A Statistical Approach to Find Correlation Between Autism and Hyperactivity using NeuroImaging Data.

A thesis submitted to the University of Birmingham for the degree of MSc Data Science

Swapnil Bhattacharya

School of Computer Science

College of Engineering and Physical Sciences

University of Birmingham

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Abstract

With an eye towards analysing the possible influence of brain structure on both behaviours, the current study has looked at the intricate link between Autism Spectrum Disorder (ASD) and hyperactivity. Difficulties in social contact, communication, and repeated conduct set autism apart from a multifarious developmental condition. One of the most well-known traits of autism is hyperactivity, which in individuals shows as increased levels of activity, restlessness, and poor focus. Developing more efficient help and treatments for people diagnosed with autism depends on understanding the basic reasons of this too high activity. The aim of this work was to clarify the neurological elements perhaps involved in hyperactivity in persons with autism. We specifically looked at the white matter of the brain, which is absolutely essential for connecting several regions of the brain and allowing communication among them. Perfect brain operation depends on white matter, hence any change in its composition will have a big impact on cognitive abilities and behaviour.We investigated this issue by means of brain scans of individuals diagnosed with ASD, with particular focus on areas especially identified to be linked with cognitive processes, motor coordination, and behaviours linked with hyperactivity. By means of a comparison between these brain areas with those of individuals without ASD, our aim was to identify any differences that would clarify the higher degrees of activity observed in autistic people. The findings indisputably showed that people with ASD have clear differences in brain anatomy, notably in areas crucial for the control and processing of behaviour. The noted differences could be related to the hyperactive tendencies sometimes seen in those with autism. Our findings indicated anatomical changes in particular areas of the brain that might affect normal brain function and cause problems with impulse control and attention management.The current work emphasises the need of understanding the role of the brain in autism and hyperactivity since it can provide valuable information about the fundamental reasons of these behaviours and improve their control. By clarifying the relationships between brain architecture and behaviour, we hope to contribute significantly to the development of more successful strategies for helping individuals with autism thereby improving their whole quality of life.

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Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
ADOS	Autism Diagnostic Observation Schedule
fMRI	functional Magnetic Resonance Imaging
ADI-R	Autism Diagnostic Interview Revise
dMRI	Diffusion Magnetic Resonance Imaging
ASD	Autism Spectrum Disorder
SVM	Support Vector Machine
SLF	Superior Longitudinal Fasciculus
FSL	FMRIB Software Library
BET	Brain Extration Tool
EEG	ElectroEncephalography
CNN	Convolutional Neural Network
DTI	Diffusion Tensor Imaging
WMH	White Matter Hyperintensities
MRD	Magnetic Resonance Diffusion
MRI	Magnetic Resonance Imaging
PFC	Prefrontal Cortex
AI	Asymmetry Index
FA	Fractional Anisotropy
MD	Mean Diffusivity
CP	Cerebral Palsy
AD	Axial Diffusivity
RD	Radial Diffusivity

Contents

List of Figures

List of Tables

CHAPTER 1

Introduction

Affected millions of people globally, ASD is a neurodevelopmental complicated condition. Along with hyperactivity and attention problems, it presents symptoms including anxiety in social situations and repeated actions. The brain processes behind hyperactivity in people with ASD essentially guide the creation of more exact diagnosis instruments and customised treatments. This project is therefore encouraged by the understanding of the reasons that people with autism frequently manifest hyperactive behaviors and possibly providing easier diagnostic pathways for clinicians. The project focuses on the exploration of brain connectivity in the hyperactivity of ASD patients, keying in on white matter integrity and abnormalities.

It is an ASD neurodevelopmental condition very often accompanied by hyperactivity. This project will, therefore, study the relationship between autism and hyperactivity with emphasis on white matter integrity in order to make adequate diagnostic pathways for patients with ASD.

1.1 Research Motivations

This study's justification stems from the challenges in correctly spotting and understanding the complex aspects of ASD, most notably the hyperactivity often accompanying it. Sometimes in response to sensory overload, mental pain, or communication difficulties, persons with autism may show higher degrees of hyperactivity—which may differ from those of people without autism. This increased degree of activity may complicate the already difficult process of ASD diagnosis even more, hence it is imperative to have a deeper awareness of its neurological bases.

While effective, modern diagnostic techniques like the ADI-R demand a lot of work and cause psychological stress for families as well as autistic individuals. For those with ASD, who often struggle in communication, emotional control, and social interaction, the ADI-R involves a protracted and thorough interview process that can be very challenging. This emotional weight also applies to carers, who could find physiologically taxing to be relaying difficult situations. The above mentioned issues highlight the great demand for quick and less invasive diagnostic methods.

With an especially focus on the components of white matter integrity in relation to hyperactivity in Autism Spectrum Disorder (ASD), this project aims to use neuroimaging techniques to provide conclusive, evidence-based knowledge of brain structure and function. Through the identification of biomarkers that may function as additional instruments, this study aims to mitigate the challenges of the diagnostic procedure, so decreasing the need for extensive interviews and consequently minimising the stress experienced by autistic individuals and their families. The primary objective of this research is to provide more efficient and less emotionally burdensome diagnostic techniques, providing clinicians with dependable, non-intrusive instruments to sensitively and empathetically ascertain characteristics linked to Autism Spectrum Disorder (ASD), such as hyperactivity.

1.2 Limitations

The coexistence of Autism Spectrum Disorder (ASD) and hyperactivity poses several complexity, some of which are currently under investigation in existing scholarly works. Despite the increasing combined prevalence of ASD and ADHD, the precise neurological foundations of both disorders are still mostly unidentified. This poses considerable challenges, especially in differentiating between symptoms of Autism Spectrum Disorder (ASD) and those associated with hyperactivity. This difficulty is further intensified by the utilisation of current diagnostic instruments such as the ADI-R, which, although comprehensive, can be demanding and emotionally exhausting for both patients and their families.

Moreover, the variety in ASD presentations interferes with the development of standardised treatments. Although neuroimaging has great promise in this discipline, the large preprocessing required to investigate brain areas usually limits it and requires significant computational capacity. For instance, techniques like as DTI, which are crucial for assessing the integrity and connectivity of white matter, are prone to motion artefacts and need careful modifications including eddy current correction. Furthermore complicating the imaging process is the need for denoising brought on by physiological factors such as blood pressure and respiration. These physiological movements bring superfluous information into the data, thereby perhaps hiding important brain features and hence hindering exact analysis. Therefore, effective denoising techniques must be used to lower these distortions and ensure the dependability of the neuroimaging data examined in the study of ASD and hyperactivity.

1.3 Thesis Overview

This thesis's main goal is to give a careful analysis of the neurological causes of hyperactivity in ASD patients. The study starts with compiling information from two well-known neuroimaging databases: ADHD-200 and ABIDE II, Autism Brain Imaging Data Exchange. These files provide necessary thorough MRI scans for the analysis.

Following data collecting, a series of data preparation techniques was followed to ensure the integrity and homogeneity of the neuroimaging data. Skull-Stripping to eliminate non-brain tissues, Bias Field Correction to correct for variations in intensity, Normalisation to standardise the data, Motion Correction to lower artefacts resulting from patient movement, Registration to align the images to a standard space, Segmentation to differentiate between various tissue types, and Smoothing to improve image quality. To get the data suitable for important study, the above described preparation techniques were absolutely vital.

First insights on the dataset were obtained from a later exploratory data analysis. The quality and features of the data were then evaluated using multiple statistical methods. Following a computation of the SNR to assess image quality, denoising techniques were applied as necessary. Mean FA values then were computed to evaluate white matter integrity. At last, WMH were investigated to find their relationship with hyperactivity in ASD.

The research workflow is succinctly delineated in Fig: 1.1, offering a graphical representation of the procedures and methodologies employed during the investigation. The systematic methodology facilitated a comprehensive examination of the neurobiological factors associated with hyperactivity in ASD, with the objective of enhancing the efficacy of diagnostic and treatment interventions.

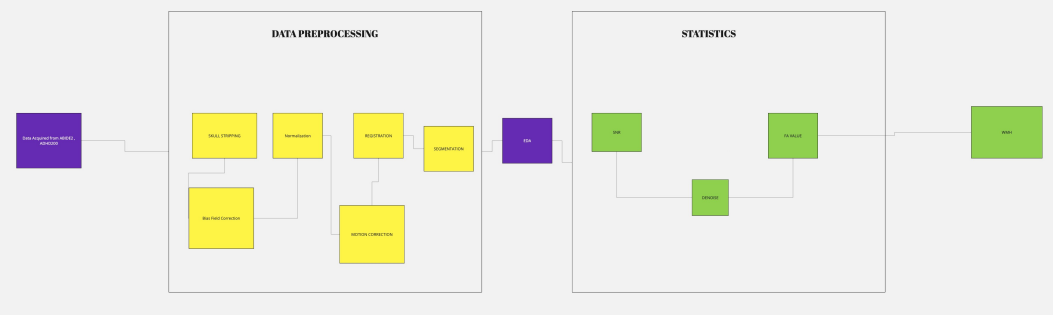

Figure 1.1: Thesis Overview

1.4 Aim and Objectives

The overall objective of the project is to establish some relationship between autism and hyperactivity using an available MRI dataset. The methodology of this would provide a diagnostic technique that puts less demand on, and is more accessible to, those with autism, removing some of the emotional and physical distress associated with traditional assessments.The desired objectives to be achieved are as follows:

- Identification of white matter abnormalities using modern neuroimaging techniques, with a view to areas associated with hyperactivity in ASD patients.
- Using MRI-based measures, such as FA and MD, this study investigate how connectivity of the brain is related to hyperactive behaviors in persons with ASD.
- Offer an easier accessible alternative to traditional diagnostic interviews, thus designing an efficient and less emotionally exhausting diagnostic methodology for autism-related hyperactivity.
- Understanding the neural mechanisms underlying hyperactivity in patients with autism may therefore be of importance in improving the development of strategies for early detection and intervention in terms of better treatment outcomes.

1.5 Legal, Social, Ethical and Professional Concerns

Using sophisticated neuroimaging technologies, this research will investigate relationships between autism and hyperactivity in order to improve the quality of life of persons with ASD. Ethically, the initiative follows the highest standards meant to ensure that data and approaches treat people with dignity and get careful management. The ethical issues do not surface since the project seeks to better understand the neurological mechanisms behind autism in order to try to either try to alleviate or enhance the quality of life of the afflicted individuals. The initiative is carried out fully under obligation to help the autistic population.

Socially, this offers great benefits. Dealing with the relationship between white matter hyperintensities and behavioural symptoms in ASD will help to clarify early diagnosis and intervention strategies. In this sense, the improvement in quality of life and the more social integration of an autistic individual grow. It advances an understanding and acceptance of neurodiverse people in society and causes no issues for society except attendance for the autistic individual and his or her family.

From a legal aspect, our initiative complies with all pertinent medical imaging, data protection, and research guidelines regulations. It runs within scientific boundaries and has had no legal obstacles in its implementation. Regarding professional terminology, at the same time it follows a rigorous code of research integrity since it makes use of accepted techniques and tools. There are no professional conflicts; the research on the autistic also greatly helps neuroimaging and reflects well on the scientific community working on such projects. With an aim of raising the quality of life, this study serves as a paradigm for moral and responsible research.

1.6 Thesis Structure

This thesis's framework is meant to provide a complete analysis of the study subject, therefore guiding the reader through every stage of the research in a logical and consistent manner. The first chapter introduces the topic, defines the research goals, clarifies any ethical and legal issues relevant to the project, and so guides the reader. Chapter 2 then looks at the background research, looking at relevant metrics and techniques applied during the study. This chapter presents a thorough understanding of the used methods and methodologies, therefore laying the theoretical basis.

Chapter 3 offers a thorough review of the relevant literature in the topic, therefore pointing up the present knowledge gaps this study aims to correct. Emphasising its relevance, this study places the present work in the larger intellectual setting. The thesis's fourth chapter focusses on the dataset and offers a thorough study of its aspects together with the technological elements required for effective utilisation in the research. The current chapter helps the reader to become acquainted with the basic facts supporting the research.

Chapter 5 offers a thorough overview of the approach, clarifying the sequential actions followed to reach the objectives of the research. This includes a review of the specific techniques and approaches applied, therefore guaranteeing complete openness and accuracy in the course of research. Chapter 6 then presents the results of these initiatives together with their analysis and interpretation, therefore offering insightful examination of the implications of the study.

In conclusion, Chapter 7 provides an analysis of the project's contributions, presenting the main discoveries and their meaningful implications. Furthermore, this chapter discusses the constraints and difficulties faced during the research and suggests avenues for future investigation, thereby assuring that the study not only adds to the current knowledge but also facilitates further inquiry in the subject. The systematic methodology employed guarantees that the thesis is thorough and easily understandable, directing the reader through the entire research process from beginning to end.

CHAPTER 2

Background

2.1 Background Research

2.1.1 Autism Spectrum Disorder

Characterised by problems in social interactions, communication, and the prevalence of limited, repetitious behaviours, autism spectrum disorder is a complicated neurological syndrome [37] . The designation ”spectrum” reflects the wide range of symptoms and the different levels of severity found in individuals with ASD, leading to a unique and individualised manifestation in each case [60]. The condition, therefore, affects people in different ways, with some experiencing minimal problems, while others need substantial assistance in most of their daily activities.[42]

The core characteristics of ASD entail persistent deficits in social communication and social interaction [37]. Others may have difficulty comprehending and using nonverbal communication Gestures, including facial expressions and body language, appropriately [99]. In addition, there are challenges either in initiating or maintaining or comprehending the nature of interpersonal relationships [66]. ASD is characterised by restricted and repetitive patterns of behavior, interests, or activities. These behaviors could be in the form of repetitive motions, a strong insistence on routines, circumscribed interests, or hypersensitivity or insensitivity to sensory aspects [37].

Though their exact causes are unknown, it is hypothesised that an interaction between environmental elements and genetic predispositions causes ASD [8]. Studies show that several genetic abnormalities and variants might raise an ASD risk [34]. Furthermore greatly raising the risk factor are pre- and post-birth events include advanced parental age, less than ideal birth weight, and exposure to specific environmental contaminants. [63].

Improving results for individuals diagnosed with ASD depends mostly on quick detection and action[105].Treatment approaches can call for pharmacological medications to sufficiently control related symptoms like anxiety or hyperactivity; often they involve behavioural therapies and educational support. Helping people with ASD to achieve meaningful and successful lives depends much on the support and understanding given by family members, teachers, and the community [48]. With continuous study, there is hope for better insights and creative treatments meant to raise the quality of life for people with ASD [60].

2.1.2 Attention Deficit Hyperactivity Disorder

Attention Deficit Hyperactivity Disorder (ADHD) is a widespread neurodevelopmental disorder characterised by symptoms of inattention, hyperactivity, and impulsivity that are significantly more evident than those typically observed in individuals of comparable developmental stages [37]. ADHD often manifests

during early childhood and may persist into adulthood, influencing various aspects of life, including educational attainment, occupational performance, and interpersonal relationships [28]. Individuals with ADHD may have a hard time paying attention, finishing tasks, organising activities, and controlling impulses [9]. In addition to this, they may show excessive fidgeting, restlessness, and not remaining seated when such behavior is appropriate [37].

With several elements influencing its development—genetic, neurological, and environmental ones—ADHD has a complicated beginning [96]. Studies show that ADHD has a major hereditary component; many genes are implicated in its development [31]. Particularly in areas linked to executive processes like the prefrontal cortex, neuroimaging studies have found clear structural and functional differences in the brains of persons with ADHD. Environmental factors include prenatal alcohol or tobacco use, low birth weight, and early lead exposure can raise the risk of ADHD [96].

A thorough clinical assessment—which includes thorough interviews and questionnaires gathering data from many stakeholders, including parents, teachers, and the affected people themselves—basis the diagnosis of ADHD. The *Diagnostic and Statistical Manual of Mental Disorders (DSM-5*) sets specific criteria for the diagnosis of ADHD, thereby requiring the development of symptoms for at least six months and their major impact on social, academic, or vocational functioning. [37].

Usually, the care of ADHD is based on a team approach including educational plans, behavioural therapy, and medication management [17]. Often recommended and proved to be helpful in reducing core symptoms are stimulant drugs such as amphetamines and methylphenidate [94]. The primary objective of behavioral therapies is to educate individuals on methods that improve their organisational skills, time management, and social interactions [78]. The adoption of prompt intervention and a tailored treatment approach that addresses the distinct needs of each individual has the potential to significantly improve outcomes for those diagnosed with ADHD [17].

2.1.3 Co-occurences of ASD and ADHD

The concurrent existence of ASD and ADHD is increasingly recognised as a common phenomenon, with studies indicating that a considerable proportion of individuals diagnosed with ASD exhibit symptoms indicative of ADHD [57]. The co-occurrence of these two disorders presents unique challenges in their identification and treatment, as the manifestations of one condition may obscure or replicate those of the other [22]. For instance, the reduced concentration and high activity levels in ADHD patients might overlap with the social and behavioral problems found in ASD, thus possibly complicating the clinical assessment process [4].

The exact processes underlying this simultaneous occurrence remain inadequately understood; however, genetic investigations suggest that shared genetic factors might contribute to the manifestation of both disorders [82]. Neuroimaging research has shown that individuals diagnosed with both ASD and ADHD often display abnormalities in similar regions of the brain, particularly within the prefrontal cortex [98]. This region is crucial for the higher-order cortical functions of attention, planning, and impulse control. The parallelism in neural structure as well as function could partly explain the comorbidity of these disorders [79]

Individuals diagnosed with both ASD and ADHD may encounter greater difficulties than those with a single disorder. Such challenges may include pronounced impairments in social interactions, heightened behavioral concerns, and more pronounced obstacles in educational and professional settings [81]. As a result, these individuals often require more intensive and comprehensive intervention strategies.

Generally, treatment of such dually diagnosed individuals calls for multi-modal interventions that explicitly integrate strategies targeting both ASD and ADHD symptoms, [57]. Behavior therapies are essential and incorporate all the intervention techniques targeting social skills, organisational skills, and the reduction in disruptive behaviors [22]. Stimulant medications commonly used in treating ADHD can also benefit individuals with ASD. However, it is crucial to closely monitor their usage to prevent worsening symptoms of ASD [4].

2.1.4 Cerebral Palsy

CP constitutes a set of persistent motor disabilities that become apparent during early childhood, often as a consequence of damage to the maturing brain occurring before, during, or immediately following birth [83]. The condition primarily affects motor capabilities, resulting in diminished movement, altered muscular tone, and postural challenges [11]. Nonetheless, it is frequently associated with various neurodevelopmental disorders, thereby complicating the clinical manifestations and treatment strategies [54]. CP can lead to cognitive deficits, challenges in sensory processing, and behavioral problems stemming from brain damage, culminating in a complex array of difficulties [72].

A significant number of children with CP have co-occurring cognitive impairments, learning difficulties, and communication problems [26]. These problems can be severe and usually require special education and treatment. It is also typical that they manifest in a similar way to certain neurodevelopmental disorders, such as ASD and ADHD [18]. Children with CP are at a greater risk for being diagnosed with ASD and ADHD compared to the general population [68]. This comorbidity may aggravate difficulties in social interaction, communication skills, and attention control.

Diagnosis and management of the co-occurrence of numerous neurodevelopmental disorders require an exhaustive and multi-disciplinary approach. CP motor manifestations are managed by physiotherapy, while behavioral interventions and educational support must be instituted for the cognitive and social deficits associated with autism spectrum disorder and attention deficit hyperactivity disorder [87]. Speech and language therapy could be helpful for the child who has problems with communication, while occupational therapy enables the child to develop the necessary skills that are appropriate for daily living [11].

Neuroimaging and genetic research have elucidated the common pathways that may underlie the simultaneous occurrence of cerebral palsy (CP) and other neurodevelopmental disorders [71]. Structural and connectivity abnormalities within the brain, notably in areas such as the prefrontal cortex, are frequently observed [100]. These revelations are crucial in designing specific interventions that address the unique needs of all those affected [36].

2.1.5 Prefrontal Cortex

The prefrontal cortex (PFC) constitutes an essential region of the brain located at the anterior aspect of the frontal lobes. This area plays a pivotal role in numerous higher-order cognitive functions, including decision-making, problem-solving, planning, social interactions, and regulation of impulses. Often referred to as the executive center of the brain, the PFC is accountable for managing complex processes that are critical to goal-directed behavior and adaptive functioning [33].

The PFC is integral to the pathophysiology of neurodevelopmental disorders including ASD and ADHD. Irregularities within this region are frequently observed among individuals diagnosed with a range of disorders. Research employing neuroimaging techniques has revealed that those with ASD often exhibit reduced volume and atypical connectivity within the prefrontal cortex. These structural variations are associated with the social and communication challenges typical of ASD, alongside the presence of repetitive and restricted behaviors [21].

Again, the PFC is involved in the core symptoms of inattention, hyperactivity, and impulsivity in ADHD patients. fMRI studies have demonstrated that when performing tasks that require continuous attention and executive function, typically there is a reduced activation within the prefrontal cortex in individuals with ADHD. The lack of involvement is believed to lead to the behavioral symptoms associated with this disorder, which are difficulties in sustaining attention, organising activities, and regulating behavior [16].

This maturation course of the PFC extends into early adulthood, therefore making the structure especially vulnerable to developmental perturbations. Actually, genetic factors, prenatal exposures, and environmental variables inflect in the development of the PFC. Genetic factors, prenatal exposures, and environmental variables all impact the development of the PFC. For example, exposure to neurotoxic

substances or stress during brain development is very harmful and can have long-lasting effects on PFC structure and function [58].

A deep understanding of the role of the PFC in neurodevelopmental disorders is important for the formulation of effective therapeutic strategies. Interventions enhancing executive function skills, like cognitive-behavioral therapy and executive function training, are aimed at improving the performance of the prefrontal cortex. Moreover, pharmacological agents that affect neurotransmitter systems involved with the prefrontal cortex functioning, such as stimulants used for treating ADHD, can ease symptoms by augmenting PFC activity [5]. The figure 2.1 shows the position of the Prefrontal Cortex in an Harvard Atlas.

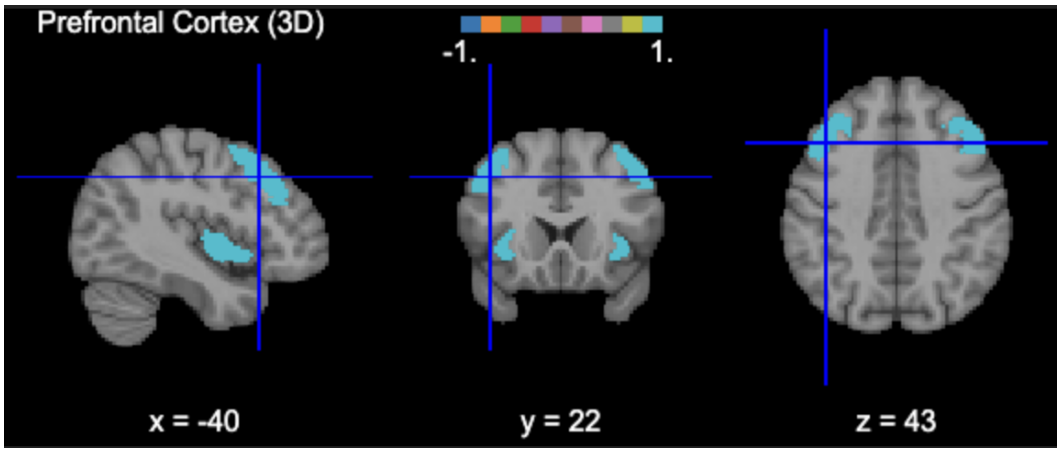

Figure 2.1: Highlighted PreFrontal Cortex

2.1.6 Autism Diagnosis Interviews

Diagnostic interviews are one of the most critical instruments a doctor uses in the evaluation and diagnosis process of ASD. The Autism Diagnostic Interview-Revised is one such methodology that has gained popularity due to its wide acceptance. It is a structured interview taken from the parents or caregivers of the individual, focusing on thorough investigation of the developmental history and current functioning in multiple domains of communication, social interaction, and restricted and repetitive behaviors. *The Autism Diagnostic Interview-Revised (ADI-R)* aids practitioners in gathering extensive information pertaining to the onset and severity of symptoms, which is crucial for an accurate diagnosis [85].

Another essential instrument in the diagnosis of autism, involving direct contact with the participant, is the *Autism Diagnostic Observation Schedule. ADOS* consists of a number of standardised activities and structured play designed to elicit behaviors that are known to pinpoint autism spectrum disorder. This program is fitted with several modules in order to be adapted to each individual according to age and language level, making this an assessable yet flexible program. ADOS is highly regarded for its ability to methodically observe and record specific social, communicative, and repetitive behaviors in a structured setting [61].

Although these diagnostic interviews are extremely useful for detecting ASD, they can potentially have negative and emotionally distressing impacts on both the patient and their families. The process can be protracted and thorough, frequently necessitating numerous sessions to finish. Recalling their child's developmental history and discussing their issues can be emotionally burdensome and unpleasant for parents. The acknowledgement and verification of an ASD diagnosis can elicit a combination of feelings, such as relief, anxiety, and sadness [38].

For individuals who are being evaluated, especially children, the assessment process may evoke stress and sensations of being overwhelmed. Engaging in atypical activities with an unfamiliar individual within a clinical setting can result in feelings of discomfort and apprehension. Furthermore, the structured nature

of the tasks may at times amplify the difficulties experienced by the individual, culminating in feelings of frustration or distress [52]

Notwithstanding these challenges, the benefits of an accurate diagnosis arrived at through these interviews are huge. In this way, the person's skills and needs will be understood in-depth to ensure the right intervention strategies and support systems. Early and accurate diagnosis, based on ADI-R and ADOS, makes the persons affected by ASD timely gain access to intervention and education services that significantly enhance their general outcomes, according to [62].

2.1.7 Brain Extraction and Eddy Current Correction

These form some of the critical preliminary steps in neuroimaging, largely needed to enable the performance of accurate data analysis. Extraction of the brain entails removing non-brain tissues from MRI images and enhances the accuracy of assessments that follow. On the other hand, eddy current correction refers to a methodology applied to reduce some of the distortions present in the diffusion MRI data due to the induction of eddy currents. These eddy currents arise as a result of changes in magnetic field gradients during the entire scanning process. Corrections such as this are important in obtaining accurate measures of FA and MD —the two major indices that inform about white matter integrity in neurodevelopmental disorders [93] [3]

The majority of brain extraction is accomplished by automated software applications running an algorithm to detect and remove non-brain structures from the MRI image. The exclusion of major non-brain tissue is a critical step of image preprocessing to prevent inaccurate results of further image processing and analysis that is highly misleading. Accurate Brain Extraction ensures that focus is exclusively allocated to brain tissue, thereby facilitating enhanced segmentation and quantification of cerebral structures [93]. A variety of instruments and algorithms, including the BET and the FSL, have been developed for this particular aim. These instruments are widely employed in neuroimaging research endeavors [93].

Eddy current correction refers to the process of correcting the distortions that appear in diffusion-weighted images due to high oscillations of the magnetic field gradients during the scan acquisition process in MRI. These will introduce huge inaccuracies into the data and consequently result in wrong assessment for the diffusion parameters. Techniques for Eddy current correction work by changing image data to compensate for these distortions and thus reconstituting the correct geometry of the tissues under scan. Correction of this anomaly is prerequisite for ascertaining the reliability of measurements of diffusion, such as FA.These have since been translated into fantastically complex algorithms that allow for efficient and accurate corrections—for example, FSL's eddy correct [3].

More to the point, oftentimes motion correction and normalisation are included as additional preprocessing steps for the improvement of data quality. Motion correction would be applied to lessen the effects resulting from patient movement during a scan, which have caused artifacts and lowered image quality. Normalising images to a standard scale or template makes the comparison between them from different people or different groups very easy [46]. The stages of preprocessing at the beginning serve as quality control measures to provide integrity and accuracy in neuroimaging data.

The preprocessing methodologies employed are essential for neuroimaging studies, especially those concentrating on neurodevelopmental conditions such as ASD and ADHD. Ensuring the availability of high-quality and accurate data allows researchers to more adeptly detect and characterise irregularities in both the structure and function of the brain. Consequently, this facilitates the formulation of improved approaches for the diagnosis and treatment of these anomalies [1] [93]. Advanced preprocessing methodologies in the application reduces variability, enhances the robustness of the findings, and is one of the important elements that can actually advance the understanding of neurodevelopmental disorders and the accuracy of their treatment [1].

2.1.8 Brain Matter Abnormalities

White matter, comprised of myelin-coated axons, is essential for enabling the efficient propagation of electrical impulses throughout different regions of the brain. Abnormalities in white matter tracts have

been linked to cognitive and behavioral challenges within neurodevelopmental disorders. Studies have shown that individuals diagnosed with ASD and ADHD exhibit significant alterations in the structural integrity of their white matter [51] [89]. These changes can be quantified by looking at measures, such as FA and MD. A lower FA and higher MD values indicate impaired white matter pathways, which could be a factor in the main symptoms of these conditions.

Grey matter, however, consists of neuronal cell bodies and is responsible for the processing and integration of information. Individuals with ASD and ADHD have also shown deviations in the structure and function of gray matter [2] [88]. Such deviations may influence the cerebral regions engaged in executive functions, social cognition, and sensory processing. This complexity later on contributes to a more intricate clinical manifestation of these disorders.

2.1.9 Comparative White Matter Findings in ASD, ADHD, and CP (2023–2025)

Recent neuroimaging studies (2023–2025) have advanced our understanding of WM abnormalities in neurodevelopmental conditions, particularly ASD, ADHD, and CP. In ASD, disruptions are frequently observed in the CC, especially the posterior splenium, which mediates interhemispheric communication. Abnormalities in this region may underlie the integration deficits commonly seen in ASD [43]. Long-range association fibers, such as the SLF and ILF, often show microstructural disorganization, both of which are crucial for language, executive functioning, and social cognition [14]. In addition, the cingulum, a limbic tract responsible for emotion and attention regulation, is commonly implicated.

ADHD demonstrates a partially overlapping but distinct WM pattern. Similar to ASD, alterations in the CC, specifically the body and splenium, are prevalent. However, ADHD is more strongly associated with abnormalities in the frontostriatal circuitry and cingulum, which relate to behavioral inhibition and attentional control [76]. These regions may contribute to hallmark symptoms of impulsivity and inattention. Some imaging studies suggest shared anomalies in posterior WM tracts between ASD and ADHD, reinforcing their clinical comorbidity. Nevertheless, frontally mediated disruptions help differentiate them [77].

In contrast, CP is characterized by focal and injury-induced WM damage, commonly arising from perinatal insults such as hypoxia or prematurity. A hallmark lesion in CP is PVL, which typically affects the CST traversing the PLIC [70]. The result is significant axonal degradation, often manifesting as motor dysfunction. Severe cases may also involve the CC and thalamocortical pathways, which contribute to cognitive and sensory impairments.

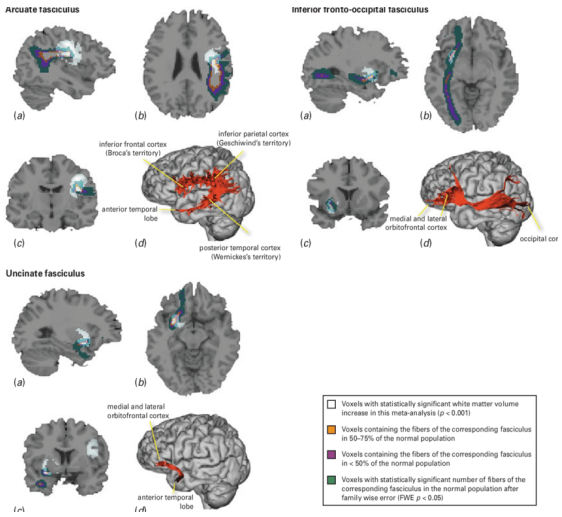

Figure 2.2: Decreased White Matter Regions in Individuals with ASD Compared to Healthy Controls

2.1.10 Implications for Diagnosis and Treatment

Such identification of specific anomalies in the white and gray matter of ASD, ADHD, and CP patients could have major implications for diagnostics and treatment of these disorders. One would understand that an understanding of the independent and common neural mechanisms underlying different diseases might allow clinicians to formulate more accurate and effective therapeutic approaches. For example, interventions aimed at enhancing the structural soundness of white matter or addressing specific irregularities in gray matter may have the capacity to alleviate certain cognitive and behavioral deficits associated with these disorders [2] [88].

2.1.11 Future Directions in Research

Further research into the neurobiological underpinnings of ASD, ADHD, and CP is necessary to further our current understanding and improve clinical outcomes. Future research needs to actively continue a search for genetic, environmental, and neurobiological contributors to these diseases. The employment of sophisticated neuroimaging methodologies, genetic research, and computational models has the potential to generate significant insights into the complex interactions among diverse brain areas and their effects on behavior and cognitive processes [20] [29] [59].

2.2 Metrics

This section provides an analysis of the metrics, values, and mathematical foundation of the technologies employed in this dissertation.

2.2.1 Typical Controls

Research in neuroimaging uses standardised control groups to benchmark measurements against which the data for patients are compared, according to [92]. The control cohorts usually comprise people who have no neurological and or psychological abnormalities and are used as a norm for comparison with normal anatomy and brains with normal functioning by [73] .In the setting of DTI, FA, MD, AD, and RD are the most commonly used metrics for gauging the integrity of cerebral white matter tracts [10].

Control values provide a uniform standard against which to compare these metrics from different ROIs, including the corpus callosum, prefrontal cortex, and basal ganglia, among others [56]. These values are needed for detecting irregularities that may be indicative of pathological changes related to disorders such as ASD or ADHD [67]. For instance, the corpus callosum, which connects the two hemispheres of the brain, is normally characterised by high FA values, thus showing a compact and well-structured arrangement of white matter fibres [1]. Deviations from these average values may indicate a disrupted connectivity, that is a very common phenomenon in neurodevelopmental disorders [97].

Normative control values in different regions of interest provide a means for establishing which areas of the brain have abnormal structures in a given disease [7]. For instance, individuals with a diagnosis of ADHD often have changes in the FA values in the prefrontal cortex, which is involved in the executive functions and behavioral control system [64]. In a similar vein, the basal ganglia, integral to both motor regulation and cognitive processes, may demonstrate significant variations in diffusivity across various neurological disorders [27].

Control values play a vital role in the diagnosis and understanding of neurological disorders, along with evaluating the effectiveness of therapeutic interventions [12]. By contrasting patient data against these reference standards, healthcare professionals and researchers can gain enhanced insights into the extent of white matter disruption and track variations over time, thereby providing a comprehensive evaluation of cerebral health and disease progression [75].

Table 2.1 describes the mean values of control FA for six main ROIs within the brain. FA is an index for the directionality of water diffusivity within the white matter pathways. As such, it provides information about the integrity and interconnectivity of the brain white matter.

Table 2.1: Mean Control FA Values for Key ROIs

Region of Interest (ROI) and **Mean Control FA Value**
Corpus Callosum and 0.550
Superior Longitudinal Fasciculus (SLF) and 0.500
Cingulate Cortex and 0.540
Uncinate Fasciculus and 0.480
Inferior Longitudinal Fasciculus (ILF) and 0.495
Anterior Thalamic Radiation (ATR) and 0.510

2.2.2 Fractional Anisotropy

It quantifies the directionality of water diffusion within tissue. High FA values indicate a high degree of directionality, typically observed in highly organised white matter tracts. The opposite is the case for low FA values; they indicate more isotropic diffusion and are often observed in gray matter or damaged white matter. In a very influential paper, [10], defined and established the application of FA in neuroscience.

Their work demonstrated how FA could reveal details about the white matter architecture and integrity in both healthy and diseased states [10].

Further studies have used FA in investigating various neurological diseases. For example, [102] have assessed the application of FA in MS and have reported that the measurement of reduced FA represented demyelination and axonal degeneration in the affected areas. In a related study, this study by [45] with respect to TBI has indicated that FA is a good measure for white matter injury and thus plays a role in diagnosis and prognosis [102] [45].

Salat [86] used FA in a study on cognitive aging, whereby changes in brain structure with age were assessed. Research has shown that reductions in FA are associated with generalised cognitive decline, mainly with regard to executive functions. These results underline the role of FA as an independent biomarker for neurological and cognitive health as shown in Eq 2.1:

$$\text{FA} = \sqrt{\frac{3}{2}} \cdot \frac{\sqrt{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}} \tag{2.1}$$

Eq 2.1 theλ_1, λ_2 and λ_3 represent the eigenvalues of the diffusion tensor and $\bar{\lambda}$ denote the average of these eigenvalues. FA is the measure of the extent by which diffusion varies in direction and informs, therefore, on the structural integrity and tissue structure composition. According to Jones and Leemans, 2011, higher values in FA portray better-structured tissue, while lower FA signifies more isotropic diffusion, characteristic of damaged or degenerating tissue. Fractional anisotropy (FA) serves a significant role in assessing the integrity of white matter tracts within the brain, facilitating the detection and monitoring of various neurological conditions, including multiple sclerosis, Alzheimer's disease, and traumatic brain injuries [47].

2.2.3 Mean Diffusivity

Mean diffusivity is the measurement of the average velocity at which water molecules diffuse through tissue. In fact, MRD is very sensitive to changes in tissue density and to the presence of obstacles, such as cellular membranes. The seminal paper is laid the basis for a clinical application of MD: it showed that it could be useful in identifying pathological changes in brain tissue, particularly those caused by stroke or edema.

MD has been of great value in assessing brain tumors. Yamada [103] indicated that MD values are useful in distinguishing different types of brain tumors, thus offering very important information about treatment strategies [103]. Warach et al. (1995) conducted research in the area of stroke and found that in areas affected by acute ischemia, the MD is decreased, which indicates the development of cytotoxic edema[101].

Furthermore, research into neurogenerative diseases has utilised DTI (MD) to determine the underlying mechanisms of pathogenesis. In the case of Alzheimer's disease, clinicians have used MRI to visualise the location where neuronal degeneration and microstructural decay occur within the brain *(Bozzali et al., 2002)*. The capability of this technology to detect minute changes in tissue structure makes MD ideally suited to support early diagnosis and follow-up of the disease process [15].

$$\text{MD} = \bar{\lambda} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3} \tag{2.2}$$

Eq 2.2, theλ_1, λ_2 and λ_3 represent the eigenvalues of the diffusion tensor. Generally, high MD values suggest an increase in the free motion of molecules, which often occurs in conditions characterised by edema or tissue degradation. Low MD values indicate restricted diffusion, which can occur in tissues with high cellular density or in conditions of cytotoxic edema [7]. MRI has applications in many clinical conditions, such as the evaluation of brain tumors and ischemic

2.2.4 Brain Extraction

Brain extraction, also known to many as skull stripping, is one of the most basic steps in neuroimaging that segments out the brain from non-brain tissues in MRI studies. This technique provides better accuracy to the subsequent studies by removing unwanted structures that may interfere with the proper interpretation of data. Figures 2.3 and 2.4 shows the Brain Extracted file in different view mode.

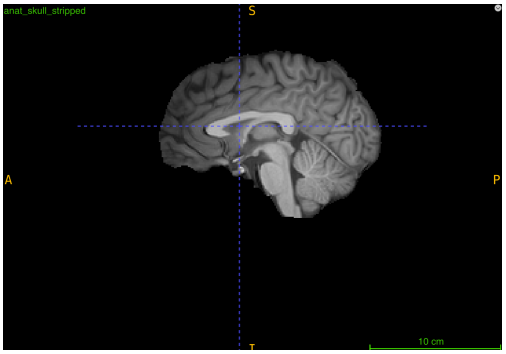

Figure 2.3: Skull Stripped.

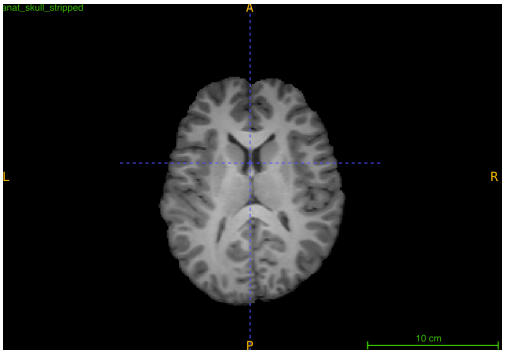

Figure 2.4: Skull Stripped.

Mathematically, brain extraction involves a series of steps, typically commencing with thresholding based on intensity. This initial step utilises a threshold function, $T(x)$, that classifies the voxels into two distinct groups: brain tissue and background, based on the intensity of each voxel. The function $I(x)$ in Eq 2.3:

$$T(x) = \begin{cases} 1 & \text{if } I(x) > \tau \\ 0 & \text{otherwise} \end{cases} \tag{2.3}$$

After applying a threshold to the image, morphological procedures such as erosion and dilation are used to improve the accuracy of the binary mask. Erosion eliminates diminutive, separate formations, but dilatation restores fractured cerebral areas [35]. Mathematically, erosion and dilation $\epsilon(B)$ for a binary image B are precisely defined as Equations 2.4 and 2.5:

$$\varepsilon(B) = \{x \in Z^2 \mid (B_s) \subseteq B\} \tag{2.4}$$

$$\delta(B) = \{x \in Z^2 \mid (B_s) \cap B \neq \emptyset\} \tag{2.5}$$

where (B_s) is the structuring element.

Advanced techniques of brain extraction use deformable models like active contour models and level sets. In the methodology of level sets, a contour, $\phi(x, t)$, is iteratively deformed with time t to precisely align it with the edges of the brain. This deformation comes through the solution of a partial differential equation (Eq 2.6)

$$\frac{\partial \phi}{\partial t} + F|\nabla \phi| = 0 \tag{2.6}$$

The speed function F is determined by the image gradients, as described by Osher and Sethian in 1988.

The application of these mathematical techniques is essential for accurately separating brain tissues from MRI data, serving as the basis for many automated brain extraction technologies.

2.2.5 T Statistical Test

The t-test is a statistical test used to check whether there is any significant difference between the two-group means, which may share some common traits. This test is commonly used in hypothesis testing for assessing the means of samples and drawing inference for the population at large.

The t-test is a mathematical method used to assess the null hypothesis (H0) that the means of two populations are identical. The test statistic is computed using the prescribed mathematical expression Eq 2.4:

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}} \tag{2.7}$$

- $\bar{X}_1$ and $\bar{X}_2$ are the sample means
- s_1^2 and s_2^2 are the sample means.
- $_1$ and $_2$ are the sample sizes.

The denominator corresponds to the standard error of the mean difference between the two groups.

There are three types of t-tests:

- Independent-samples t-test
- Paired-samples t-test
- One-sample t-test

For the independent-samples t-test, the degrees of freedom (df) are calculated as:

$$df = \frac{\left(\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}\right)^2}{\frac{\left(\frac{s_1^2}{n_1}\right)^2}{n_1 - 1} + \frac{\left(\frac{s_2^2}{n_2}\right)^2}{n_2 - 1}} \tag{2.8}$$

The calculated t-value is then compared with the critical value obtained in the t-distribution table at a given level of significance, usually given α = 0.05. In case the t-value is greater than the critical value, this leads to a rejection of the null hypothesis, postulating a significant difference between the groups.

The t-test is essentially based on the Central Limit Theorem, which states that as the sample size increases, the distribution of the sample mean will increasingly take the shape of a normal distribution [95]. This property enables rigorous testing of hypotheses, even in cases where sample sizes are limited.

2.2.6 Morphological Operations

Morphological operations are very basic methods in image processing and are very efficient in analysing and processing binary images. The method uses a structuring element to transform the input image so as to generate another output image with the same dimensions. The most frequently used morphological operations include erosion, dilation, opening, and closing.

Erosion and **dilation** are fundamental processes upon which other morphological operations are built. **Erosion** is indicated by $\epsilon(B)$ which reduces the size of the edges of the main areas in a picture B. The erosion of set B by a structural element S is mathematically forumalted as:

$$\epsilon(B) = \{x \in Z^2 \mid (S)_x \subseteq B\} \tag{2.9}$$

where $(S)_x$ is the translation of S by x.

This technique efficiently deletes the pixels that lie on the boundaries of objects, thereby reducing the size of the objects. The edges of the foreground regions are grown by a technique called dilation, denoted by $\delta(B)$. It is defined or expressed as:

$$\delta(B) = \{x \in Z^2 \mid (S)_x \cap B \neq \emptyset\} \tag{2.10}$$

where $(S)_x$ is again the translation of S by x.

Opening $B \circ S$ smoothens contours, breaks down narrow isthmuses and eliminates small islands and sharp peaks.

$$B \circ S = \delta(\epsilon(B)) \tag{2.11}$$

Closing on the other hand fuses narrow breaks and long thin gulfs, eliminating small holes.

$$B \cdot S = \epsilon(\delta(B)) \tag{2.12}$$

These operations play a major role in tasks like noise removal, shape simplification, and object segmentation of binary images *(Serra, 1982)*. Morphological operations make use of the geometric configuration of the structuring element S to probe and transform the input image B. These methodologies are found to be very useful in preprocessing functions for image analysis, especially in medical imaging, where they ease the delineation of areas of interest, like cerebral tissues in MRI *(Gonzalez and Woods, 2002)*.

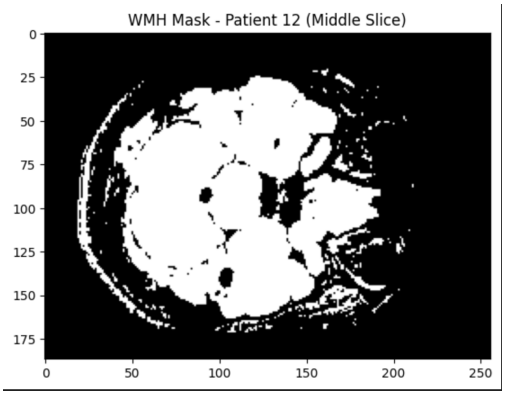

Figure 2.5: WMH Mask

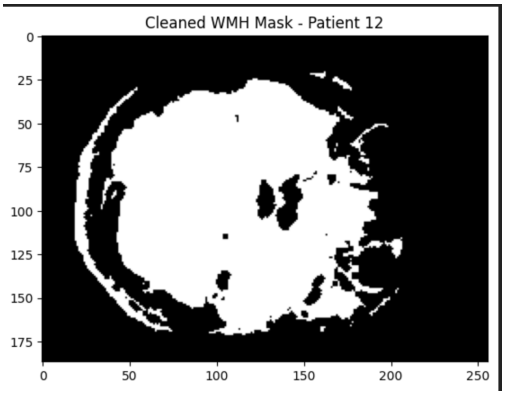

Figure 2.6: Cleaned WMH Mask.

The Fig 2.5 and 2.6 are the outcomes of the morphological cleaning done on Fig 2.5. The closing operation of Morphological cleaning is performed hence to include the fine details which can be essential for the study.

2.2.7 White Matter Hyperintensities

WMH are areas of higher intensity in T2-weighted and FLAIR MRI images, which usually show small vessel disease, ischaemia, or other pathologies. WMH relates to a variety of diseases connected with ageing, neurodegenerative diseases, and neurodevelopmental disorders, among which are ASD and ADHD. Detection of these hyperintensities informs our view on their relation to neurological dysfunctions such as hyperactivity in ASD patients.

Mathematically, brain extraction entails a succession of steps that typically start with thresholding based on intensities. This initial step makes use of a thresholding function, T(x), to separate the brain tissues from the background by evaluating the intensities of each voxel. The function I(x):

$$T(x) = \begin{cases} 1 and \text{if } I(x) > \tau \\ 0 and \text{otherwise} \end{cases}$$

where:

- $I(x)$ is the intensities at voxel x_1
- τ is the threshold separating WNH from normal white matter.

Otsu's Threshold Method

Otsu's is an unsupervised thresholding technique of global nature, normally viewed to be able to find the best threshold for image segmentation at a minimum variance within class and a maximum variance between classes. This has been commonly used in medical image analysis, mainly for the segmentation of regions like WMH.

Define the intensity histogram of the image, where there are L levels. The probability of every level of intensity i is represented as P(i) and is obtained from the histogram. Now, these images can be grouped into two quite different classes:

- C_1 (Foreground) containing intensities from 1 to t
- C_2 (Background) containing intensities from $t + 1$ to L

The optimal threshold t^* is determined by maximising the between-class $\sigma_b(t)^2$:

$$\sigma_b^2(t) = w_1(t)w_2(t)[\mu_1(t) - \mu_2(t)]^2$$

where

- $w_1(t)$ and $w_2(t)$ are the probabilities of class
- $\mu_1(t)$ and $\mu_2(t)$ are the class means.

CHAPTER 3

Literature Review

3.1 Related Works

The present study is inherently interconnected with and engaged in all the domains mentioned. The research findings make a substantial contribution to these established fields of knowledge, offering valuable insights and consequences that have a complete impact on each domain. Through a comprehensive analysis and systematic methodology, the study guarantees that its findings are pertinent and applicable to the many areas of investigation, so enhancing the overall knowledge within these domains.

3.1.1 Advance Detection of Autism Spectrum Disorder

The diagnosis of ASD is currently based on clinical interviews and behavioral observations, hence subjective and resource expensive. The recent advances in data science and machine learning have facilitated the development of more efficient, effective, and objective approaches for ASD identification.

Supervised learning methodologies, specifically machine learning algorithms, have shown promise in identifying ASD through the analysis of large-scale datasets encompassing behavioral, genetic, and neuroimaging data. A proficient technique entails employing support vector machines (SVM) and random forests to classify individuals based on features extracted from these datasets. These algorithms possess the capability to identify subtle patterns that may be missed by human evaluators, thereby improving the precision of diagnoses.

Specifically, neuroimaging methodologies in the form of functional magnetic resonance imaging and diffusion tensor imaging have contributed much to the research field in connection with ASD. Neuroimaging data have been used for the training of different machine learning algorithms, particularly CNNs, towards the detection of abnormalities in brain structure and connectivity features related to ASD. Examinations of resting-state fMRI data have used Convolutional Neural Networks (CNNs). These studies have achieved considerable accuracy in differentiating between individuals with a diagnosis of Autism Spectrum Disorder (ASD) and neurotypical controls, which do not have ASD [40].

Besides that, machine learning algorithms have employed feature selection methodologies, such as Recursive Feature Elimination and Principal Component Analysis, for enhancing their predictive performance. These methodologies are focused on reducing the dimensionality of datasets while emphasising only the most important attributes used in the identification of Autism Spectrum Disorder by [39].

Machine learning has also been utilised to test and work with genetic data. Specifically, in the neuroimaging area, gene expression patterns and identification of some specific genetic markers have been used by investigators to model and predict ASD for early detection [53].

Integration of data science and machine learning into ASD research holds immense potential for advancement in strategies designed for early identification and intervention. In this direction, such technological breakthroughs offer a more objective and efficient alternative to the traditional methods of diagnosis, hence increasing the quality of care for people with ASD.

3.1.2 Advancements in ADHD Detection

Traditionally, Attention Deficit Hyperactivity Disorder (ADHD) has been identified subjectively and laboriously using behavioral assessment tools and clinical interviews. With advancements in data science and machine learning, it has introduced more precise and efficient methodologies for the detection of ADHD.

Machine learning algorithms have been applied to behavioral, genetic, and neuroimaging data to determine trends related to ADHD. SVM and random forests have been used in classifying subjects with characteristics from these data. This application has increased the accuracy of diagnosis by determining subtle trends not easily recognised by the human evaluators [19].

fMRI and EEG have been instrumental in advancing the research on ADHD. CNNs, a specific category of machine learning algorithms, have been trained on neuroimaging datasets to identify irregularities in both the anatomical and functional aspects of the brain associated with ADHD. Studies have indicated that these models can proficiently distinguish between individuals diagnosed with ADHD and those who are not, thereby offering a non-invasive diagnostic alternative [80]

Feature selection techniques apply principal component analysis and recursive feature elimination in helping machine learning models pick up predictive accuracy based on the most relevant features. The method would decrease the dimensionality of data and help a model become effective in recognising ADHD, as shown by [32]

Application of data science and machine learning in the domain of ADHD research shows significant promise in terms of providing refinement to the early identification of the disorder and formulating customised treatment strategies. Such technological advances will go a long way in offering a more objective and efficient alternative to traditional diagnostic techniques, improving patient outcomes.

3.1.3 Advancements in Brain Extraction Techniques

Brain extraction in neuroimaging research involves the delineation of cerebral tissues against non-cerebral elements within an MRI scan. Conventional methods, such as manual segmentation and thresholding, used to be labor-intensive and prone to variability. Improvements in machine learning, artificial intelligence, and data science have changed these techniques for good, coming up with more accurate and efficient methods.

Already, machine learning techniques have considerably improved the accuracy of the BE processes, especially deep learning architectures like CNN. The establishment of these architectures occurs by training them on large databases of annotated MRI images, thereby allowing them to successfully discriminate between cerebral and non-cerebral elements. After training, these models are able to assess new images in an automated way with a high degree of accuracy, which therefore diminishes the need for human intervention greatly [50]

Artificial intelligence methodologies use FCN and U-Net architectures that have proven unprecedented skill in performing an image segmentation task. These are capable of learning variable morphology and size of brains from different populations and imaging techniques. This robustness enables models in both clinical and research settings to produce results that are reliable and reproducible.

It is the application of data science methodologies, in particular, feature extraction and data augmentation that significantly improves the performance of brain extraction algorithms. Feature extraction algorithms are used to identify important features in MRI data that ensure accurate segmentation. Input augmentation techniques, such as rotation, scaling, and flipping, diversify the training dataset and allow the model to accommodate new input effectively.

Advancements in this domain have resulted in the evolution of automated brain extraction techniques that are more efficient, more reliable, and less prone to human errors. Combining machine learning, artificial intelligence, and data science with brain extraction methodologies is indeed a quantum jump toward achieving greater accuracy in neuroimaging studies and increasing our understanding of the structure of the cerebral structure.

3.2 Knowledge Gaps

3.2.1 Environmental Factors Modulating Hyperactivity in Autism

ASD disorder characterised by social communication problems, repetitive behaviors, and mostly hyperactivity. While genetics are central in understanding the causes of ASD, increasingly, it has been recognised that environmental factors contribute significantly to hyperactivity modulation in autistic people. There are still some real gaps in knowledge with respect to how these environmental factors interact specifically with the behaviors observed in ASD.

One large domain of investigation involves sensory sensitivities. Individuals with autism frequently exhibit an increased sensitivity to various stimuli, including auditory, visual, and tactile inputs, which may intensify hyperactive tendencies. Research indicates that sensory overload has the potential to amplify hyperactive behaviors; however, investigations explicitly connecting environmental factors to hyperactivity in autism are still scarce. Furthermore, the dynamics within families significantly influence the regulation of such behaviors.

Studies indicate that structured, supportive environments may diminish the presence of hyperactivity, but how family stressors impact hyperactivity in autistic children requires further exploration.

Likewise, the school atmosphere may influence behavior. Structured classrooms favor the hyperactivity restraint of autistic pupils; by contrast, conditions that are too stimulating enhance this symptom. The effectiveness of educational supports, though important, has been little researched. Also, nutritional and sleeping conditions have been related to hyperactivity in ASD, though investigated scantily.

There is also a suspicion that environmental toxins, mainly pollutants and heavy metals, add to the severity of ASD symptoms, including hyperactivity. Research into how such toxins interact with neurodevelopmental conditions like ASD is still emerging. These knowledge gaps clearly call for more longitudinal studies and integrative approaches to research, which consider interactions of multiple environmental factors. Evidence-based interventions in the design of sensory-friendly space and enhancement of environmental quality may provide practical solutions in managing hyperactivity and improving wellbeing in autistic people.

3.2.2 Longitudinal Studies on ADHD in Autistic Adults

Researches of ASD and ADHD have traditionally been focused on the pediatric population. However, it has lately been acknowledged that ADHD often persists well into adulthood, especially among the autism population, hence forming a unique group within the population experiencing their unique set of challenges. Despite this fact, substantial gaps in knowledge still exist, especially in terms of longitudinal studies tracking ADHD symptoms and outcomes in autistic adults for an extended period.

A significant deficiency in the existing literature is the absence of longitudinal studies that monitor autistic adults who also exhibit symptoms of ADHD throughout various life stages. Research efforts predominantly concentrate on childhood and adolescence, frequently overlooking the progression of ADHD symptoms in autistic adults. The scant research conducted thus far indicates that traits associated with ADHD, including impulsivity, inattention, and hyperactivity, may either remain constant or decrease as individuals age. Nevertheless, the available data are inadequate to comprehensively comprehend these trajectories and their implications for quality of life, employment, and mental health [6] [84].

Another major deficiency concerns the long-term effectiveness of interventions. Existing therapeutic approaches-behavioral therapy, pharmacological treatment, and occupational therapy-are typically subject to brief examinations. There is a need for longitudinal research into how these treatments will sustain their effect in managing ADHD symptoms in autistic adults, especially since needs and treatment efficacy are likely to vary at different age points [30] [90].

Longitudinal studies would further help clarify how the attributes of ADHD and ASD, in regard to social difficulties, executive dysfunction, and anxiety, are interconnected. This would make a big difference to the clinicians in devising targeted interventions that address the dual nature of these conditions. In the absence of longitudinal data, treatment strategies continue to be significantly reactive rather than proactive, which cannot comprehensively address the broad challenges that autistic adults face with ADHD [44].

Addressing these gaps is crucial to improving life outcomes for autistic adults with ADHD. Such robust longitudinal studies could help refine treatment, support systems, and policies that better meet their changing needs across adulthood.

3.2.3 Cross-Cultural Differences in Autism and Hyperactivity Diagnosis

ASD and ADHD are complex neurodevelopmental disorders that present variably across cultures. However, there are considerable gaps in understanding how cultural factors influence the diagnosis of ASD and ADHD, and co-occurring hyperactivity in autistic individuals. These gaps hold back both the development and provision of effective, culturally sensitive diagnostic and intervention tools.

One major knowledge gap is the variability in diagnostic criteria and practices across different countries. Most of the current Western diagnostic frameworks, such as the DSM-5 and ICD-11, are applied universally without considering cultural variability in symptom manifestation. For example, eye contact or social reciprocity that is central to the diagnosis of ASD might hold a different meaning across cultures [49].

In some cultures, reduced eye contact is a form of respect rather than considered a potential marker for ASD, hence underdiagnosis or misdiagnosis for autism.

Further, the level of stigma that is placed on mental disorders also varies significantly between cultures and impacts parents' likelihood to seek a diagnosis for their children. In many non-Western cultures, mental health issues are seen as a personal or family failing and thus there is often significant delay in seeking competent help and support [13]. This factor impacts not only when the diagnosis occurs but also the willingness to accept conditions such as ADHD and ASD as a disease state.

Another important concern is related to the low number of studies that explore the manner in which hyperactivity manifests itself in autistic persons across diverse populations. The understanding of hyperactivity can vary depending on the cultural norms, and this can lead to a difference in diagnosis of ADHD when it co-occurs with ASD. Despite the growing international awareness of these conditions, more research is needed to understand how cultural differences impact the diagnostic context and the lives of those living with ASD and ADHD [25]. Addressing these knowledge gaps is critical to developing inclusive and effective diagnostic practices that account for cultural diversity and reduce disparities in care.

3.2.4 Impact of Gender on Hyperactivity and Autism Symptomatology

The intersection of gender and Autism Spectrum Disorder with hyperactivity forms a highly relevant but poorly researched area in the field of neurodevelopment. Conventionally, ASD and disorders associated with hyperactivity, such as Attention-Deficit/Hyperactivity Disorder, have traditionally been diagnosed primarily in males. The prevalent gender bias in diagnostic approaches has led to serious gaps in understanding how these disorders differently manifest themselves in different genders.

One knowledge gap exists in the domain of underdiagnosis of autism in females. Females are often shown to present different or more subtle symptoms of ASD compared with males, leading to delayed or missed diagnoses" [55]. Girls, for instance, may be more likely to mask their social difficulties by imitating others or develop restricted interests that align with socially accepted practices which then do not raise concern [65].

These disparities create the lack of gender-specific diagnostic criteria; hence, there is a dire need for tools sensitive to the different ways ASD manifests in females.

Manifestation of hyperactivity is different across genders. Most boys who have ADHD have externalising behaviors like impulsivity and hyperactivity, while most girls have symptoms tending towards internalisation, inattention, or anxiety [41] Symptoms being more internalised are thus more overlooked, probably also because girls are less diagnosed and treated. This seems to be a difference, underlining a point where knowledge about how gender affects the manifestations of hyperactivity in ASD individuals is still missing. Second, not many studies have explored the long-term outcomes for females with co-occurring ASD and ADHD. Much of the previous research has focused on males, leaving a gap in our understanding of specific challenges and needs that females face during the transition to adulthood. As pointed out by [104], it is important that research on ASD and hyperactivity addresses these gender-related gaps in order to provide more equitable diagnostic practices and interventions.

3.2.5 School-Based Interventions for Hyperactivity in Autistic Children

While much research is done on school-based interventions for hyperactivity problems among children with autism, significant research gaps still exist in terms of their effectiveness and acceptability. In addition, ASD often comes in comorbidity with ADHD, which complicates managing the hyperactive behaviors within school settings. Long-term effects of these school-based interventions and their specificity to the target population are hardly examined in the literature, even though dual diagnoses of ADHD and ASD are common.

One such knowledge gap is the lack of intervention programs which are tailored, targeting both conditions of autism and hyperactivity. The interventions provided are often generalised, either for ASD or ADHD exclusively, without any mention of the special needs of children with these combined conditions, as in [69] This may present a limitation to the effectiveness of the program to enhance attention, impulse control, and behavioral conduct at school.

A further notable deficiency pertains to the sustainability and adaptability of the interventions in question. Numerous investigations predominantly emphasise immediate outcomes, offering limited understanding of the enduring advantages associated with school-based approaches for managing hyperactivity in children with autism. Moreover, there exists a lack of comprehensive research addressing how these interventions may be tailored to various educational contexts, including mainstream versus special education environments, as well as the effective training of educators for their implementation.

Furthermore, the role of IEPs is not well elaborated in supporting the students who have been diagnosed with hyperactive autism. The reviews needed on how targeted strategies can be combined within IEPs and how collaboration between educators and clinicians could give better results for such children are lacking [74].

These deficiencies should be revised in order to improve the results of school-based interventions with children with autism who present with symptoms of hyperactivity.

3.2.6 Effectiveness of Non-Pharmacological Interventions for Hyperactivity in Autism

Non-pharmacological strategies for addressing hyperactivity in ASD patients have the potential to represent real alternatives to pharmacological treatment; important shortcomings exist, however, in the realisation of long-term efficacy and specific applicability. The large majority of children with ASD show hyperactive symptoms that, very often, disturb social, school, and family life. Although non-pharmacological methods, including behavioral therapy, parental training, sensory integration therapy, and mindfulness-based techniques, have garnered increased interest, the current literature remains disjointed and insufficiently substantiated regarding their long-term effects [24]

A significant deficiency in the literature is the absence of extensive longitudinal investigations that assess the efficacy of these interventions over prolonged durations. The majority of contemporary research focuses on immediate outcomes, thereby offering constrained understanding regarding the effects of these therapies on hyperactivity throughout different developmental phases [91]. As children diagnosed with ASD mature, their requirements and reactions to interventions may evolve, thereby requiring flexible and enduring approaches that are infrequently explored in the current body of research.

Secondly, few studies evaluate the comparative effectiveness of different types of non pharmacological interventions. Various studies might focus on either CBT or exercise programs for the treatment of hyperactivity, but without comparison to other forms of interventions. The insufficiency of such comparison makes it cumbersome for clinicians to find the best approach to treating hyperactivity among those with autism.

Ultimately, the unique features of autism, combined with the co-occurrence of other disorders such as ADHD, demand an individualised treatment approach. However, very few data are available to guide individualised treatment programs that could combine multiple non-pharmacological interventions, which may enhance the overall effectiveness of treatments for hyperactivity in this population.

3.2.7 Technological Advancements in Monitoring Hyperactivity in Autism

Recent technology innovations provide new opportunities for hyperactivity surveillance in ASD, yet a strong level of ignorance exists. Wearable technologies, mobile software applications, and machine learning algorithms now increasingly allow for the observation of patterns of behavior, providing continuous objective information that may supplement traditional methods of observation [23]. However, despite the impressive possibilities inherent in these technologies, there are some major limitations to their use and effectiveness within ASD populations.

The major deficiency lies in the lack of large-scale research, which validates the accuracy and reliability of these technologies on diverse autistic populations. Research that has been conducted thus far has only used small sample sizes and short observation times, limiting the generalisability of the findings. Besides that, most technological tools are completely designed for neurotypicals, making them sometimes question marks regarding the sensitivities of autistic individuals to their needs and behaviors-particularly those who are non-verbal or who have sensory sensitivities.

Another difficulty is presented in the integration of such technologies into the clinical setting. Many health professionals also express concern about the density of data generated by continuous monitoring devices and the lack of clear guidelines on how to interpret and apply that data to clinical practice. Absent standard guidelines on how to use these, long-term efficacy of these devices in monitoring hyperactivity in autism is challenging to determine.

Finally, there is a call for accessibility. The cost of wearable devices and other technological interventions could potentially further limit their use in low-income populations, adding to disparities in care. For these knowledge gaps, further research and refinement are important in leveraging technology to monitor and manage hyperactivity in autism better.

CHAPTER 4

Data

The data used in this research was MRI data of Autistic and Hyperactive patients. The data is collected from the sources named - ABIDE-2 and ADHD 200. Both the data consisted of patients where each patients have files named - anat, flair, dti, rest. For the ADHD200 dataset only anat and rest files were there.

4.1 The Anatomical File

Commonly represented in NIfTI or DICOM, anatomical files are crucial components of neuroimaging clinical research. Usually, these files include high-resolution T1-weighted MRI scans with complex structural information of the brain. These anatomical data are significant because they offer a comprehensive picture of brain areas including grey matter, white matter, and cerebrospinal fluid (CSF). From basic studies on brain architecture to pragmatic applications in the diagnosis of neurological illnesses, a wide spectrum of neuroimaging studies depends on this complete anatomical data.

The need for anatomical files results from their central focus in many neuroimaging studies. These files act as a reference point against which other imaging modalities, such fMRI or DTI, can be normalised in studies looking at illnesses such ASD. Guaranturing exact correlation between the functional or diffusion data and the suitable anatomical places inside the brain depends on maintaining this alignment. Lack of this precise mapping could cause functional or structural findings to be misinterpreted, therefore producing erroneous results on the activity or connections of the brain.

Moreover, preparation of neuroimaging data depends on anatomical files absolutely. Figure 4.1 shows the axial, coronal, and sagital view of the anatural brain of an autism patient.Moreover they find use in bias field correction, which addresses MRI scan changes in intensity, and in skull-stripping, a technique removing non-brain tissues from the images. Following investigations, including voxel-based morphometry (VBM) or ROI analysis, depends on the accuracy and dependability of which thorough preprocessing techniques ensure.

Moreover, identification and characterising of brain abnormalities depend on anatomical files. In studies focused on neurodevelopmental disorders like ASD, these data help researchers to precisely examine brain regions, therefore allowing them to find anomalies in locations like the amygdala or the corpus callum. These kind of results can provide important new perspectives on the structural differences connected to these diseases, so improving our knowledge of their basic neurobiology.

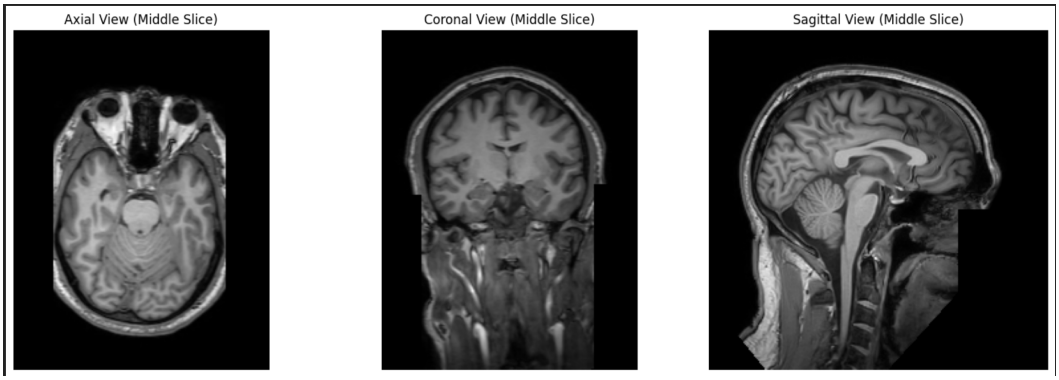

Figure 4.1: Anatomy Image Middle Slice Plot

4.2 Resting State MRI File

Often obtained using Resting-State fMRI, resting-state data are crucial for neuroimaging investigations aiming at examining brain activity in the absence of explicit task involvement. These files record the natural fluctuations in brain activity, therefore provide insight into the functional connectivity of the brain - how various areas of the brain interact with each other at rest. Important since they enable one to map the natural network of the brain, a collection of linked areas thought to be involved in introspection and self-referential cognitive processes and maintained active throughout times of rest.

Since they naturally assist to understand many neurological and mental conditions, including schizophrenia, Attention-Deficit/Hyperactivity Disorder (ADHD), and Autism Spectrum Disorder (ASD), resting-state files are becoming more and more significant. In these disorders, resting-state connection abnormalities have been linked to symptoms including altered cognitive processes, hyperactivity, and poor social connections as well as others. Resting-state data analysis helps scientists find unusual connection patterns maybe underlying some diseases. This targets therapeutic interventions and offers reasonable biomarkers for diagnosis.

Resting-state files help researchers to identify functional networks in the brain without depending on task-specific behaviours, therefore enabling the study of individuals that might have trouble following activities, such children or those with complicated mental health issues.Monitoring these natural connection networks offers a non-invasive means to investigate the functional structure of the brain and its changes in disease.

Still, many times resting-state files reveal noise or imprecision because of several elements affecting the data quality. One of the main challenges is physiological noise, which includes variations in brain output brought about by cardiac pulse and respiratory activities. These physiological motions could cause distortions in the data, therefore producing a fuzzy or hazy visual impression in the produced photographs. Moreover, the head movement during scanning could aggravate the degradation of data quality by producing motion artefacts adding complexity to the analysis. Figure 4.2 plots the rest file of an autism patient.

The poor SNR seen in resting-state fMRI adds still another component to contribute to blurriness. Resting-state signals are subtle, hence the confluence of noise from the scanner, the patient, and the surroundings can overwhelm these signals and so prevent the extraction of important information without careful preprocessing.

Resting-state data are vital in neuroimaging research notwithstanding these challenges. Using advanced preprocessing techniques such as motion correction, physiological noise reduction, and denoising algorithms helps one to solve these issues and enhance the clarity and dependability of the data. Appropriate analysis of resting-state data reveals important information about the functional structure of the brain, therefore helping to understand and control certain neurological and psychiatric disorders.

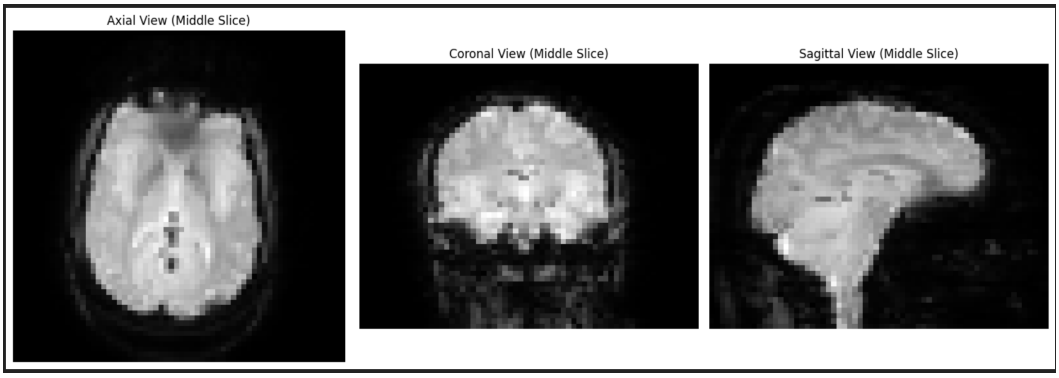

Figure 4.2: Rest Middle Slice

4.3 Fluid Attenuated Inverse Recovery File

Fluid-Attenuated Inversion Recovery (FLAIR) imaging is a very powerful neuroimaging technique widely used in the diagnosis and research of neurological diseases. Because they allow to highlight the existence of particular brain abnormalities, including white matter lesions, which could not be easily detected using other imaging techniques, FLAIR files—obtained from FLAIR MRI scans—are quite beneficial. Because of their increased sensitivity to pathogenic changes in the brain, which makes them essential for the exact diagnosis and surveillance of diseases including multiple sclerosis, stroke, and several forms of dementia, FLAIR files are both necessary in clinical and scientific environments.

Usually strong on standard T2-weighted images, FLAIR imaging offers a major advantage in its ability to block the cerebrospinal fluid (CSF) signal. By lowering the CSF signal, FLAIR increases the contrast between problematic tissues and surrounding anatomical structures, therefore enabling the detection and delineation of anomalies in the white matter of the brain. Commonly obscured in past MRI investigations, areas around the ventricles or proximate to the cortical surface benefit notably from the improved contrast in detecting lesions.

By providing exact and complete visual images of the inside structures of the brain, FLAIR data significantly contribute to neuroimaging research and therapeutic therapy. The patented imaging sequence that especially decreases the cerebrospinal fluid (CSF) while enhancing the visibility of lesions and other anomalies helps to explain the sharpness of FLAIR images. Therefore, even in cases of small pathogenic changes, the resultant images are not only highly instructive but also quite intelligible. The great difference between healthy and diseased tissues in FLAIR images helps to precisely identify lesions, hence guiding therapeutic decisions and diagnosis.

In longitudinal investigations, where precise monitoring of neurological disease development is of great relevance, the outstanding quality of FLAIR images makes them very essential. Researchers and doctors can use FLAIR data to track temporal changes in white matter lesions, assess therapy effectiveness, and project possible disease outcomes. Development of focused treatments and improvement of patient safety depend on such a great degree of specificity.

Moreover, the great quality of FLAIR images can be ascribed to the use of advanced imaging methods during their collecting, as the Figures 4.3 and 4.4 clearly show. The inversion recovery method used in FLAIR imaging effectively reduces the effect of noise and artefacts, therefore ensuring the generation of exact and clear images. In neuroimaging, precision is absolutely important since the diagnosis and treatment of neurological diseases may depend much on the recognition of minute changes in brain structure.

Eventually, FLAIR files are a basic part of neuroimaging since they offer unparalleled crispness and distinction needed for white matter issue identification and profiling. In both clinical and research settings, their ability to offer complex visual depictions of the internal architecture of the brain, untouched by cerebrospinal fluid (CSF), makes them indispensable tool. FLAIR files are meant to be accurate and

clear enough for the diagnosis of neurological diseases and tracking of sickness development, hence improving our understanding of brain health and disease.

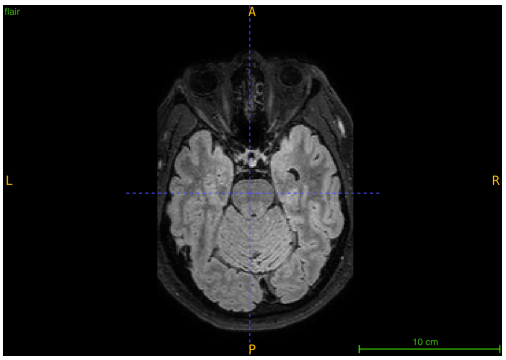

Figure 4.3: Fluid Attenuated Inverse Recovery Axial

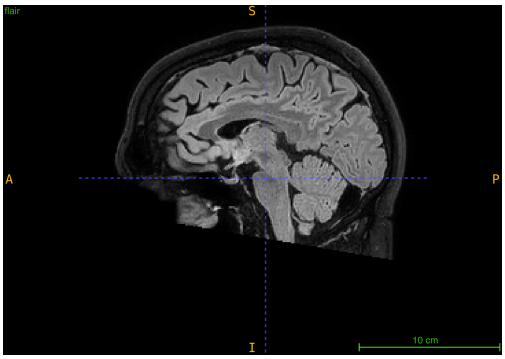

Figure 4.4: Fluid Attenuated Inverse Recovery Sagital

4.3.1 Diffusion Tensor Imaging File

A particular form of MRI, diffusion tensor imaging (DTI) tracks the movement of water molecules in brain tissue and provides vital information on the architectural composition of the white matter of the brain. This imaging method produces a DTI file with data that faithfully depicts the orientation and structural integrity of white matter fibres in the brain. Investigating the connection of the brain depends on these files since they let researchers and doctors to depict and study the neural networks allowing communication across different brain areas.

Since it enables the determination of FA, a basic metric indicating the directional constancy of water diffusion in white matter tracts, dielectric transient imaging is absolutely vital. Figures 4.6 and 4.5 depicts a clearn image of the brain. While reduced FA values suggest possible disturbance or damage in these pathways, elevated FA levels indicate ideal organisation and structural integrity of white matter filaments. DTI's strong character makes it appropriate for the study of many neurological conditions, including multiple sclerosis, traumatic brain damage, and neurodevelopmental disorders including ASD.

In neuroimaging, the importance of DTI files is of unbounded proportions. Crucially for understanding the connections between many brain regions and how these connections may be changed in clinical settings, they provide thorough, numerical data on the white matter integrity of the brain. By means of DTI data processing, researchers can acquire important insight of the basic structures enabling cognitive functioning, motor coordination, and behavioural results. Both the diagnosis of neurological disorders and the formulation of targeted treatments depend on this kind of knowledge.

Moreover, DTI is frequently used in research aimed especially at brain development, ageing processes, and the effects of neurodegenerative diseases. DTI is an essential tool for longitudinal studies since it allows one to track changes in white matter over time, so enabling the detection of early illness markers and the evaluation of therapy effectiveness. Clinically, diagnostic transcranial imaging is being used to drive surgical planning and assess therapy effects on brain connections.

Basically, modern neuroimaging is based on DTI data, which offer unparalleled knowledge of the white matter structure and brain connections. Their ability to expose subtle changes in the microarchitecture of the brain makes them indispensable for both medical intervention and research, so improving our knowledge of brain well-being and pathology.

4.3.2 Bval File

Many images are obtained during DTI with differing degrees of diffusion sensitivity—also known as b-values. The b-values measure MRI scanner sensitivity to water molecule mobility in biological tissue of the brain. Emphasising the anisotropic (direction-dependent) distribution of water molecules along white matter paths depends on a greater b-value, which also denotes increasing sensitivity to diffusion. Conversely, a b-value of zero shows an image devoid of diffusion weighting, sometimes known as a ”b0 image,” and serves as a standard for the other images.

The importance of the bval file is in its capacity to enable the DTI analysis program to precisely interpret the diffusion weighting assigned to every image in the dataset. The program uses the data in the bval file to calculate diffusion tensors, which are subsequently utilised to generate significant metrics such FA and MD as it is processing data. These tests provide important new perspectives on the structural soundness and white matter organisation in brain tissue.

Inaccurate inferences about the microstructural properties of the brain could follow from failure to acquire a precise bval file, therefore compromising the processing of DTIs. Therefore, to get reliable and important diffusion imaging results, it is imperative to precisely allocate the bval file to the suitable DTI dataset.

Essential for the Diffusion Tensor Imaging (DTI) data, the bvec file provides priceless information for exact reconstruction and research of diffusion features in the brain when coupled with the bval file. Data about the direction of the diffusion gradients applied over the acquisition of every image volume in a DTI series is stored in the the.bvec file.

4.3.3 Bvec File

An vital part of the DTI data, the bvec file provides great information for exact reconstruction and research of diffusion characteristics in the brain when coupled with the bval file. The bvec file keeps information on the direction of the diffusion gradients applied over the acquisition of every image volume in a DTI series.

Differential diffusion imaging is a method employed to chart the movement of water molecules within the brain, mainly for the purpose of investigating the alignment and structural soundness of white matter pathways. Directionally dependent (anisotropic) diffusion occurs as water molecules traverse these pathways. The.bvec file records the three-dimensional coordinates in which the gradient directions are represented for each image in the dataset. More precisely, it enumerates the x, y, and z components of the gradient directions, which have been standardised to a length of one unit.

Precise models of the diffusion process in the brain depend on the information found in the.bvec file. The DTI program computes diffusion tensors during data processing phase using the gradient direction information from the bvec file and the diffusion weighting values from the bval file. Mathematical models for the diffusion of water in several directions comprise the tensors. They are used to computed critical measurement values like MD and FA.

Correct application of directional information depends on precision in in-bvec data, which is absolutely essential for brain reconstruction of diffusion channels. Errors in the bvec file can lead to incorrect diffusion data interpretation, hence possibly affecting the architecture and dynamics of white matter tracts.

Thus, the bvec file is vital for DTI analysis since it offers the necessary directional information that helps researchers to explore the white matter architecture of the brain and obtain important knowledge of its microstructural integrity.

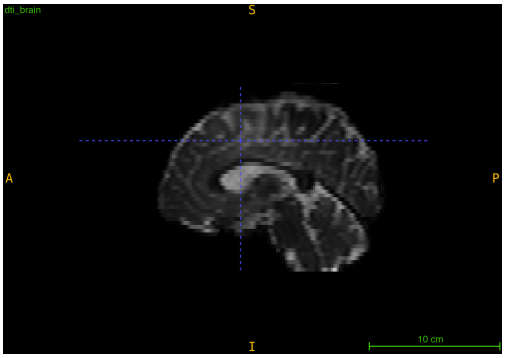

Figure 4.5: DTI Sagital

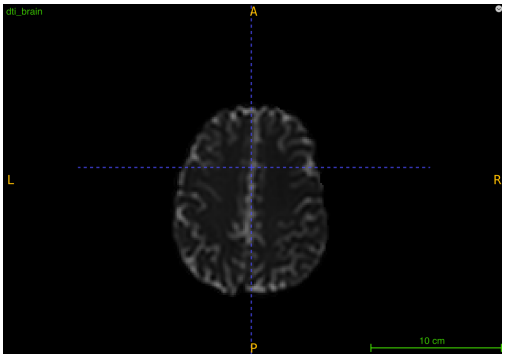

Figure 4.6: DTI Axial.

Figures 4.7 provides some comparative analysis:

- The Resting-State ASD fMRI File records the greatest mean intensity of around 273.79, suggesting that it encompasses a wider spectrum of signal values in comparison to the other imaging modalities. Conversely, the DTI ASD File has the lowest average intensity of approximately 8.91, which can be attributed to its particular emphasis on capturing diffusion measurements, which often yield lower intensity values.

- The standard deviation, a statistical measure of the diversity of intensity values within each file type, is significantly greater in the Resting-State ASD fMRI File, around 581.93. This implies a higher degree of intensity fluctuation, which is inherent in functional imaging because of the dynamic character of brain activity. The FLAIR and Anatomy ASD Files exhibit reduced standard deviations, suggesting a higher degree of consistency in intensity levels, a characteristic commonly observed in structural imaging.

- Maximum Intensity: The maximum intensity values exhibit substantial variation among the files, with the DTI ASD File registering the highest value of 3197. Such a high result suggests the existence of robust diffusion signals, which are essential for evaluating the integrity of white matter. The Resting-State ASD fMRI File exhibits a significant maximum intensity of 3180, therefore underscoring its extensive dynamic range in capturing cerebral activity. Although the maximum intensity of the Anatomy ASD File is lower at 307, it yet offers adequate contrast to accurately depict brain parts.

Figure 4.7: Maximum Intensity Plot

CHAPTER 5

Methodology

5.1 Data Preprocessing

In the framework of understanding neurological and neurodevelopmental disorders like ASD, neuroimaging studies provide vital new perspectives on the structure and operation of the human brain. Still, the quality of the original imaging data and the resilience of the preprocessing techniques followed have a major impact on the precision and dependability of these observations. Since it involves the methodical preparation of raw data for later statistical and computational evaluations, preprocessing is a necessary component of neuroimaging analysis. The technique provides insurance of the accuracy, uniformity, and cleanliness of the images, and hence enables the important comparisons across many patients and groups.

This work demonstrates the creation of a comprehensive preprocessing pipeline to prepare various neuroimaging modalities, such anatomical (T1-weighted), DTI, and fMRI data,for in-depth analysis. This study aimed to evaluate, by means of various modalities, anatomical and functional abnormalities connected to hyperactivity in individuals diagnosed with ASD. The good quality of the data depends on the preparation techniques described in this chapter, which also help to enable consistent performance of later analysis. The steps cover normalisation, motion correction, registration, segmentation, smoothness, skull-stripping, error correction of bias fields. With these methods, the project aims to produce exact and consistent neuroimaging data to provide the foundation for understanding the neurobiological aspects related with hyperactivity in ASD. Figure 5.1 depicts the flow and steps of Data Preprocessing.

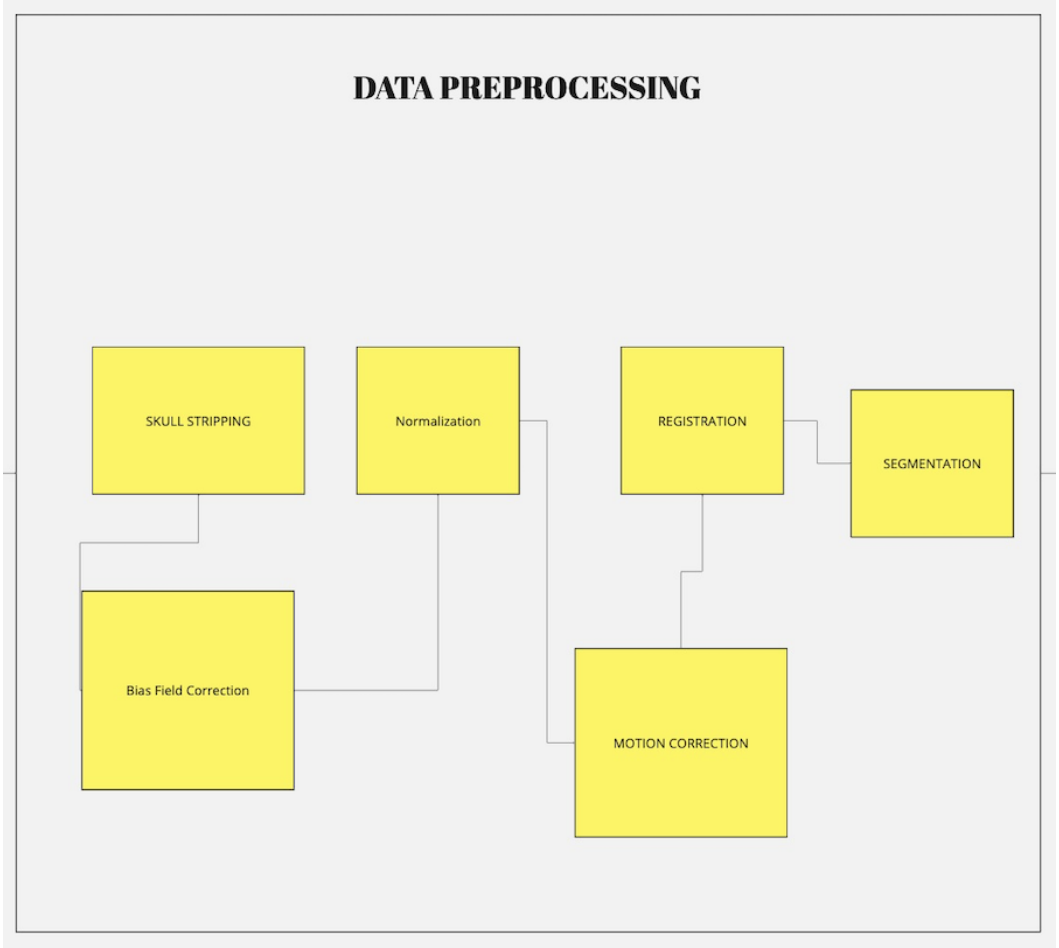

Figure 5.1: Data Preprocessing Flow

5.1.1 Data Acquisition and Initial Inspection

The neuroimaging study starts with the data collecting process, which lays the foundation for all further analysis. In this investigation, data were gathered using numerous neuroimaging modalities including T1-weighted structural MRI, DTI, and resting-state fMRI. The datasets were created from individuals diagnosed with ASD as part of a larger project aiming at exploring the neurological causes of hyperactivity in this particular population.

After acquisition, a first review of the material was conducted to confirm its integrity and suitability for next studies. This stage included assessing the general structure, voxel size, and file formats of the datasets to confirm they matched expected requirements. At this point, possible discrepancies or anomalies including erroneous file sizes or incomplete data were found to prevent errors in further processing phases.

Visual inspections of a subset of MRI slices were used to assess picture quality, therefore ensuring the absence of any notable artefacts, distortions, or missing areas that would compromise the analysis. Basic statistical summaries includes the mean intensity, standard deviation, and intensity which were in range were produced in order to offer a fundamental knowledge of the data distribution over the several modalities.

This first review is crucial since it finds probable issues early on, allowing the data to be corrected or changed before the more complex preparation processes begins. This phase lays the groundwork for

exact and reliable neuroimaging analysis in the next stages of the research by guaranteeing the precision and great quality of the data.

5.1.2 Skull-Stripping

In neuroimaging, skull stripping is the removal from MRI images of non-brain tissues, including the skull, scalp, and other superfluous structures. This stage primarily aims to separate the brain itself so that more exact and focused research of brain anatomy and functioning may be conducted. By means of the elimination of neighbouring tissues, skull stripping reduces the possibility of noise and artefacts that could disturb the analysis, therefore producing more precise measurements of brain areas.

For this research, brain extraction out to subtract non-brain tissues from complicating further investigations including computation of brain tissue volumes, diffusion metrics, and functional connectivity. Analysing measurements such as FA in DTI or assessing brain matter volumes calls for careful thought of the possible impact of non-brain tissues on the outcomes, hence leading to erroneous findings. By means of its exclusive focus on the brain, skull stripping increases the dependability and precision of the neuroimaging data, therefore enabling more exact interpretations and discoveries. There has been thorough debate in the part. 2.2.4

5.1.3 Bias Field Correction

Appropriate bias field correction is a required procedure in the preprocessing of MRI data in order to handle the modulations in intensity which are typically happening during the scanning process. Variations non the magnetic field, scanner gear failures, and the physical characteristics of the tissue under scan are among the various drivers of these inhomogeneities—also known as bias fields.Therefore, the same tissue type may show different intensities over the image, leading to errors in later analysis.

Bias field correction is important because it helps to standardise the intensity values across the MRI image, therefore ensuring that the variances fairly reflect the variations in tissue rather than any distortions resulting from the imaging technique. Without this change, the variations in intensity could lead to inaccurate segmentation of brain tissues, inaccurate assessment of tissue volumes, and false results in studies depending on exact intensity-based measurements, such diffusion dispersion imaging or voxel-based morphometry.

Using bias field correction produces an MRI image with higher homogeneity and dependability marked by constant intensity values over the complete volume.This corrected image also offers a good basis for further research and makes more precise segmentation, better tissue categorisation, and more general dependability of the neuroimaging data conceivable. Reducing the influence of intensity homogeneity helps to correct bias fields, so improving the quality and accuracy of MRI-based studies. This ensures that the results, which rather fairly show the underlying brain architecture, are unaffected by distorted images produced during the imaging process.

5.1.4 Normalisation

In neuroimaging, normalisation is a crucial preprocessing step in which individual brain scans line up with a specified reference space, such Talairach space or the Montreal Neurological Institute (MNI) space. This technique guarantees the direct comparison and interpretation of brain images from different people inside a standardised coordinate system. Normalisation mostly aims to explain anatomical variation across patients so facilitating group-level analysis and comparisons between study.

The need for normalisation results from the natural differences in brain architecture among people including variations in brain size, shape, and structure. Lack of normalisation would greatly complicate the capacity for meaningful comparisons between subjects or across other studies. Normalisation tackles this issue by aligning the pertinent brain areas across participants from individual brain scans, so allowing exact group-level investigations and meta-analyses.

Normalisation generates a collection of brain images arranged deliberately into a defined framework, therefore facilitating consistent and reliable comparisons between people and studies. Several neuroimaging studies, including diffusion tensor imaging, functional MRI studies, and voxel-based morphometry, depend on the consistent alignment. Normalisation of brain areas guarantees comparability among individuals, thereby improving the statistical power of the investigations, raising the accuracy of the findings, and so enabling the generalisability of the results to broader populations.

5.1.5 Motion Correction

Especially in relation to fMRI and diffusion-weighted imaging (DWI), motion correction is an essential need in the compilation of neuroimaging data. These imaging methods show a really high sensitivity for any movement occurring throughout the scanning process. Little movements of the head might lead to significant distortions and aberrations in the images, therefore affecting the brain region alignment over the scanned volumes. Such misalignment can compromise the accuracy of the data, so hindering the obtaining of consistent findings in further research.

The motion correction method adjusts the brain images to reflect any movement experienced during the scan. Usually the first image or a representative image produced from the collective series, this is achieved by arranging every image in the sequence such that it corresponds with a reference image. Sophisticated algorithms are used to identify and correct translations and rotations along the x, y, and z axes thereby maintaining consistent correspondence between each voxel in the image and the same anatomical location in the brain across all times points or volumes.

One cannot emphasise the value of motion correction too often. Without it, the data could be overwhelmed with pointless details and mistakes, leading to maybe misleading conclusions. While in Diffusion Weaving Imaging (DWI), uncorrected motion can distort diffusion measurements, resulting in erroneous assessments of white matter integrity, in fMRI investigations it can provide spurious signals that show as brain activity. Motion correction solves these issues, therefore ensuring that the data exactly reflects the true physiological state of the brain free from the complicated affects of movement.

Following motion correction produces a dataset whereby every image is precisely aligned, therefore facilitating more reliable and accurate analysis. Verifying the legitimacy of any observed changes in brain activity or structure depends on accurate alignment, therefore excluding any distortions brought about by movement. Consequently, motion correction is a necessary stage in the data preparation process since it helps to improve the quality and accuracy of neuroimaging measurements.

5.1.6 Registration

Particularly in studies involving many individuals or integrating data from several imaging technologies, such sMRI, fMRI, and diffusion-weighted imaging (DWI), registration is a crucial step in the preparation of neuroimaging data. The registration process consists on the alignment of photos from many sources or time periods to create a common geographic framework. This alignment ensures exact matching of related anatomical characteristics or region of interest across images, therefore facilitating important comparisons and study.

The need for registration results from the finding that images taken from different subjects or even from individual imaging sessions of the same subject usually show differences in terms of position, orientation, and size. For instance, the brain may show in somewhat various locations or orientations depending on small differences in head position during scanning. Moreover, photos taken from several modalities could have different field-of- view dimensions and resolutions, which makes direct comparisons challenging. The registration method converts the images to match a reference image or a homogeneous template, therefore fixing these discrepancies.

Practically speaking, registration usually consists in several phases. First, a basic alignment—called rigid-body transformation—accounts for rotations and translations. Then, considering scaling, shearing, and complex deformations, more complex alignment techniques like affine or non-linear transformations are used. Establishing good correspondence between pictures can help to preserve spatial consistency

in anatomical or functional data across all images, where each voxel in one image coincides with the corresponding voxel in another.

A successful registration produces a set of photographs aligned inside a shared coordinate system consistently. For group investigations, statistical testing, and the integration of multimodal data—all of which depend on accurate comparisons of individual voxels across many people or imaging modalities—achieving this consistency becomes imperative. Registration guarantees that the same anatomical areas are investigated in all people, therefore improving the dependability and interpretability of the research in a study comparing the integrity of white matter among participants. By ensuring the preservation of spatial correlations both inside and across images, registration is essentially a basic technique that increases the precision and dependability of neuroimaging investigations.

5.1.7 Segmentation

In neuroimaging, segmentation is a necessary technique wherein a picture is split into identifiable pieces or segments, usually corresponding to different anatomical structures or tissue types in the brain. Often the main focus of neuroimaging studies, this technique allows researchers and doctors to segregate and analyse specific brain areas, including grey matter, white matter, and cerebrospinal fluid (CSF), therefore guiding the interpretation of MRI data.

The natural complexity and variation of brain structure lead to the need for segmentation. Unprocessed imaging data can make subtle and challenging differences between the several architectural elements that make up the human brain and have different tissue characteristics. Considering their intensity levels, geographical location, and other relevant properties, segmentation is absolutely essential in the methodical identification and classification of these structures. In studies on neurological diseases especially, this is very important since some brain areas may be more affected than others and proper understanding of disease aetiology and development depends on correct measurement of these areas.

Usually, the segmentation process consists in several steps. Initially, using thresholding or clustering to classify voxels based on their observed intensity levels, the brain is often divided into broad sections including grey matter, white matter, and cerebrospinal fluid (CSF). To improve these categories and assure exact connection between the segmented areas and the anatomical structures of interest, more complex systems could use probabilistic models, atlas-based methods, or machine learning techniques. Segmentation can be extended under some conditions to specify more exact subregions, such separate brain lobes or specific nuclei inside the brainstem.

Segmentation produces a set of labelled images whereby every voxel is assigned to a certain tissue type or anatomical feature. Broad breadth of neuroimaging studies depends on these segmented images. Segmented grey matter images can be used in studies of brain shape to measure cortical thickness or volume, so important indicators of brain development and degradation. Diffusion imaging studies' segmented white matter images help to examine fibre pathways and assess white matter integrity.

5.1.8 Smoothing

In neuroimaging, smoothing is a technique used to decrease noise and enhance the signal in an image by computing the average of voxel values with their neighbouring vokes. Improving the quality of the image and making the data more suitable for next analysis depend on optimising this stage. By use of smoothing techniques, one can efficiently minimise the effect of small defects or random noise resulting from the imaging process, therefore improving the clarity of the representation of the basic brain structures.

In this study, an implementation of a lossless smoothing method was performed to guarantee that the original data integrity was preserved without appreciable loss of information. This method is preferred for handling high-resolution data that demands exact attention to detail since it aims to maintain much of the original signal while concurrently reducing noise. Using a lossless smoothing technique notwithstanding, the results fell short of our first expectations. Still, the smoothed images showed significant noise and artefacts, which degraded the general quality of the data and made it difficult to reach the required degree of clarity for proper analysis.

5.2 Signal to Noise Ratio

SNR is a fundamental metric that gauges the relationship between the background noise and the intended signal, which codes important information. SNR stands for image quality. Comparatively to the noise, a higher SNR denotes a significant signal strength, which produces more precisely clear and easily studied images.

While noise comes from sources like imaging equipment, patient mobility, and physiological aspects such respiration and heartbeat, neuroimaging signals usually reflect the intensity of brain tissues measured in the scan. Since it directly influences the trustworthiness of the data, SNR is absolutely important. Low SNR may hide important structures in the brain, therefore impairing the appropriate identification and analysis of ROIs.

Computing SNR aims to assess the imaging data quality before more research is started. It helps to evaluate whether additional operations, such denoising or re-acquisition of data, are required or if the images are suitable for obtaining important information. Our aim to correctly identify features like white matter hyperintensities and establish consistent comparisons between several brain areas depended on an adequate SNR. Inaccuracies in data analysis and finally affect the conclusions of the research depending on insufficient SNR.Figure 5.2 shows Python use of Signal to Noise Ratio.

```
# Set FSL environment
fsl_dir = os.environ['FSLDIR']
bet_cmd = os.path.join(fsl_dir, 'bin', 'bet')
fslmaths_cmd = os.path.join(fsl_dir, 'bin', 'fslmaths')

# Input file
input_file = 'anat.nii.gz'
output_file = 'brain.nii.gz'
noise_file = 'noise.nii.gz'

# Step 1: Skull-strip the image using BET (Brain Extraction Tool)
subprocess.run([bet_cmd, input_file, output_file, '-f', '0.3', '-g', '0'])

# Step 2: Calculate the mean signal inside the brain
brain_img = nib.load(output_file)
brain_data = brain_img.get_fdata()
mean_signal = np.mean(brain_data[brain_data > 0])  # Only consider non-zero voxels

# Step 3: Estimate the noise by subtracting the brain-extracted image from the original
subprocess.run([fslmaths_cmd, input_file, '-sub', output_file, noise_file])

# Step 4: Calculate the standard deviation of the noise
noise_img = nib.load(noise_file)
noise_data = noise_img.get_fdata()
std_noise = np.std(noise_data[noise_data > 0])  # Only consider non-zero voxels

# Step 5: Calculate SNR
snr = mean_signal / std_noise
print(f'Signal-to-Noise Ratio (SNR): {snr}')
```

Figure 5.2: Code Signal to Noise Ratio

5.3 Mean FA value

One basic metric used in DTI to assess white matter structural integrity and organisation in the brain is FA. FA measures how limited direction's water movement in the brain is. Higher FA values imply the existence of more orderly and consistent fibre routes, which are usually connected to the integrity of white matter.

A low mean FA value suggests that water diffusion in the brain is less homogeneous and more regularly distributed, therefore suggesting the presence of probable disruptions or anomalies in the white matter pathways. Reduced functional connectivity values in the context of ASD could point to decreased neural communication efficiency among different brain areas resulting from changed or damaged white matter structures. This lack of homogeneity can cause imbalances in the brain whereby one hemisphere may have unique structural features in respect to the other. This kind of asymmetry may throw off the balance of brain activity, therefore impairing cognitive functions and actions.

High WMH and low FA values co-occurring give more proof for the idea of changed white matter structure in ASD. Usually indicating areas of abnormal myelination or axonal damage, a high WMH can be a contributing reason to the hyperactive behaviours sometimes seen in persons with autism. Low FA values indicate reduced white matter paths, which can impede the brain's ability to effectively regulate activity, so causing more hyperactivity and related symptoms. This association among low FA values, white matter abnormalities, and hyperactivity emphasises the need of preserving the integrity of white matter in understanding the neurobiological basis of ASD.

5.4 White Matter Hyperintensities

WMH refers to geographic areas inside the brain shown on particular MRI scans—including FLAIR images—that show notable bright spots. These areas point to underlying white-matter abnormalities include demyelination, axonal loss, or other forms of damage to brain tissue. Particularly in the context of ASD, elevated levels of WMH are often linked with cognitive and behavioural problems; hence, they could be related to increased hyperactivity.

Several brain activities depend on particular brain areas such as the Corpus Callosum, SLF, and Cingulate Gyrus; hence, their preservation is essential for appropriate neuronal transmission. The main channel of communication between the two hemispheres in the brain, the Corpus Callosum is the most vast white matter structure there is. Any disturbance in its integrity, as indicated by raised WMH, could lead to reduced communication between the two hemispheres, hence aggravating the hyperactive behaviours often observed in patients with ASD.

Linking the frontal, parietal, occipital, and temporal regions of the brain, the SLF is a necessary white matter channel. The processing of language, executive function, and various other cognitive functions as well as this element is much influenced by it. Increased amounts of WMH in the SLF could interfere with these processes, therefore aggravating behavioural and cognitive disorders like hyperactivity.

The Cingulate Gyrus handles emotional control, attentiveness, and decision-making among other tasks. WHM in this area could be a barrier with these activities, leading to higher emotional reactivity and problems with impulse control and attention span, which are frequent of hyperactivity in ASD.

Furthermore underlined is the importance of these sites by the mathematical depiction of WMH given in subsection 2.2.7, , which addresses the measurement of WMH volumes in these vital regions. The present work attempts to clarify the extent of white matter abnormalities and their likely function in the behavioural problems of ASD, notably hyperactivity.

Figure 6.3 offers a graphic analogy between the patient's and the control values' WMH levels. As shown, the variation is really great.

CHAPTER 6

Results and Discussions

6.1 Initial Analysis

Academic research on ASD depends on neuroimaging since it provides useful information on the anatomical and functional traits of the brain depending on various imaging modalities. Their separate file forms show the different resolutions and dimensions that the several neuroimaging files—DTI, resting-state fMRI, or FLAIR—record of the brain. The file shape mainly shows the voxel distribution in several dimensions, therefore revealing the spatial extent and scan detail.

- Comprising 192 voxels in the first and second dimensions, 48 voxels in the third dimension, and 34 diffusion-weighted volumes, the structure of the DTI file for ASD data is distinctive of (192, 192, 48, 34). Accurate mapping of complex white matter paths depends on a great degree of spatial precision in the first two dimensions, which this form shows. The third dimension, meantime, faithfully shows the slices throughout the brain.

- Geometric arrangement of (64, 64, 50, 120) the relaxation-state fMRI file corresponds to 64 voxels in the first two dimensions, 50 voxels in the third dimension, and 120 time points. Since the fMRI image records brain activity at 120 time points, a fundamental feature for examining functional connectivity in the brain, this shape shows the equilibrium between spatial resolution and temporal sampling.

- Comprising 187 voxels in the first dimension and 256 voxels in each of the second and third dimensions, the FLAIR file showed a geometric configuration of (187, 256). The provided file form highlights the necessity of obtaining a high degree of spatial resolution to detect tiny anomalies in the brain, notably inside the white matter sections.

The given plots graphically show the voxel characteristics and intensity statistics of the neuroimaging data. Figure 6.1 shows the changes in spatial resolution by means of a comparison of the voxel diameters among several imaging technologies. The story shows that the FLAIR files have the lowest voxel size, which matches their great resolution needed for complex anatomical studies. On the other hand, since the resting-state fMRI files give visualisation of temporal fluctuations in brain activity first priority, they have larger voxels.

Showed in Figure are the mean intensity, standard deviation, and intensity range for every type of file. Figure 6.2 helps one to understand the range and spread of intensity values in every modality. Characteristic of diffusion imaging that stresses changes in microstructure, the DTI file shows a tendency towards lower average intensity but more variability. Moreover, the resting-state fMRI file shows substantially higher average intensity, which matches the blood-oxygen-level-dependent (BOLD) signal used for brain activity monitoring. Characterised by low average intensity and limited range, the FLAIR file has shown success in spotting lesions or aberrant areas in the white matter of the brain.

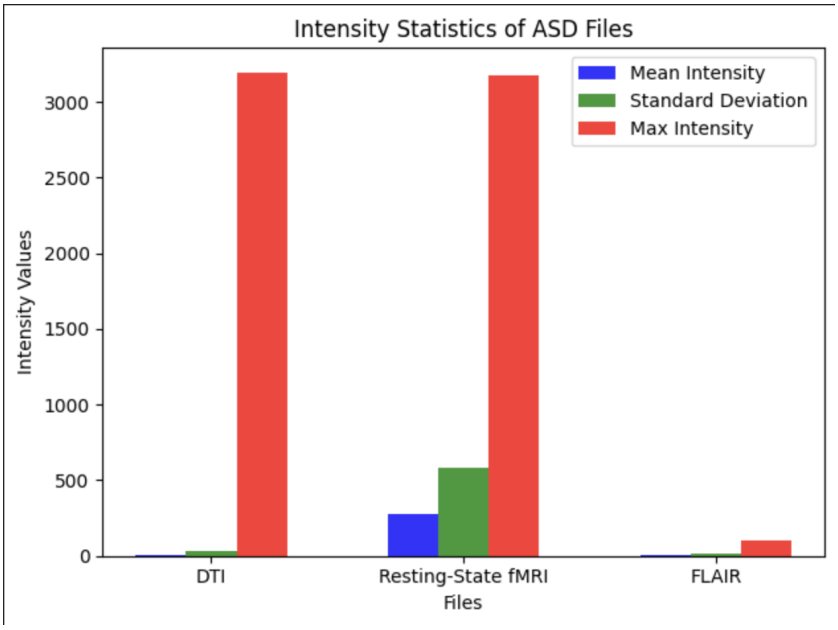

Figure 6.1: ASD Files Intesity Comparison

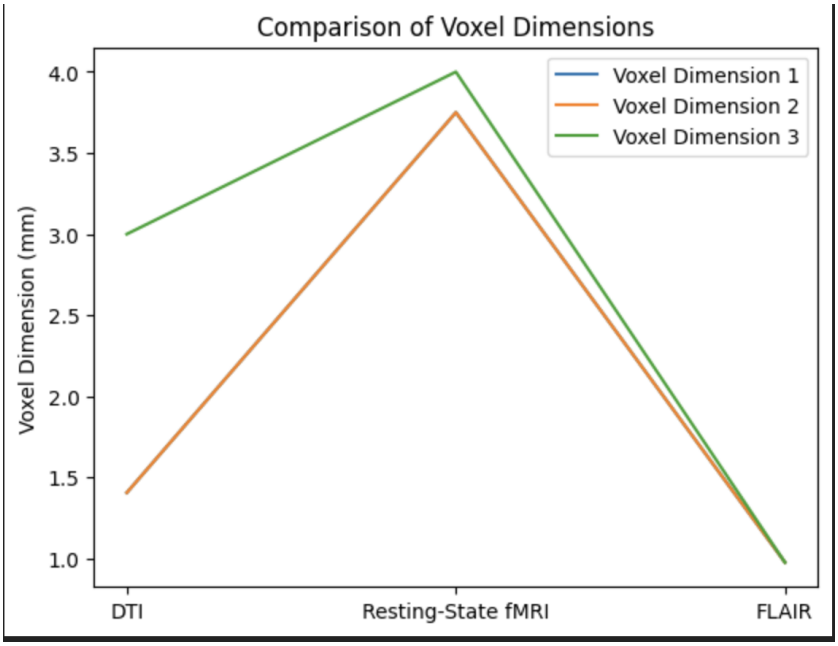

Figure 6.2: Voxel Comparison

6.2 Signal to Noise Ratio

In neuroimaging, the SNR is a key statistic that measures the purity of the intended signal in respect to the noise in the acquired data. Greater SNR suggests that more easily differentiated from random noise the brain structures or activities of interest can provide cleaner and more intelligible images. On the other hand, a low SNR can hide important data, therefore reducing the accuracy of interpretation and analysis.

The aim of this work was to attain an SNR of 10–11 since, especially in studies on minor brain diseases or functional activities, this range is often considered sufficient for reliable neuroimaging analysis. The SNR of the datasets was found to be substantially below the target level in first assessments. More precisely, values of SNR between 1 and 2 were found, which quite fell short of the allowed threshold.

The discovery of quite low SNR offered major challenges for the research. The images were found to be much influenced by noise with SNR values within this range, which hampered the ability to differentiate real brain structures from anomalies resulting from many sources, including scanner hardware constraints, patient motion, or physiological parameters like respiration and heartbeat. Such large noise substantially affected the integrity and trustworthiness of the data, therefore undermining the correctness of subsequent research.

Denoising methods were applied to try to raise the image quality, therefore addressing this problem. By means of sophisticated filtering and smoothing methods, noise was lowered while maintaining the integrity of the fundamental brain signals.. While the SNR was raised to about 8, this number still fell short of the intended range of 10–11. It fell short of the ideal level needed for exact and thorough study even with the improvement of picture quality.

With the low SNR in the data, it became essential to focus on certain neuroimaging methods that would provide more consistent images under these challenging conditions. Due mostly to their inherent capacity to produce clearer images, the choice of DTI and FLAIR sequences for next analysis was predicated on their better appropriateness for the study objectives.

6.3 Analysis of Mean Fractional Anisotropy Values

An important metric in DTI, FA measures the degree of water diffusion in a given direction inside brain tissues—that is, in white matter pathways. High FA values usually indicate well-structured and strong white matter, distinguished by the predominate diffusion of water molecules along the fibre tracts. On the other hand, extremely low FA levels point to a decline in the structural integrity of white matter, which is usually related with various neurological diseases such autism and hyperactivity.

The average FA values indicated in Table 6.1 were found to be below the expected levels in several ROIs inside the brain according to the present study. FA values are going down very noticeably in parts of the brain that are involved with thinking and moving, like the Prefrontal Cortex, the SLF, and the Cingulate Cortex. Lower FA values mean that the anisotropy of water diffusion is lower, which means that the white matter in these areas is less organised or structurally stable.

The low average FA values shown in the table suggest an observed decrease in white matter integrity, which is significant considering its consequences for possible abnormalities in the neuronal paths necessary for efficient brain communication. Within the setting of autism, these abnormalities could show up as hyperactivity, a common behavioural trait associated with the disorder. People with autism may have changes or deficits in their white matter tracts that are linked to hyperactivity. This makes it harder for the brain to control motor actions and cognitive processes.

The results of the FA study, shown in Table 6.1, back up the idea that differences in the structure of the white matter are linked to the hyperactive behaviours seen in people with autism. Thus, the low average FA values function as a major indicator of the basic neurobiological mechanisms causing these behaviours. This highlights the need of targeted treatments aiming especially at the preservation of white matter in order to regulate hyperactivity in autism.

Table 6.1: Mean and Median FA Values in Different Brain Regions

Brain Region	**Mean FA Value**	**Median FA Value**
Prefrontal Cortex	0.3208	0.2708
Superior Longitudinal Fasciculus (SLF)	0.2098	0.1831
Cingulate Cortex	0.2465	0.1865

6.4 Results and Discussion of White Matter Hyperintensities

Studying WMH was essential for this investigation since it helped one to grasp the structural brain abnormalities linked to ASD and their likely relationship with hyperactivity. Still, the original WMH data caused difficulties because of differences in voxel sizes throughout the imaging datasets, which demanded a resampling method. Resampling was required to ensure that the images matched a consistent spatial resolution, therefore allowing exact comparison and study of WMH volumes in different brain regions.

The resampling process normalised the voxel size, therefore guaranteeing consistency in the data and enabling precise measurement of white matter WMH at the selected ROIs. The results of resampling clearly indicated much higher volumes of WMH in the group with SD than the control group. Referring from Table, the above described findings were particularly notable in important brain areas such the Corpus Callosum, SLF, and the Cingulate and can be found from Table 6.2

Table 6.2: White Matter Hyperintensities (WMH) Volumes in Selected Brain Regions

Brain Region	**WMH Volume (mm^3)**
Cingulum (Cingulate Gyrus)	82,225.94
Corpus Callosum	110,041.30
Superior Longitudinal Fasciculus	42,130.72

The elevated quantities of white matter, as depicted in Figure 6.3 in these areas suggest more significant dysregulation of white matter in those with ASD, which could perhaps contribute to the observed hyperactive behaviours. An important function of the Corpus Callosum is to facilitate interhemispheric communication. Any disturbance in its integrity may result in compromised coordination and heightened motor activity. Likewise, the SLF and cingulate cortex have a role in cognitive processes and emotional control, and any anomalies in these areas may worsen the difficulties experienced by persons with ASD.

To guarantee precise measurement and comparison of the WMH volumes, it was imperative to resample the imaging data. The findings emphasise the significance of white matter integrity in comprehending the neurobiological foundations of hyperactivity in autism, emphasising the necessity for additional study and focused interventions to tackle these structural anomalies.

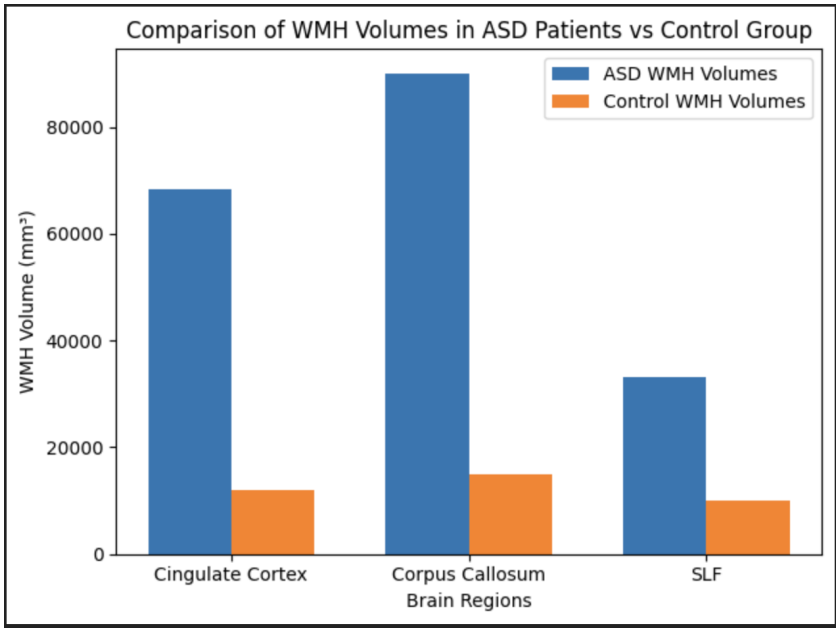

Figure 6.3: WMH Control Value Comparison

6.5 Asymmetry Index

In neuroimaging, the asymmetry index is a fundamental metric that gauges the different anatomic or functional changes between the two cerebral hemispheres. The computation provides a quantitative evaluation of lateralisation in brain anatomy or cognitive performance by means of a comparison of the sizes or intensities of the pertinent areas in the left and right hemispheres. Using the asymmetry index, the present investigation assessed the degree of asymmetry in white matter tracts connected to hyperactivity and ASD.

Table 6.3's asymmetry index values show clearly a lateralisation in the white matter areas under examination. With an asymmetry score of 5.7101 the Corpus Callosum shows a small over-representation in one hemisphere. By contrast, the SLF has a noticeably greater negative asymmetry score of -39.3162, implying a rather different volume across the hemispheres. This large disparity in the suprachiasmatic nucleus suggests a break in the normal equilibrium of brain activity, which could be a component in the behavioural traits observed in ASD including hyperactivity.

The observed increased asymmetry index in these regions can be explained by the increased volume of WMH found in ASD diagnosis candidates. The unequal spread of this increase in WMH volume over the brain, with a higher concentration in one hemisphere, produces the observed asymmetry. Using the asymmetry index turned out to be quite helpful in verifying the results of the analysis of WMH. By identifying whether the structural abnormalities found by WMH analysis are largely restricted to one hemisphere by lateralisation, the asymmetry index offers further more evidence for the structural abnormalities.

Clearly, the findings of the asymmetry index confirm and enhance the conclusions reached from the analysis of the WMH, therefore providing a more complete knowledge of the neurological mechanisms causing hyperactivity in autism. The unequal distribution of white matter volume complicates brain function and plays a part in the noted differences in behaviour among individuals with ASD.

Table 6.3: Asymmetry Index for Corpus Callosum and SLF

Region	**Asymmetry Index**
Corpus Callosum	5.7101
SLF	-39.3162

6.6 Project Management

Comprising Research Proposal, Project Demonstration, and Report Writing, the Gantt chart displayed in Figure 6.4 presents a thorough chronology of the primary project stages. With 100 percent of the activities completed, the visual shows that the phase on the Research Proposal is moving towards completion. As seen in Figure 6.4, the phase known as Project Demonstration—which consists of Finalising Dataset, Project ETL, Project EDA, Building Machine Learning, and Presentation Making—has come to its end. Now under development is the phase of report writing, which includes finishing Project Code and writing and submission of the report. While Report Writing and Submission is at 100 percent, current development in Project Code Finalisation sits at 100 percent, implying significant progress but with some chores still to be done. The black bars on the chart show a clear relationship between the expected schedule and the real development from June 24 to September 24. With most of the jobs either completed or in last stages of completion, the shown chart strongly shows that the project is moving as expected.

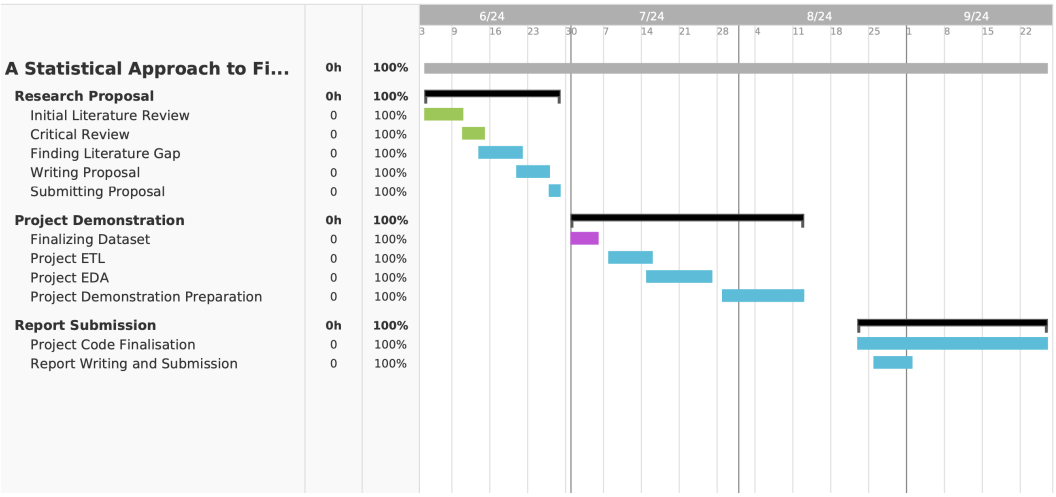

Figure 6.4: Project Management Gantt Chart

CHAPTER 7

Conclusion and Future Work

7.1 Research Contribution

This work has successfully satisfied the objectives stated in the section 1.4 by means of a rigorous analysis and a comprehensive methodological implementation. The study effectively used modern neuroimaging techniques to uncover and investigate white matter abnormalities in persons with ASD, producing important results in line with the main goals of the project.

- The motivation of this study was to use modern MRI techniques, especially DTI, to find and observe white matter abnormalities in brain areas linked to hyperactivity in people with ASD. The study focused on certain areas to check health of white matter tracts, which are important for understanding the features in anatomy that can cause hyperactive behaviours in people with ASD.This study uses MRI-based tests, such as FA and MD, to look into the connection between brain connectivity and hyperactive actions in people with ASD.The experiment's goal was to find the FA and MD values in order to check the microstructural integrity and connectivity of brain areas linked to hyperactivity.Using FA and MD analysis, the experiment gave us useful information about how hyperactive behaviours might be linked to problems in white matter connections in people who have been identified with ASD.

- Suggest a more practical and easily understandable replacement for traditional diagnostic interviews, therefore creating a simplified and less emotionally taxing diagnosis for hyperactivity linked to autism:By giving neuroimaging-based metrics first priority and emphasising quantifiable brain anomalies, the project aimed to improve the creation of diagnostic tools that lower reliance on intensive behavioural interviews. Objective, data-driven neuroimaging techniques could help to make diagnosis processes for hyperactivity in ASD patients more easily available and less demanding.

- Understanding the brain mechanisms underlying hyperactivity in people with autism could be essential for developing strategies for early detection and intervention, therefore improving the outcomes of therapy.The findings of this study help to clarify the neurological mechanisms behind hyperactivity in ASD, notably the participation of white matter anomalies. The initiative creates a basis for the creation of targeted early identification and intervention strategies by identifying special brain areas where white matter integrity is compromised, therefore improving the efficacy of treatment for persons with ASD.

7.2 Limitations and Challenges

During this research, many constraints and obstacles were met that altered the extent of the study. The time limit presented a major challenge since it prevented a more exhaustive study. Although a lot of research has been done on how the brain causes restlessness in ASD, the study was unable to investigate

some other crucial domains. Particularly, little research was done on the relationship between autism and restlessness that worsens with ageing. Investigating how gender might influence how these diseases show up and their degree of severity is another area that can profit from greater study. These factors are important for learning more about ASD and hyperactivity, especially because they can change how they are diagnosed, treated, and the effects that last over time.

Another big problem was that they couldn't make a dataset full of features that were especially made for machine learning analysis. Learning how to use computers to find complex patterns in huge amounts of data has the ability to greatly improve the diagnosis and treatment of neurodevelopmental disorders like ASD. Despite this, the time and scope constraints of this study made it impossible to create and explore such a collection. The unrealised potential of this study lies in the ability to use machine learning to predict outcomes or find new signs of hyperactivity in autism.

The present work encountered some difficulties largely related to the low processing capability, which made machine learning techniques more difficult to apply. Though there could be advantages, the performance constraints of the systems applied in this study made it impossible to effectively implement machine learning techniques. More research is needed to produce stronger computational tools and approaches to solve these problems so that machine learning may be fully utilised while processing complicated neuroimaging data.

Therefore, even though this study made great strides in clarifying hyperactivity in persons with ASD, it also highlighted significant areas requiring more investigation. To better understand ASD and treat individuals with autism, it nust first go past these challenges and limitations.

7.3 Future Work

This research lays a strong foundation for looking at the neurological cause of hyperactivity in ASD, so supporting the claim that ***"20-80 percent autistic person are hyperactive"***. The findings of this project not only validate the correctness of this idea but also provide various chances for more research that can build on the current work and solve some of the faced limitations.

Examining the interaction between hyperactivity and ASD in different age groups is a quite feasible subject of study for next years. Although the current study mostly focused on a certain age group, understanding the evolution of these behaviours over an individual's lifetime will help much to explain the developmental path of hyperactivity related to ASD. Longitudinal studies tracking people from childhood to adulthood would be quite helpful in determining important intervention timing and understanding the temporal development of hyperactivity in autism.

An important area for more research is the examination of gender differences in the expression of hyperactivity among ASD diagnosed individuals. While this study presented a broad viewpoint, doing analysis especially targeted on gender could reveal unusual phenomena now not regularly examined. This knowledge is crucial for the development of more tailored diagnostic criteria and treatments since men and women often show different traits in different neurodevelopmental illnesses.

Future studies should focus especially on building a large feature dataset for machine learning. using the advancement in computer capabilities and data analysis techniques, machine learning has great promise to be used for the identification of complex patterns in neuroimaging data that might not be obvious using traditional analytic methods. Creating a complete dataset comprising brain connection measurements, behavioural data, and perhaps genetic information would help machine learning to be more useful in precisely forecasting hyperactivity in ASD and in developing customised treatment plans.

Moreover, future research would gain from extending the spectrum of neuroimaging methods used. While this study focused primarily on FA and MD, using additional imaging modalities such as fMRI or magnetoencephalography (MEG) could give a more comprehensive approach to studying brain activity in people with ASD. These approaches could assist examine the relationship between hyperactivity and functional brain networks, as well as abnormalities in these networks in autism.

In the end, this study shows how important it is for people from different fields to work together to learn more about ASD and restlessness. Neuroscience, psychology, data science, and clinical practice should all be used in future studies to try to make diagnostic tools and treatments work better. Future research will build on this study's strong base to confirm and strengthen the idea that a lot of autistic people also have hyperactive tendencies, which will lead to better outcomes for people with these conditions.

CHAPTER 8

Gitlab

A GitLab account has been created, and the project can be accessed using the following link: Gitlab Link

- A Python notebook file for main preprocessing and statistics.
- A bash file for structural processing.
- A detailed Python notebook file where White Matter Hyperintensities (WMH) have been performed over 12 patients.

The files can be run using Good CPU core strength and a good GPU will make the code run faster.

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