Neural Correlates of ADHD and Treatment

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Abstract

Attention-Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by continuous patterns of inattention, hyperactivity, and impulsivity. This study aims to explore the neural correlates associated with ADHD, environmental and genetic factors that might play into the disorder, and investigate the efficacy of current treatment methods. Furthermore, this research sheds light on personalized treatment approaches and discusses the importance of tailoring interventions based on individual neural profiles using cutting-edge technologies which would help the development of novel therapeutic strategies. This research seeks to create a bridge between neuroscientific data and behavioral assessment tools to advance our comprehension of ADHD and ultimately improve the quality of life for individuals affected by ADHD.

1 Introduction

In the last 20 years, attention-deficit/hyperactivity disorder (ADHD) has become a popular topic of scientific research, spurred by its significant prevalence and its complex structure as it involves neurological, psychological, and environmental factors. ADHD is one of the most common neurobehavioral disorders with an onset age of as early as 3 years old and often lasts into adulthood (Mayo Foundation for Medical Education and Research, 2019). ADHD presents itself through consistent patterns of inattention and/or hyperactivity-impulsivity. The disorder has three subtypes: Predominantly inattentive presentation (e.g. defects in sensory processing, poorly focused attention, etc.), predominantly hyperactive-impulsive presentation (e.g. non-stop talking, trouble sitting still and doing quiet tasks, etc.), and combined presentation [Mag23].To be diagnosed with ADHD, symptoms must have been present in two or more contexts for at least six months before the age of 12, and the individual must have decreased or impaired social, intellectual, or occupational functioning. Adults and adolescents aged 17 and older should exhibit five symptoms from each category, and it is recommended to use established assessment tools for adults [Dre20].According

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to the 2016 National Survey of Children's Health (NSCH) - 5.4 million children in the U.S. between the ages of 2-17 suffer from ADHD of which 62 percent received pharmacological treatment, 46.7 percent received behavioral therapy, and 23 percent received no treatment [Dan16].In addition, it was found that boys(13%) are more likely to be diagnosed with ADHD than girls (6%), and black, non-Hispanic children and white, non-Hispanic children are more often diagnosed with ADHD (12% and 10%, respectively), than Hispanic children (8%) or Asian, non-Hispanic children (3%) (Centers for Disease Control and Prevention, 2022).These statistics emphasize the need for continued efforts to ensure equitable access to diagnosis and treatment for all children, while also encouraging a diverse and personalized approach to ADHD management. The exact percentage of individuals with ADHD who do not receive a formal diagnosis can vary depending on factors such as geographic location, access to healthcare, awareness, and cultural differences. The findings suggest that a significant portion of individuals with ADHD may go undiagnosed. In [Gin14] Gingsberg and his colleagues highlighted the underdiagnosis of ADHD in adults.They found that approximately 2.5% to 5% of adults in the general population were affected by ADHD. Interestingly, when they looked at adult psychiatric patients attending clinics for other conditions, a much higher percentage, ranging from 17% to 22%, were also suffering from ADHD. An important point to note is that ADHD in childhood has a strong association with another disorder known as oppositional defiant disorder. This condition is characterized by negative, hostile, and defiant behaviors, often directed towards authority figures. The implications of this association are significant. It has been observed that individuals with a history of ADHD in childhood are at an increased risk of developing oppositional defiant disorder. Moreover, this pattern of behavior can persist into adulthood. A substantial proportion of imprisoned men, approximately 40%, have been found to have both ADHD and oppositional defiant disorder. This suggests that when these two conditions co-occur, they may contribute to difficulties in behavioral and social functioning, potentially affecting various aspects of a person's life, including their legal and interpersonal relationships. It is also known that ADHD is a disorder with high comorbidity such that patients often also experience autism spectrum disorder (ASD), learning disorders, tic disorders, and internalizing and externalizing disorders [Gna19].These findings and the intriguing structure of the disorder captivated researchers' attention from various fields, investigating the underlying neurological and cognitive mechanisms along with treatment methods to understand the ADHD brain better. Therefore, this paper will dive into a comprehensive exploration of current knowledge surrounding ADHD, combining insights from different research papers to provide an understanding of the key neurobiological mechanisms underlying ADHD and treatment methods. First, the paper will discuss the neuroanatomy and functions associated with ADHD. Then, it will examine brain differences as well as genetic and environmental factors that play into the disorder. At last, the article will shed further light on current treatment methods, their limitations, and future directions. This topic is crucial to address regarding the disorder's prevalence and symptoms because it affects millions of people's academic, pro-

fessional, and personal lives. Ultimately this paper will demonstrate that by investigating the neural underpinnings of ADHD and creating a neurophysiological model, it is possible to foster the development of more targeted strategies for assessment, treatment, and support.

2 Neural Anatomy and Function in ADHD

2.1 Prefrontal Cortex Dysfunction: Impaired Executive Functions

Executive Functions are neurocognitive processes that are critical for guiding and regulating attention, affect, and action. Because EFs are believed to link underlying genetic, neural, or environmental mechanisms to behavioral actions of psychopathology and to predict present and future functional impairment, such as quality of life and educational attainment, there is great interest in the EF profiles of ADHD [Tow23]. One of the EF problems that are present in almost every ADHD case is impairment in response inhibition - an inability to inhibit inappropriate thoughts and actions [Mia17]. Multiple studies showed that inhibitory problems are one of the main neurophysiological effects of ADHD [DSAJ23]; [Ble10]; [Zhe22]. Other studies suggested dysfunctions in working memory, planning, cognitive flexibility, attention, processing speed, and visuospatial abilities ([A.97]; [CA13]; [CF16].Given that EFs are supported mainly by the prefrontal cortex(PFC), research points to a possible dysfunction in the regions of the PFC.

2.2 Striatal Abnormalities in ADHD: Dopaminergic System Dysfunction

The striatum comprises a collection of linked nuclei within the basal ganglia, contributing to various functions related to decision-making. These include tasks like regulating motor control, processing emotions, shaping habits, and processing rewards [Bam19].Malfunction in this striatal area is believed to play a part in ADHD, as the behavioral traits that define ADHD align with the behaviors regulated by these networks [Old16].In the research of [D.10a] it is seen that dopamine is released from the dorsal striatum during emotional processing, and increased regional cerebral blood flow in these areas during the processing of self-generated negative emotion of sadness and transiently elicited sadness was observed. The malfunction of the dopaminergic system within the brain has been linked to numerous neuropsychological disorders, including Parkinson's disease, Tourette's syndrome, ADHD, addiction, and schizophrenia. In the context of ADHD, the dopamine (DA) hypothesis suggests that DA systems play a vital role in motor functions, motivation, and reward processes, which exhibit anomalies in individuals with ADHD [Wu12]. Moreover, [Swa07] noted that the caudate nucleus and globus pallidus which both contain a high density of DA receptors are smaller in the ADHD than in the control groups. In

addition, norepinephrine, which is synthesized from dopamine, as a neurotransmitter increases alertness and attention, it affects the sleep-wake cycle, mood, and memory. When norepinephrine levels are low health conditions like anxiety, depression, ADHD, etc. might occur (Cleveland Clinic, 2022).

2.3 Frontostriatal Network Dysfunction

The striatum and PFC are fundamental components of the neural network that governs various cognitive and motor functions. On their own, the striatum, located deep within the brain, is essential for tasks involving reward processing, habit formation, and motor control. Meanwhile, the PFC, often referred to as the brain's executive center, is responsible for higher-order thinking, decision-making, and goal-directed behaviors. However, it's the connectivity between these two regions that truly underscores their importance. The frontostriatal network enables seamless coordination between the emotional and executive aspects of our brain, allowing us to make adaptive choices, learn from experiences, and execute complex actions. This intricate interplay between the striatal and PFC regions highlights the dynamic nature of neural networks and their pivotal role in shaping our behavior and cognition [Lev21]. Recently it was stated that poor inhibitory function, dyspraxia, and spatial working memory of the central nervous system are associated with insufficient dopamine and norepinephrine secretion caused by dysfunction in the frontostriatal networks [Cha22]. Also, the frontostriatal network appears to be underactive in ADHD in most studies [Vai08]. Particularly, the dysfunction observed in ADHD often points to the impairment of frontostriatal and frontoparietal networks, which play a role in top-down or executive functions. These functions involve areas like the dorsolateral prefrontal cortices, anterior cingulate cortices, and interconnected striatal regions, all of which are frequently mentioned in relation to ADHD-related issues [Dic06].

3 Brain Differences in ADHD

3.1 Structural Brain Differences: Grey and White Matter Alterations

Structural connectivity responds to the anatomical links or white matter pathways connecting distinct brain regions [Som23]. Disruptions in functional and structural connectivity can result in impairment across a range of cognitive functions and increase the risk for neurodevelopmental disorders such as ADHD [Par23]. Grey matter is a tissue in the brain and the spinal cord that plays a crucial role in everyday functioning, like memory, emotions, and movement (Cleveland Clinic, 2023). White matter is the tissue that lies beneath the grey matter, in the subcortical regions and connects neurons from different brain regions to make them function as a circuit [D.10b]. A systematic review detected significant changes, primarily decreased fractional anisotropy in individ-

uals with ADHD, affecting the frontostriatal pathways, cingulum, and corpus callosum [Par23]. Fractional anisotropy (FA) is a measure that quantifies the directionality or anisotropy of water diffusion within the brain's white matter tracts, in regions with well-organized and intact white matter, such as in neural pathways, the diffusion of water molecules tends to be more directional or anisotropic. Therefore, a reduction in FA values can be indicative of damage or alterations in the white matter structure. Another study by [Ros23] stated that children diagnosed with ADHD exhibited diminished fractional anisotropy (FA) within pathways that connect the orbitofrontal cortex (OFC) to the ventral striatum, irrespective of gender. However, lowered FA in the tracts connecting the OFC to the amygdala, as well as the ventral anterior cingulate cortex (ACC) to the amygdala, were specifically observed in boys with ADHD. These findings suggest that ADHD patients have reduced white matter, especially in the striatal and frontostriatal regions, with some gender differences in connectivity between different areas, which likely play a critical role in cognitive dysfunctions seen in ADHD.

3.2 Functional Brain Differences

3.2.1 Default Mode Network Alterations

Functional connectivity (FC) refers to the statistical correlation or relationship between the time series of blood oxygenation level-dependent (BOLD) signals recorded from two distinct brain regions, sometimes in the context of a specific cognitive task. The default mode network (DMN) is a distinct set of brain regions that are primarily active when an individual is at rest or engaged in spontaneous, self-referential thoughts. It includes regions like the posterior cingulate cortex, the medial prefrontal cortex, the angular gyrus, and parts of the parietal lobe [Sem21]. It is theorized that dysfunction within the default mode network (DMN) contributes to attentional interference and fluctuations in response consistency among individuals with ADHD, as suggested by [SB07]. A possible explanation for the reduced connectivity within the DMN observed in individuals with ADHD during rest is that this network appears to have difficulty adjusting or "turning down" its activity when transitioning to a task-focused mental state. In simpler terms, when people with ADHD are not actively engaged in a specific task and are at rest, their DMN might remain overly active, which can make it challenging for them to switch to a more focused and goal-oriented state of mind when needed. This altered connectivity within the DMN may contribute to difficulties in attention regulation and cognitive control that are commonly associated with ADHD [rou22]. Additionally, when comparing adult patients with persistent ADHD to healthy individuals, several noteworthy differences were observed. Specifically, there was a decrease in functional connectivity within the default mode network (DMN), and the connection between the dorsal anterior cingulate and the DMN showed less typical behavior and coherence. Furthermore, the relationship between the dorsolateral prefrontal cortex and the DMN appeared to be notably stronger in these

individuals [Mos16].

3.2.2 Task-Positive Network Alterations

In terms of anatomy, the task-positive network is composed of various regions, including but not limited to the dorsolateral prefrontal cortex (dLPFC), the dorsal anterior cingulate cortex (dACC), cortical regions along the intraparietal sulcus (IPS), and the middle temporal area (MT) [Nai13]. The task-positive network (TPN), also known as the central executive network (CEN) or the frontoparietal network (FPN), is a functional brain network that becomes active when an individual is engaged in goal-directed cognitive tasks or activities that require focused attention, problem-solving, decision-making, and working memory. Key features of the task-positive network include increased activation in areas of the prefrontal cortex, particularly the dorsolateral prefrontal cortex, as well as the parietal cortex and other brain regions associated with executive functions. These regions work together to support concentration and cognitive control during tasks that demand mental effort [Bro17]. A study builds upon an emerging collection of research that proposes the negative functional connectivity within this system as a focal point of dysfunction in ADHD, indicating a developmental delay in the disorder. Additionally, it illustrates that irrespective of group status, these networks exhibit negative connectivity in females. Moreover, the study suggests that the malfunction of this system might be linked to attentional deficits present in childhood ADHD [Mil18].

4 Genetic and Environmental Factors

4.1 Genetic predisposition of ADHD

According to the results of family and twin studies, the heritability of ADHD is approximately 80%, indicating a substantial genetic element in the disorder's underlying causes. Nonetheless, the specific genetic impacts on the risk of the condition, the severity of symptoms, and its persistence remain uncertain [Bal22]. In 2018, [Far22] stated in their paper that a study involving 894 individuals diagnosed with ADHD (referred to as "ADHD probands") and 1135 of their siblings aged 5–17 years old revealed a significant ninefold increase in the risk of ADHD among siblings of ADHD probands compared to siblings of controls. They also demonstrated that findings from adoption studies indicate that the factors contributing to the familial occurrence of ADHD are primarily genetic rather than shared environmental influences. In fact, a recent adoption study demonstrated higher rates of ADHD in biological relatives of non-adopted children with ADHD than in adoptive relatives of adopted children with ADHD. Interestingly, adoptive relatives exhibited a similar risk for ADHD as relatives of control children [Spr00].

4.2 Gene-Environment Interactions

A pathway to comprehend the complex interactions between genetic and environmental factors in ADHD is the concept of gene-environment interactions. This concept emphasizes that the significance of genetic influences might be contingent on specific environmental factors. Research has shown that environmental exposures have the capacity to influence gene expression through mechanisms like epigenetics, particularly relevant in psychiatric disorders. Detecting and understanding gene-environment interaction effects holds significance as it contributes to advancing our comprehension of the genetic and clinical diversity of ADHD symptoms as they evolve [Li21]. In an investigation, Wong and colleagues conducted an analysis of DNA methylation within the promoter regions of three specific genes: DRD4, the serotonin transporter gene (SLC6A4/SERT), and the MAO-A gene. Their research involved the examination of DNA samples obtained from 46 pairs of monozygotic twins and 45 pairs of dizygotic twins, resulting in a total sample size of 182 participants aged between 5 and 10 years. The study findings provided compelling evidence that differences in DNA methylation can be observed early in childhood, even among individuals who share identical genetic makeup, and these differences in methylation levels do not remain consistent over time. Overall, Wong and colleagues' research contributes to our understanding of how gene-environment interplay may manifest in ADHD. It suggests that epigenetic modifications, such as DNA methylation, are sensitive to environmental influences, which can impact the expression of genes associated with ADHD. This underscores the need for a holistic approach to understanding and addressing ADHD, considering both genetic predispositions and environmental factors in diagnosis, treatment, and prevention strategies. While this study presented the epigenetic side of the disorder, other studies demonstrated the importance of environmental factors such as exposure to alcohol and substances, maternal smoking, and low birth weight, etc ([Ban07]; [Kia22]).

4.3 Prenatal and Early Life Factors

4.3.1 Maternal smoking and substance use

Epidemiological investigations have highlighted numerous environmental factors that contribute to the context of ADHD. These include maternal substance use, stress, exposure to environmental toxins during the prenatal or perinatal phase, and low birth weight. Similarly, the risk of developing ADHD is heightened in instances of preterm birth, the presence of psychosocial challenges during early childhood, or suboptimal nutritional conditions [Bal22]. ([Zhu14]) saw in their research that both maternal and paternal smoking during pregnancy was linked to an increased risk of ADHD as determined by hospital diagnoses, medication, and hyperactivity/inattention scores. However, this association was notably stronger for maternal smoking compared to paternal smoking. In cases where mothers smoked but fathers did not, children faced a heightened risk of ADHD compared to those born to non-smoking mothers and smoking fathers.

Additionally, it observed that children born to mothers who utilized nicotine replacement during pregnancy had an elevated risk of ADHD. Another research also revealed that maternal smoking increased the risk of ADHD in offspring, indicating a positive correlation between maternal smoking during pregnancy and ADHD in children [Hua18].Nonetheless, findings strongly suggest that maternal smoking and substance use affect ADHD.

4.3.2 Premature Birth and Low Birth Weight

[Hat14] reported that several studies showed a relationship between low birth weight and ADHD, children who were born underweight were 3.8 times more likely to meet the diagnostic criteria for ADHD. A twin-pair analysis showed that a distinct connection exists between low birth weight and ADHD symptoms, maintaining its significance even after accounting for shared environmental and genetic variables among twin pairs. These results indicate that restricted fetal growth, as observed in the variations of birth weight among twin pairs, along with the potential influence of associated environmental factors, contributes to the causal pathway that leads to ADHD [Pet15]. All findings suggest that genetics and environmental factors greatly impact the prevalence of ADHD.

5 Treatment Implications

5.1 Medication Based: Stimulant and Non-stimulant Medications

Pharmacological intervention remains the primary approach to treating ADHD in the majority of clinical settings. Approximately 90% of children diagnosed with ADHD ultimately undergo medication-based treatment [Cay19]. ADHD medications are divided into two: stimulant and non-stimulant. Stimulant medications like amphetamines (e.g., Adderall) and methylphenidate (e.g., Ritalin and Concerta) work by increasing the level of neurotransmitters: dopamine and norepinephrine. Also, studies using functional magnetic resonance imaging (fMRI) have revealed that stimulant medication results in heightened activation of inferior frontal and striatal regions, along with their interconnections. Simultaneously, the medication leads to reduced activation in regions associated with the default mode network [RK14]. The increase in these neurotransmitters helps ameliorate functions like hyperactivity, shortness of attention span, impulsive behavior, etc (Cleveland Clinic, 2022). However, [Ban04] reported that 10 to 30% of all children and adults with ADHD either do not respond to or do not tolerate treatment with stimulants. In addition, due to their effects like appetite suppression, heightened wakefulness, and improved focus and attention, these stimulants are often abused which entails consuming them in quantities exceeding the prescribed dosage or using them in ways not intended by a medical professional (National Institute on Drug Abuse, 2014). As a result, non-stimulant medications like specific norepinephrine re-uptake inhibitors and Alpha-2 no-

radrenergic agonists along with antidepressants have been examined for their effectiveness in treating ADHD ([Bud05]; [Cay19]; [O'C23]). Norepinephrine re-uptake inhibitors atomoxetine (eg. Strattra) function by increasing the concentration of norepinephrine and dopamine in the prefrontal cortex. Clonidine, an alpha-2 agonist, operates by stimulating alpha-2 adrenoceptors situated in the brain stem, which activates inhibitory neurons. This activation leads to a decrease in sympathetic outflow from the central nervous system (CNS). Consequently, this reduction in sympathetic outflow results in lowered peripheral resistance, renal vascular resistance, heart rate, and blood pressure. In the treatment of ADHD, the precise mechanism of action for these drugs remains unclear. Within the CNS, there exist numerous subtypes of alpha-adrenergic receptors that are broadly distributed. The main theory suggests that stimulation of postsynaptic alpha-2 agonists regulates subcortical activity within the prefrontal cortex, thereby modulating symptoms of inattention, hyperactivity, and impulsivity ([Bro18]).

5.2 Cognitive-Behavioral Therapy

Cognitive behavioral therapy (CBT) is a psychological treatment approach that has shown its effectiveness in addressing various issues such as depression, anxiety disorders, substance abuse, eating disorders, and severe mental illnesses. CBT treatment aims to change one's harmful thinking and behavior patterns [APA17]. In 2018, the current treatment plans for children between the ages of 6 to 11 were medication and/or CBT, preferably a combination of both according to the American Academy of Pediatrics ([Pan21].([aL17]) noted that behavioral therapy combined with stimulants had better responses compared to stimulant or non-stimulant monotherapy, cognitive training, and neurofeedback. Another study on the effects of CBT on adults with ADHD showed that patients who are receiving CBT alongside medication reported improvements in their anxiety symptoms but this change wasn't seen in patients receiving treatment as usual [Jen16]). These findings support the idea that CBT can be an important part of the treatment for both adults and youth.

5.3 Neurofeedback and Neurostimulation

Neuroimaging studies of ADHD in the last decades provided key neurofunctional abnormalities that have pointed targets for neurotherapeutics. With the help of these neurotherapeutics abnormalities of the disorder could be improved. Neurofeedback techniques involve measuring a patient's brain activity, which is then processed in real-time and transformed into signals that are returned to the patient. Through this feedback the patient can learn to self-regulate their brain activity, thereby influencing the underlying neural mechanism of cognition and behavior ([EG19]). ([K.18]) noted that fMRI-neurofeedback has the advantage of higher spatial resolution compared to EEG-neurofeedback and it can target the key cortical and subcortical brain function deficits that have been established in ADHD. Another method is neurostimulation which is often done with

transcranial direct current stimulation (tDCS), transcranial magnetic stimulation (TMS), and trigeminal nerve stimulation (TNS) ([K.22]). Repetitive TMS is a safe and non-invasive technique for brain stimulation. It involves delivering short but intense pulses of electric currents to a coil placed on the subject's head, which creates an electric field within the brain through electromagnetic induction. Typically, high-frequency rTMS enhances cortical excitability, while low-frequency rTMS inhibits cortical excitability. Compared to transcranial direct current stimulation (tDCS), rTMS offers higher precision in targeting specific neural regions. However, it is expensive and can be uncomfortable, which makes it less suitable for children ([Wes21]). tDCS is used mostly with children due to high tolerability and low side effect profile. External trigeminal nerve stimulation (TNS) is another non-invasive intervention that has few side effects. TNS involves delivering low-level electrical currents through the skin to stimulate action potentials in the supratrochlear and supraorbital branches of the ophthalmic nerve (V1), which are situated beneath the forehead skin. The supraorbital nerve has extensive connections within the brain, especially with regions like the reticular activation system, locus coeruleus, brain stem, thalamus, frontal cortex, and other cortical areas ([K.22]).

5.4 Precision Medicine Approaches

Precision medicine (PM) aims to provide evidence-based individualized assessment and treatment to each patient and thereby is an advancing field of healthcare that is informed by each person's unique clinical, genetic/genomic, biomarker, and environmental information. Ultimately recommendations and decisions in clinical practice will be targeted to well-defined groups of patients with very similar clinical, genetic, or biomarker profiles rather than be directed at a one-on-one level. However, PM for psychiatric conditions encounter many challenges such as comorbidity and complex genetic structures based on different types of genetic variants and gene-environment relations ([Bui22]). So PM depends on identifying biomarkers that are dependable, and that align with the existing interventions ([Mam22]). Therefore, the field needs to have more in-depth knowledge of the neural correlates of ADHD in order to create better-suited assessment and treatment tools.

6 New Idea: Harnessing Advanced Technologies and Personalized Approaches for Understanding and Treating ADHD

In recent years, there has been a growing recognition of the need for more personalized and technologically advanced approaches to understanding and treating Attention-Deficit/Hyperactivity Disorder (ADHD). This emerging shift in perspective seeks to utilize cutting-edge technologies, such as neuroimaging, genetic profiling, and digital health tools, to gain deeper insights into the neural

correlates of ADHD. By combining these advanced diagnostic methods with a personalized medicine approach, it is possible to move beyond the one-size-fits-all model of ADHD diagnosis and treatment. This new idea represents a significant change from traditional approaches, which often rely on symptom-based assessments and generic treatment protocols. The main point of this innovative approach is to tailor ADHD interventions to the unique neurobiological and genetic profiles of each individual. Advances in neuroimaging, such as functional MRI (fMRI) and diffusion tensor imaging (DTI), functional NIRS (fNIRS), enable the identification of specific neural patterns associated with ADHD subtypes. Genetic and epigenetic profiling further refines the understanding by uncovering the genetic variants and epigenetic modifications that contribute to an individual's susceptibility to ADHD. Additionally, digital health tools, including wearable devices and smartphone apps, offer real-time monitoring of symptoms and behaviors, allowing for continuous tracking and personalized feedback. By integrating these data streams, clinicians can create highly individualized treatment plans that target the underlying neural mechanisms of ADHD, ultimately improving treatment efficacy and patient outcomes. This shift toward advanced technologies and personalized approaches has the potential to revolutionize the field of ADHD research and clinical practice, ushering in a new era of precision medicine for this complex neurodevelopmental disorder.

7 Conclusion: Implications, Future Directions, and Limitations

This review paper explored the neural correlates of attention-deficit hyperactivity disorder (ADHD) and current treatment methods. First, the paper examined the neural anatomy and function in ADHD, it stated that ADHD patients show problems in executive functions which points to an abnormality in the prefrontal cortex. Also, it suggested that dysfunctions in the striatal and fronto-striatal regions, like a dysfunction in the dopaminergic system, significantly impact the human brain, potentially leading to the emergence of ADHD symptoms. Then the review looked at the findings of the neuroimaging studies in ADHD and described the roles of grey matter and white matter in the brain, and how disruptions in structural and functional connectivity can contribute to cognitive impairments and the risk of neurodevelopmental disorders like ADHD. Furthermore, the review went into a short explanation of the interplay of genetic and environmental factors on the global prevalence of ADHD and stated that genetics as well as prenatal factors such as maternal smoking and substance use, etc., might contribute to triggering the disorder. At last, the paper reviewed current treatment strategies like stimulant and non-stimulant medicine, cognitive-behavioral therapy and examined their effects, it also discussed emerging methods like neurofeedback and neurostimulation. In addition, the paper introduced the idea that the utilization of advanced technologies and personalized approaches for understanding and treating ADHD holds the capacity to

transform the field of ADHD research and clinical practice. One limitation of this review was the lack of sufficient neuroimaging findings on the neural correlates of ADHD. Furthermore, the focus of this study was the neural basis of ADHD however because of the complex psychological, environmental, and physiological structure of the disorder as well as it is high comorbidity it is not possible to find a causal relationship between the disorder and specific brain regions. Another limitation is that most studies didn't have a large enough sample size, which caused a problem in the validity of the findings. In addition, the ideas presented in this review are propositions drawn from existing literature, as a result, more research is needed to ascertain the neural correlates of ADHD. As new neuroimaging techniques emerge, more detailed research on the neural correlates of ADHD will be possible which will enable the researchers to find better targeted treatments. Thus, the neural underpinnings of neurodevelopmental disorders like ADHD will be further investigated. In conclusion, this review aimed to explore the key neural mechanisms underlying ADHD and the treatment methods that are currently available. There are several findings on the subject pointing to the PFC and the cerebrum, nonetheless, further research is needed to determine a neurophysiological model that could help determine targeted assessment, treatment, and support systems.

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