole, we can say the benefit of an intelligent tutoring system in K-12 education is an increase in the productivity of the education sector.

Total expenditure on education can be used as the measure of education output.²⁹ However, that might be an overestimate because the study focuses on a single AIED project. Therefore, the total public expenditure on education technology is considered to estimate the quantifiable value of the benefits of the intelligent tutoring system.

In the 2022 budget, the public expenditure on education technology is \$29547,000. Due to the lack of real-world data, we assume that all of it is used for AIED implementation. The study considers this as the value of expected efficiency increase from implementing an intelligent tutoring system in K-12 schools. Additionally, AIED has the potential to decrease the cost of education in terms of private tuition, transportation, hostels, books, etc. It also can potentially reduce the learning gap between students in lower-income schools and those in high-income schools by providing them with personalized learning opportunities.³⁰ To quantify this expected benefit of ITS, the study uses private investment in AI technology, which is \$111497296. Assuming a discount rate of 5%, its present value is calculated as follows:

$$PV = \$111497296 / (1 + 0.05)^5 \approx \$87,343,676.80$$

Thus, total benefits are \$29547,000 + \$87,343,676.80 = \$116,890,677

$$CBA = \text{Total Benefits} / \text{Total Costs} = \$116,890,677 / \$57,813,097.45 = 2.02$$

A CBA ratio greater than 1 indicates that the benefits outweigh the costs. Therefore, the ITS implementation is feasible and advisable.

Key Policy Implications of CBA

A hypothetical CBA analysis is conducted in the study based on logical reasoning and proxies to quantify the costs and benefits of an intelligent tutoring system in K-12 education. It is noteworthy

²⁹ The output of the education sector is often measured in terms of its inputs (Gu and Wong).

³⁰ For more information, see (Diebold and Han)

that legal and ethical costs contribute significantly toward the total cost of implementation. The current analysis is conservative, and the results show that ITS has net benefits. However, by reducing the ethical and legal costs of implementation, the benefits may be further maximized. Therefore, it is implied that for any such project to be beneficial in the long term, policies to minimize such costs must be considered (Bright and Cortes). Government policies aiming to increase transparency and accountability at the development stage of AI-based technology would reduce future costs by eliminating the risk of intentional and unintentional biases and social and economic inequalities.

Additionally, reducing environmental costs should be another priority for policymakers (Wu et al.), (Degot et al.). As it stands, these costs contribute considerably toward the total costs. Thus, policies toward managing electronic waste, employing sustainable technology, and reducing greenhouse gas emissions should not be ignored at the early stage of discussion.

Another important implication of the analysis is assigning monetary value to the benefits. As the study uses total expenditure on education technology to quantify the benefits, it is implied that the greater funds allocated to education technology result in better performance. Thus, the allocation of education expenditure plays a key role in this regard, and its importance cannot be downplayed. Taking the framework presented in the study as a guideline for key policymakers to comprehensively understand the objectives of AIED implementation, emphasis should be paid to reducing ethical, legal, and environmental costs, as well as increasing the budget allocation of K-12 education.

Limitations of the Study and Recommendations for Future Research

The CBA is a useful technique to determine whether a planned action is beneficial for society or not (Mishan and Quah). It is frequently used in public policy. However, it has its limitations (Posner), (Sassone and Schaffer). One of the most difficult to overcome is quantifying certain costs and benefits that might not have monetary value. To overcome this hurdle, proxies are used based on available data and the nature of the variable (Sassone and Schaffer). The current study is limited because the choice of proxies is heavily dependent on the availability of data rather than accuracy. As the data availability is improved, future studies should quantify the social, ethical, legal, and environmental costs of AIED more accurately. In this regard, surveys should be conducted at regional and national levels to collect data that gives more insights into society's willingness to accept AI-based systems in K-12 education costs of lawyers and courts in case of lawsuits. Moreover, future research should take into account that depending on the objectives and type of AI-based system used, there might be costs associated with ensuring it complies with privacy laws, etc. Hence, such costs should be included in the analysis. In conclusion, the limitations of the current analysis pave the road for future analysis.

Conclusion and Future Recommendations

The demand for AI in education is increasing rapidly. Where AI-based systems have an array of advantages for education, there are several risks and challenges that need due consideration. The current study discusses some of the most pressing technical, fiscal, and ethical challenges of AIED implementation in K-12 education.

The discussion reveals that technical biases can potentially increase societal inequalities and hinder future economic progress regarding job opportunities and legal costs. Furthermore, the increase in AIED poses a challenge when it comes to the allocation of scarce resources and preventing ethical issues. Unfortunately, the current policies are insufficient to deal with these challenges, thus creating a need to formulate policies focused on decreasing the technical, social, economic, environmental, and legal costs of implementing AIED in K-12 schools.

The study proposes a cost-benefit analysis framework to simplify the cumbersome task of policymakers when they might not have a comprehensive understanding of AI-based systems and how they work. A hypothetical case study shows that from the policy perspective, ethical, legal, and environmental costs need to be focused on. Minimizing these costs would make AIED beneficial at the societal level. Maximizing budget allocation of K-12 education is another important implication of the analysis.

However, it is observed that data on AIED, its implementation, and trends is not readily available. Therefore, the study has limited applicability. As more data becomes available, the cost-benefit analysis may be re-evaluated and improved upon. The interdisciplinary nature of AIED cannot be ignored. Therefore, holistic approaches focused on analyzing interlinked aspects of AIED are better suited for such a study than isolated case studies that might underestimate the complexity of the issue at hand.

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The Effects of Social Media on Adolescents

Introduction

In today's digital time, social media has powerfully reflected ways in which adolescents communicate, interact, and look at the world. Instagram, TikTok, and Snapchat are among those that make up the dominating social life, and a question arises—to what extent such changes in adolescent development are impacted. This is one of the most dramatic periods in one's life because of the high rates of cognitive and emotional changes; therefore, adolescents are reported as the most vulnerable age group to the influence of social media. Understanding how social media impacts the developing adolescent brain goes a long way in grasping, generally, the effects modern technology has on the youth. This paper describes how social media shapes cognitive functions and emotional well-being through a comprehensive overview of its impacts on adolescents in their development.

Cognitive Impact of Social Media

Among the big impacts social media has on adolescents are those which are cognitive. This includes its impact on attention span and focus. Studies have hence shown that the constant stream of information from sites may decrease focused attention ability since teens become accustomed to browsing through numerous posts in a short time. Frequent use of social media may decrease the sustained attention and increase the distractibility. The barrage of information in small chunks, delivered through sites like TikTok and Instagram, generates attentional fatigue and interferes with teenagers' abilities to deal with longer-term tasks and sustain attention on them. Another crucial impact of social media doesn't leave much hope for great memory retention either.

Switching between applications, notifications, and executing different activities in social media creates a fragmented cognitive experience incompatible with deep information processing. Multithreading between sites could hurt the memory of adolescents to retain information correctly either academically or personally (Best et al. 2). What this means is that with the continual diversion brought about by social media, it can affect the cognitive development of adolescents as far as being able to concentrate continuously and retain memory effectively. Social media influences decision-making among adolescents, primarily via social comparison. The presence of peers' achievements, lifestyle, and appearance naturally builds an environment where comparison could be bred. Social comparison on the social networking site may lead adolescents to increase anxiety and self-doubt in order for them to match their peers' perceived social standards (O'Keeffe 45). Increased social comparison negatively impacts their self-regulation; it more often than not makes them more vulnerable to outside influences and less apt to independently make choices based on one's personal values.

Emotional Effect of Social Media

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Social media has a big impact on the self-esteem and body imagery of adolescents. Since they are constantly exposed to idealized images, pressures present themselves in the form of a curated life, which can make one feel inadequate and more self-conscious. This, in turn, may encourage negative body image and low self-esteem among girls, particularly the younger ones who are more sensitive to beauty expectations set by society (Best et al. 34). The pressure inflicted on teenagers through persistent messages that they should look a certain way or otherwise encourages negative body image and feelings of inadequacy, thus affecting their emotional lives. Apart from self-esteem problems, the use of social networks is now considered one of the various reasons behind increased anxiety and depression among teenagers. Excessive use of social media is linked to increased levels of anxiety and depressive symptoms as a result of FOMO and the subsequently emerging need for continuous verification in the form of likes and comments (Best et al. 35). This need for verification from other individuals then creates a spiral of anxiety, whereby adolescents and young people are compelled to keep their online presence and race with others at a tremendous personal cost with regard to their mental well-being. Another key emotional factor linked with social media activity is the issue of how social media impacts emotional regulation. Those adolescents that regularly are exposed to negative and disturbing content are more likely to have increased levels of stress and dysregulation. Active use of social media among adolescents is bound to lead to emotional distress and impulsiveness in dealing with real-life situations emotionally (Uhls). Poor emotional regulation can deteriorate conditions such as academic performance and interpersonal performance because an adolescent would not be in a position to deal with challenges through a positive attitude.

Larger Ramifications on Adolescent Development

The influences of the practice of social media do not end here, as they influence adolescents' social traits and well-being. Those adolescents who are more dependent on digital communication may lag behind others in developing their face-to-face communication skills. Over-reliance on virtual relationships inhibits adolescents from developing interpersonal skills that are important in forging deep relationships in the physical world. The absence of non-verbal cues when conducting online interactions deprives adolescents of learning how to decode body language, facial expressions, and other forms of communication that are imperative for effective social interaction. Besides social skills, social media may influence young people's sleep and physical health. Late-night use of social media can interfere with sleep, resulting in tiredness and even lower academic achievement due to disturbed sleep (Uhls). Blue light from screens, combined with stimulation from engaging content, can delay sleep onset and reduce overall quality of sleep. Thus, sleep loss could snowball into other areas of health: mood swings, lower concentration, and resilience to stress all suffer.

Conclusion

The Effects of Social Media on Adolescents

The presence of social media in the lives of teenagers is pervasive and has significant consequences in terms of cognitive functioning, emotional well-being, and overall development. As access increases, it becomes important to understand the results of long-term exposure to social media on the developing brain of adolescents. Understanding these effects is crucial in fostering healthier adolescent development. Schools, parents, and policymakers alike should pay attention to the implications of digital literacy programs that encourage balanced use of social media as a way for adolescents to take responsibility for their experiences on the Internet. The upside of this could be that such efforts equip young people with the necessary abilities to navigate through the labyrinth of social media and minimize its negative effects.

The Effects of Social Media on Adolescents

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