Intergenerational and Transgenerational Transmission of Parental Stress and Trauma and the Mental Health Disorders in the Offspring of Survivors

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Abstract

Previously, genomics research did not consider the stress and trauma endured by an individual as cause for medical concern for that individual. However, recent epigenetics research has shown that not only do stress and trauma have the ability to alter a person's genome, it also has the potential to alter the genome of their offspring. This paper focuses on the effects of parental and ancestral PTSD on the likelihood of their offspring in developing mental health disorders and abnormalities. It was found that parental PTSD not only predicted psychological predispositions in offspring, but also that such changes could actually survive for several generations even if they came from a single, time-constrained experience of a distant relative. Generally these findings show that acute stress has far more complications on the human body than previously thought. Major changes need to be made to address such experiences in the political sphere, and better mechanisms need to be made to help people with such backgrounds in the medical sphere.

1. Introduction

The consequences of stress on human physiology has been vastly underestimated by both medicine and politics. Stress and trauma are generally considered to be something that people can get over and not have to worry about in the future once it's over. However, recent epigenetic research suggests that not only can stress cause a permanent epigenetic change within a person's genome, it can also transfer that change down the inheritance line. For instance, the current epidemic of Type II Diabetes in China was long considered to be caused by and fixable by lifestyle and diet alterations; however, new analyses suggest that one of the culprits behind it might be the epigenetic effects of early-life exposure to famine (Zimmet, Shi, El-Osta, & Ji, 2018). New literature about the genome alterations that are caused by intergenerational traumatic stress is paving the way for understanding the consequences of an individual's trauma on their own, as well as their offspring's genome.

This type of research is important because many people in the modern age vastly underestimate the long-term implications of historical events that caused mass trauma to entire populations. The aftermath of cultural traumas such as the Holocaust, ethnic cleansing of Native Americans, the Rwandan Genocide, the Armenian Genocide and more can still be seen in individuals today. Survivors of such atrocities are often at a higher risk of having mental health disorders such as PTSD, yet the reason for why these conditions are so prominent in later generations of certain populations go understudied. Further research must be done in order to properly provide these people with the resources they need, since their mental health might suffer for different reasons than that of people who do not descend from such survivors.

This paper aims to assess the effects of epigenetic stress from genocide and discrimination on the genome and mental health of the offspring of such survivors. First, the

effects of direct inheritance of trauma from parent to child is assessed, and then the effects of transgenerational trauma caused by the experience of an ancestor. In both scenarios, uncharacteristic methylation of NR3C1 — which is known to be responsible for depressive symptoms — and inherited PTSD symptoms, despite the descendants never having had experienced the trauma themselves, was found. The hope is that with more research done on this topic, it will become clear why oftentimes, survivors of such atrocities cannot simply build a new life after the traumatic experience ends — the trauma lives on not only in their genes, but in their descendants' genes. Additionally, there is potential for better treatment of mental health conditions caused by intergenerational transmission of trauma.

2. Findings of Epigenetic Inheritance of Parental PTSD

For a long time epigenetics was considered outside of the basic model of genetic research. It was thought that whatever genes a person was born with was what they would have for the rest of their lives. However, ground-breaking research like Hejimans et al (2018) on the effects of early life exposure to famine made it clear that genetic alterations are certainly possible within one's lifetime. In fact, they can even be transferred to the person's offspring. Part of the reason that this was able to be determined was unfortunately due to the fact that entire populations had gone through traumatic experiences like genocides and famines. Studying the people who came from such backgrounds showed that these types of experiences can cause dramatic changes in the genome of the survivors and their offspring.

One of the earliest findings that supported the idea of inheritable epigenetic changes in mental health was a study done on descendants of Holocaust Survivors. In the 2014 study by Yehuda et al, the researchers assessed the genetic and behavioral patterns found across people of

Jewish Ashkenazi ancestry whose parents survived Nazi Germany, and compared it to the patterns in people of the same ancestry whose parents were not in Nazi Germany during the Holocaust. They found that there was a significant difference in the methylation of NR3C1 between people of the same background who did not have this traumatic experience. Participants whose parents had PTSD after surviving the Holocaust were far more likely to develop PTSD themselves, as well as depression, anxiety and other mental health abnormalities. Additionally they found that there was a sex-linked difference in what maternal PTSD and paternal PTSD did to the genome and behavioral patterns of the offspring.

These findings were supported by study done on the survivors and children of survivors of the Tutsi Genocide. The paper by Perroud et al (2014) examined 50 women of the same ethnic background who were pregnant during the Tutsi Genocide; 25 of the women were directly exposed to the atrocities of the genocide, and 25 of the women were not exposed to it. They found that not only were the women who were directly exposed to the genocide far more likely to have PTSD and methylation of NR3C1, but also that their children had higher rates of methylation of NR3C1 as well. The study found that the exposed women's children had a higher likelihood of developing mental health disorders like depression in comparison to the non-exposed women's children. This study supported the idea that mental health conditions can be inherited from parents to children, even on the genetic level.

Additionally, continuous traumatizing experiences that go on generation after generation can create robust changes in the genome. A meta-analysis of the long history of colonization of the Native peoples of Canada has shown that in addition to having to be raised in the physical and mental effects of generational trauma and colonization, the modern Native Canadian population might also face a biological inheritance of trauma (Matheson, Seymour, Landry,

Ventura, Arsenault, & Anisman, 2022). Although many people from the native nations do not want to partake in Western research that has historically never benefitted, and even hurt them, there is a lot of concern for what hundreds of years of colonization might have done to the genetics of the survivors. It prompts discussion as to why the North American governments cannot keep treating indigenous people in the discriminatory and dehumanizing way that they have been. In a society obsessed with meritocracy, there must be an acknowledgement that people cannot reach the same point from an uneven playing field.

3. Findings of Epigenetic Inheritance of Transgenerational Trauma

One of the major downfalls in epigenetic research done on intergenerational trauma is that the results of these studies can also be explained through Social Learning Theory. An adult with PTSD from genocide would probably raise their children in a different way from a mentally healthy adult, even without knowing it. However, non-human animal studies have shown that socialization is certainly not the only factor at play here. A paper written by Ambeskovic et al (2019) demonstrated that epigenetic changes from a traumatic and stressful experience in a distant ancestor can live on generations later. They conducted experiments on three groups of rats — four generations of completely undisturbed rats, one generation that went through prenatal stress and four subsequent generations that went undisturbed, and four generations of prenatally stressed rats. They found that even if whole generations in the bloodline remain unbothered, there can still be abnormalities detected on a genetic, as well as a behavioral, level. Although the multigenerational-stressed rats were found to have the highest rates of anxiety-like behaviors, transgenerationally-stressed rats were still found to have abnormally high anxiety

rates. This study demonstrates that a single individual's epigenetic changes can live on for up to four generations later.

This transgenerational trauma effect can be found in humans as well. A study by Aintablian et al (2018) conducted research on depression, anxiety and PTSD rates in 278 Armenians. The study compared the mental health of people who had no survivors of the Armenian Genocide of 1915 in their family line, and the mental health of people who had one or more survivors of the Armenian Genocide in their family line. Overall, they found that descendants of survivors of the genocide had higher likelihood of having a mental health condition, and of taking medication for mental health disorders. The findings were astonishing because they went to show that trauma can live on for generations, and does not necessarily end after the direct descendant of the survivors. In fact, the more survivors a participant had in their bloodline, the more likely they were to have severe mental health abnormalities. In future therapeutics, it might be beneficial to first assess whether the patient has trauma in their family line. Although survivors of genocide are likely to report to a therapist that they have been through a traumatic experience, the descendants of genocide survivors are unlikely to consider the experience of their ancestors in their modern-day life. If the field of psychiatry took this kind of history into consideration, patients might be treated in more efficient and effective ways.

4. Discussion

One of the most obvious limitations to epigenetic research with PTSD is the inability to distinguish between true epigenetic changes, and changes due to being reared by a traumatized person. Previous studies have shown that parental attitude towards children has an immense influence on the psyche of the adults that they become. In fact, parental style on its own could

have large-scale influence on the mental health of the person they rear. However, looking into the epigenetic possibilities adds to the complexity of transmission of mental health disorders, and could explain the aspects of it that social learning theory cannot (Hines and Saudino, 2002). It is likely that socialization and epigenetics interact with one another, so the existence of one does not cancel out the other.

Another limitation with this research is that the field of epigenetics is still new, and there is a small volume of literature with virtually no guidance on how to standardize or validate the recent studies. Additionally, since this research specifically is looking into the epigenetics of the survivors of systems made to annihilate people of their background, the sample sizes are generally quite small. This could be because there are not a lot of survivors who could be easily reached for this research, and also because people with such PTSD might not even be willing to participate in a study like that. However, despite the lack of empirical evidence, there is plenty of anecdotal evidence within the peoples who underwent such cultural traumas that show that this hypothesis is not unfounded — trauma does in fact live on in the offspring.

5. Conclusion

Recent findings confirm that traumatic experiences within a single individual's lifetime can cause epigenetic changes that are not only inheritable to the direct offspring of the individual, but also to many generations onwards. Despite the limitations of relatively small sample sizes, and small volumes of literature done so far on this topic, there is empirical evidence that trauma can change a person’s genome and live on in their children’s genome.

With more and more research being done on this topic, it is reasonable to believe that in the future there could be better treatment for psychological conditions caused by parental and

ancestral PTSD from genocide and discrimination. Hopefully, there will also be more importance placed on the mental health of the individual within society, since it has been shown that the effects of stress can be permanently etched onto the epigenome. This research has the potential to humanize survivors of genocides and explain why it is so important to keep history from repeating in this way because, clearly, trauma lives on for generations and causes distress even when its cause has ceased.

6. Bibliography

Aintablian, H. K., Markarian, B., Irmak, I., Galoustian, N., Melkonian, C., Vardapetyan, M., ... & Aintablian, N. (2018). Direct ancestry to a genocide survivor has transgenerational effects on mental health: A case of the Armenian population. MOJ Public Health, 7(4), 233-239.

This paper is a statistical analysis of 278 ancestrally Armenian participants' mental health in relation to whether they had one or more survivors of the Armenian Genocide in their family line. They concluded that overall, the Armenians with ancestry from the Genocide more likely to have mental health condition, undiagnosed or diagnosed, as well as be taking medications for it compared to Armenians with no genocide survivors in their ancestry. Additionally, they found that the more survivors there were in the participant's family line, the more likely the were to have mental health disorders. One of the major downfalls of this paper is that there was no wet lab component to it. One of the most compelling arguments for actual genetic inheritance of mental health disorders is methylation of NR3C1, and there was no gene coding done to add on to the statistical findings. However, the statistical findings were very profound on their own, and

showed a great difference between the groups outlined in the study. Adding on the aspect of how many survivors were in the family also made the findings more consistent. This paper made me think a lot about my own ancestry, since my mother is a survivor of the Baku Pogroms of 1990. One of the things they mentioned is how the population of Armenia has uncharacteristically high levels of depression and anxiety, and that makes me think about how Westerners call us “lazy” when in reality it could very well be large-scale depression. I also really liked how this paper fit into my research of transgenerational trauma, since the documented genocide took place in 1915, and many of its descendants are now generations removed from both that land and that direct memory.

Ambeskovic, M., Babenko, O., Ilnytskyy, Y. *et al.* Ancestral Stress Alters Lifetime Mental Health Trajectories and Cortical Neuromorphology via Epigenetic Regulation. *Sci Rep* 9, 6389 (2019). https://doi.org/10.1038/s41598-019-42691-z

This study used rats to test the transmission of biological factors through generations. They had three groups: the control group of four generations of non-stressed rats (NNNN), the transgenerationally stressed group with a stressed F0 ancestor (SNNN), and the multigenerationally stressed group where all the rats were stressed (SSSS). They found that, while all of the groups with a stressed ancestor inherited genetic alterations, the multigenerationally stressed lineage in particular, produced an F4 generation with a predisposition to stress vulnerability and generated a phenotype resembling symptoms of PTSD. The study seems to be very carefully thought-through since they had the three groups with

different stress points. They did so in order to really isolate the genetic changes as compared to the effects of direct stress. While the design is sound, I wish that they reported more on the other generations of the transgenerationally stressed rats, rather than mainly on the F4. Since the F4 generation in the SSSS condition was still stressed, it seems unclear to me whether the genetic findings are related to the stress in the fourth generation or to the overall multigenerational stress. They also found that the genetic alterations were mostly present in the male rats, although other animal studies found the opposite results. I thought that this study was really promising, and I'm not sure if I misunderstood some findings because of my lack of a biology background, but I really wish they released more information on what the genetics of the F1-F3 generations looked like in the SNNN condition since the F4 results might be mild due to substantial removal from stressed ancestor. That said, it still proved that even in the F4 generation of the SNNN condition, there was still a noticeable effect despite how removed it is.

Bowers, M., Yehuda, R. Intergenerational Transmission of Stress in Humans. *Neuropsychopharmacol* 41, 232–244 (2016). https://doi.org/10.1038/npp.2015.247

This study is a meta-analysis of a lot of the recent literature on intergenerational stress. The authors, Bowers and Yehuda, outlined the professional jargon as it is used, and as it should be used in the future, went into the importance and challenges of conducting research on this topic, then sorted the recent biological correlation findings into neuroendocrine, epigenetic, and neuroanatomical categories. The authors also explained a lot of the theory and proof of intergenerational trauma. Overall, the paper is very well-balanced on the positive impacts of this

research, the challenges with understanding where the findings actually come from, and the actual experiments and what we can conclude from them. I especially appreciated that the authors included findings on paternal stress correlations, as well as the general stress that they put on the importance of more research being done in regards to the paternal lineage. This study felt like a good place to start because it consolidated everything that happened in the topic within the past, including the early days of the establishment of PTSD as a diagnosis at all. I feel like the topic of intergenerational trauma has just recently become a trending idea in the mainstream, so I really did not know that much about the actual science behind it. This paper provided a lot of background knowledge and theory behind this topic, as well as limitations that I did not really consider before starting this project. The only thing is that I wish that the authors gave a little more background on the biological and neural mechanisms that they were talking about, since reading about it from a psychology perspective felt a little confusing.

Heijmans, B. T., Tobi, E. W., Stein, A. D., Putter, H., Blauw, G. J., Susser, E. S., ... & Lumey, L. H. (2008). Persistent epigenetic differences associated with prenatal exposure to famine in humans. Proceedings of the National Academy of Sciences, 105(44), 17046-17049.

Hines, D., Saudino, K., INTERGENERATIONAL TRANSMISSION OF INTIMATE PARTNER VIOLENCE A Behavioral Genetic Perspective. Trauma, Violence, & Abuse, 3(3), 210-225 (2002). https://journals.sagepub.com/doi/pdf/10.1177/15248380020033004

This article is a literature review of previous work done in regards to intimate partner violence that suggests that aggression is not only inherited through social learning theory, but also genetically. The authors amassed all the research and statistics that have been done on the topic, and explore the weak points behind trying to explain intimate partner violence through social learning theory. They also point out that although there is considerable reason to believe that the violent behaviors are inherited through more than shared environment, there has not been much research on this topic. At some points, I thought that it was not necessarily conveying what it needed to; particularly in the reason why figuring out the genetic component is important, and how women commit violence against men as well as the vice versa. At some points you might find yourself reading the paper and wondering whether it is leaning into eugenics, until the very end where they emphasize that genetics is probabilistic, not deterministic, so knowing this information can help guide people in the right direction. They also mentioned that women commit violence against men at an equal rate as the vice versa, and the statistics of that seem questionable to me. I have a feeling that the violence against women went massively under-reported or framed in an odd way in the studies they were looking at. This paper was not quite what I was looking for, and I only realized that after I finished reading it. Still, it was an interesting read, and highlighted a lot about how aggression studies were usually done from an environmental perspective, which I did not realize.

Li, Y., Sjölander, A., Song, H. et al. Associations of parental and perinatal factors with subsequent risk of stress-related disorders: a nationwide cohort study with sibling comparison. Mol Psychiatry 27, 1712–1719 (2022). https://doi.org/10.1038/s41380-021-01406-5

The authors of this study consolidated data on over 90% of the births in Sweden between the years of 1973 and 2008, and traced prenatal and perinatal factors that could have possibly contributed to the development of mental health disorders in the population. They observed a lot of associations during the population analysis, but all of them turned out as null when they ran the sibling analysis, so their findings do not support a correlation between prenatal or perinatal conditions and stress-related health disorders. This study had its limitations though since it was done in Sweden. This environment presented both a blessing and a curse because on one hand, they were able to attain detailed results from a large population; however, Sweden is not a necessarily diverse country, and it has an extreme climate which could present itself as an ungeneralizable specification. A lot of science is done by and for middle-class white folk, so I really do wish there was more genomics research in other parts of the world that are not the U.K. or Scandinavia. I'm not really sure how useful this is for my purposes since I was actually looking for evidence to show that there can be genetic underpinnings for stress-related disorders; however, it does provide a good view of the other side, and of the importance of the environment. This paper can be used to show evidence that there is still plenty to stress-related disorders that is caused by environmental factors that people do not inherit genetically, and puts some rest on the more eugenics-leaning side of this argument to show that anyone can end up in any situation.

Matheson, K., Seymour, A., Landry, J., Ventura, K., Arsenault, E., & Anisman, H. (2022). Canada's Colonial Genocide of Indigenous Peoples: A Review of the Psychosocial and Neurobiological Processes Linking Trauma and Intergenerational Outcomes. International Journal of Environmental Research and Public Health, 19(11), 6455. MDPI AG. Retrieved from http://dx.doi.org/10.3390/ijerph19116455

Perroud, N., Rutembesa, E., Paoloni-Giacobino, A., Mutabaruka, J., Mutesa, L., Stenz, L., ... & Karege, F. (2014). The Tutsi genocide and transgenerational transmission of maternal stress: epigenetics and biology of the HPA axis. The World Journal of Biological Psychiatry, 15(4), 334-345.

The researchers of this study found 50 women who were pregnant at the time of the Tutsi Genocide, 25 of them who were directly exposed to death and murder, and 25 of them who were abroad and who had not directly been at the events at the time, and recruited them as well as their children for analysis of behavior PTSD and depression traits, as well as NR3C1 methylation in their genomes. They found that not only the women who were directly exposed, but also their children had significantly higher rates of NR3C1 methylation and behavioral PTSD. The researchers were clearly caught up on all the recent literature in the field. Every method and hypothesis was backed up by at least two other studies. Usually, when I read genetics papers, there is always a moment where I feel like one claim or another is not backed up by evidence, but this paper had reasoning every step of the way. The only downside is the small sample size

— 50 women and their children does not feel like enough to make a full claim; however, it must have been hard to find and recruit people of this specific background. I decided to look for a paper examining the survivors and offspring of the Rwandan Genocide after reading the paper about Holocaust survivors by Yehuda et al (2014), and this paper was perfect for what I was looking for. The results were very similar to the results of the Holocaust survivors, and the science is very sound in this one as well. In order to make a proper claim, I want to examine papers from many parts of the world and have a diverse set of samples and examples.

Yehuda, R., Daskalakis, N. P., Lehrner, A., Desarnaud, F., Bader, H. N., Makotkine, I., ... & Meaney, M. J. (2014). Influences of maternal and paternal PTSD on epigenetic regulation of the glucocorticoid receptor gene in Holocaust survivor offspring. American Journal of Psychiatry, 171(8), 872-880. https://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.2014.13121571#_ac_authorArticleInfoCon

This study pretty much gave me the answers to the questions that arose in my head after reading Ambeskovic, Babenko, Ilnytskyy et al (2019). The paper examines effects of maternal PTSD, paternal PTSD, a combination of both, and a control group with neither amongst adults whose parents are Holocaust survivors. The authors focused on GR-1_F promoter methylation, but mentioned that in behavioral terms, there seemed to be a parental-sex-driven difference in vulnerabilities; maternal PTSD enhanced the risk for poor emotional health, depression symptoms and anxiety, while paternal PTSD enhanced the risk for dismissing, fearful or insecure

attachment styles, as well as greater dissociative experiences and sensitivity to violence. Participants who had both parents with Holocaust-related PTSD were more likely to report being affected by trauma and psychological scars, sensitivity to violence and injustice and dissociative amnesia. This study was well-designed and executed, and although I do not fully understand how the glucocorticoid receptor relates to PTSD, I am nevertheless convinced by their work. They worked out a perfect representation of trauma passing down genetically from parents to children in two generations. This research relates directly to my research topic, and shows very strong proof towards the idea that severe trauma not only alters the genes of the people who went through it, but also the genes of their offspring. The results of this study make me want to look further into other studies done on people from similarly traumatic backgrounds (e.g. the Rwandan Genocide, the Armenian Genocide).

Zimmet, P., Shi, Z., El-Osta, A., & Ji, L. (2018). Epidemic T2DM, early development and epigenetics: implications of the Chinese Famine. Nature Reviews Endocrinology, 14(12), 738. https://link.gale.com/apps/doc/A573138198/AONE?u=mlin_w_umassamh&sid=bookmark-AONE&xid=86095d74

This paper is a sort of meta-analysis of a the literature done on the effect of harsh famine on the adult diabetes of the people who were prenatally exposed to it. Although it specifically provided a lot of data and statistics on China, it also talked about the Dutch famine, the famines in Cambodia, Nauru and more. Overall, it argued that the extreme rise in China's Type II Diabetes rates in the recent 20 or so years is correlated to the famines that people who were born around

that time were exposed to prenatally and during childhood development. The paper was dense with statistics, and had a lot of evidence to back up its claims. At times it felt like so much evidence that it was taking away from the central idea. However, the argument was very compelling, and showed a lot of proof for the idea that prenatal changes must have affected the populations. I wish they could have gotten data for the difference between the rates of diabetes in people directly exposed to the famines compared to unexposed people; however, I'm sure that it must have already been hard to publish a paper about the Chinese famines. To me this serves like great evidence for the effects of epigenetics. Although this does not really have to do with mental health or PTSD, it proves that parental stress transmits consequences to the children. I also like the fact that the paper stresses that these findings mean that we have to treat the same condition differently in different people — lifestyle and diet changes that have been pushed for so long in society are just not applicable to everyone, and epigenetic research is going to help us find better medicine.