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| Literature Review

Psychobiological Markers, Coping Mechanisms, and Family Well-being in Attention Deficit Hyperactivity Disorder (ADHD)

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| ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental condition arising from a complex interplay of genetic and environmental factors, reflected through diverse psychobiological markers involving neurophysiology, neurochemistry, neuroimaging, and molecular profiles. Various biomarkers, including electrophysiological changes, alterations in functional connectivity, neurotransmitter variations, and miRNA expression, have been associated with ADHD, although none have yet demonstrated consistent diagnostic sensitivity. Individuals with ADHD frequently display maladaptive coping strategies such as avoidance and escape behaviors, contributing to emotional dysregulation and reduced quality of life. These difficulties extend to the family environment, where caregivers often experience heightened stress, strained interactions, disrupted daily routines, and increased psychological burden. Studies indicate that family functioning, parenting quality, and stress levels are closely linked to ADHD symptom severity, affecting both the individual and their caregivers. However, the use of adaptive coping strategies, such as problem solving, cognitive restructuring, and social support, can strengthen resilience, reduce psychological strain, and improve overall family well-being. Integrating knowledge of psychobiological markers with patterns of coping and family dynamics provides a more comprehensive understanding of ADHD and highlights the importance of supporting adaptive coping mechanisms to improve outcomes for individuals with ADHD and their families.

| KEYWORDS

ADHD, psychobiological markers, coping mechanisms, family well-being, stress responses, neurodevelopmental disorder

| ARTICLE INFORMATION

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1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) represents a neurodevelopmental disorder that commonly impact both children and adults worldwide. ADHD correlates with both rare and common genetic variants, suggesting genetic factors. Moreover, it has also been found that environmental factors also play a role in the disorder. However, determining the lying cause of ADHD has consistently proven to be a significant challenge (Faraone *et al*., 2024). Based on its clinical symptoms, ADHD is commonly divided into three distinct presentation types: predominantly inattentive (ADHD-PI), predominantly hyperactive-impulsive (ADHD-HI), and combined type (ADHD-C) (Zhu *et al*., 2023). A previous study analyzing 588 research reported that the prevalence of childhood ADHD globally is roughly 8% with the observed rate being twice as high in males (10%) as in females (5%) (Ayano *et al*., 2023). A study conducted in Indonesia reveals that of 314 students of primary school aged ranging from 6-12 years old, around 45.85% were exhibiting characteristics consistent with the symptoms of ADHD (Wimbarti & Kusrohmaniah, 2023). In ADHD, varied biomarkers have been reported in several studies from the fields of neurophysiology, neurochemistry, neuroimaging, to genetics. A range of biomarkers, including electrophysiological, genetic, peripheral, and miRNA-based, are objective tools for identifying ADHD (Mehta *et al*., 2020). When faced with a stressor, individuals tend to deal with varying ways referred to as coping mechanisms. Coping can be defined as the thoughts and behaviors made by an individual as a result of being faced to either internal and/or external stress (Algorani & Gupta, 2023). These coping mechanisms can influence overall family well-being levels,

like emotional stability and adaptability. For instance, when parents rely on maladaptive coping styles, their children are more likely to exhibit disruptions in emotional functioning (Vladislav *et al*., 2024). Well-being refers to the interpretation and evaluation of one's life that is shaped by an individual's emotional states and internal experiences. Well-being is associated with better emotional and physical health (Susmarini *et al*., 2024).

2. ADHD

Attention Deficit Hyperactivity Disorder (ADHD) is a hyperkinetic disorder involving disturbances in activity and attention that is considered as a psychiatric disorder and is commonly characterized in children with symptoms like hyperactivity, impulsive behavior, and difficulties in maintaining attention (Mirnawati & Amka, 2019). Over time, the terminology of ADHD has undergone significant changes over time. Fundamentally, as stated in DSM I, ADHD was described as a hyperkinetic disease and considered as minimal brain dysfunction in the 1900s. DSM II then redefined it as a hyperactive reaction of childhood upon identifying attention deficits as a core component. This was then subsequently updated in DSM-III as attention deficit disorder with or without hyperactivity (Cabral *et al*., 2020). Formerly, there were two separate diagnoses: Attention Deficit Disorder and Attention Deficit Hyperactivity Disorder. However, as later stated in DSM-IV, these two diagnoses are merged into one disorder consisting of three presentations: predominantly inattentive, predominantly hyperactive, and combined type. In 1950, the prevalence of ADHD progressively rose as schools for children were becoming standardized. Usually, ADHD symptoms arise at a young age and interfere with daily activities in more than one environment. ADHD is often correlated with abnormalities of the brain affecting daily functioning and cognitive processes. Compared to normal individuals, ADHD exhibited shrinkage of the anterior cingulate gyrus and the dorsolateral prefrontal cortex (DLPFC). Functional Magnetic Resonance Imaging also reveals that individuals with ADHD indicate reduced activity in the frontostriatal region. However, no consistent laboratory findings or imaging results have been established in individuals diagnosed with ADHD (Magnus *et al*., 2023).

According to DSM-IV, individuals should present a minimum of six symptoms to be considered as ADHD. This was then reduced to a minimum of five symptoms in DSM-5 (Musullulu, 2025). In predominantly inattentive type (ADHD-I) one would need to meet the cut off score of ≥6 (≥5 for adults) of several features including difficulty focusing on details, clumsiness, struggles maintaining focus, unresponsive to direct communication, difficulty executing and finish task, avoidance, unwilling to engage in effortful work, frequent items misplacement, prone to distraction from the environment, and/or often. On the other hand, individuals with predominantly hyperactive impulsive type (ADHD-HI) would need to meet a minimum criteria of ≥6 (≥5 for adults) of symptoms like tendency to leave seat at inappropriate times, fails to remain seated when required, fidgeting hands or feet while sitting, frequently moves around, fails to remain quiet while involved in tasks, restless, make thoughtless remarks, talks excessively, difficulty waiting for their turn, and interrupts on others. (Yacoub *et al*., 2025).

ADHD is associated with hereditary and environmental influences. The likelihood of ADHD is nearly doubled among siblings compared with individuals in the broader population. Other factors like maternal smoking, viral diseases, inadequate nutrition, and prenatal alcohol exposure might also potentially be contributors to ADHD (Magnus *et al*., 2023). Various maternal and lifestyle factors, like pre-pregnancy overweight and obesity, pre-eclampsia, hypertension, exposure to acetaminophen, as well as atopic conditions during childhood, have also been identified to have a strong correlation with ADHD (Kim *et al*., 2020). A recent meta-analysis study assessed 12 independent genome-wide significant loci and identified that FOXP2 on chromosome 7 is associated with ADHD. Exposure to diverse range of toxins, like heavy metals such as Hydragyrum and Plumbum, as well as chemicals such as organophosphate pesticides, has also been suggested as a contributing factor, indicating a significant association with ADHD. Past studies have also revealed the association of nutrition with ADHD, indicating reduced levels of zinc and omega-3 fatty acids in individuals affected with ADHD (Cabral *et al*., 2020).

In individuals with ADHD, delays in temporal processing are commonly identified from five years of age. A delay of approximately three years in prefrontal cortex development is expected in children with ADHD, with 50% of peak cortical thickness reached at roughly 10.4 years, whereas typically developing individuals could reach it in about 7.5 years, and is associated with overall decreased volume of the brain in the prefrontal region. The development of the prefrontal cortex is fundamental for planning, attention control, and decision making, which are among the things commonly compromised in individuals with ADHD. Cognition and emotional functioning in individuals with ADHD are affected by the decline in functional connection from nucleus accumbens to the right hemisphere of paracingulate gyrus. Consequently, a dysregulation in reward pathways between the nucleus accumbens and its downstream targets is a key component in the manifestation of ADHD symptoms. The cerebellum, involved in controlling movement, balance, coordination, regulation of attention, cognitive control, memory, linguistic abilities, and visuospatial processing, is expected to exhibit a developmental delay, with 50% of cortical maturation reached at about 10.5 years, whereas typically developing individuals could reach it in about 7.5 years. A reduced volume of the corpus callosum is recognized as one of the mechanisms underlying coordination impairments observed in children with ADHD. However, corpus callosum size reductions are then normalized to levels as typically developing individuals once they reach adulthood (Yacoub *et al*., 2025).

3. Psychobiological Markers in ADHD

A biomarker is a broad term referring to any measurable feature that supports identifying a condition and tracking how it develops over time. In neuroscience, one of the most highly used biomarker methods is imaging, following the discovery of

distinct functional regions, commonly referred to as 'maps' (Chen *et al*., 2023). Hit reaction time (RT) interstimulus interval (ISI) change and hit standard error (SE) have been shown to have a significant correlation with ADHD, indicating that the higher the attention of individuals with ADHD, the smaller both the hit of RT change and hit ISI SE change. This implies that the greater the activity levels are associated with the greater the impulsive behavior in ADHD (Chu *et al*., 2020). A significant reduction of Oxy-Hb in the right frontal cortex was observed in children with ADHD, alongside extended NoGo-P3 latencies and decreased NoGo/Go-P3 amplitude responses, with a significant correlation between NoGo/Go-P3 amplitude and Oxy-Hb (Kaga *et al*, 2020). Adults with ADHD exhibited smaller Cz mismatch negativity (MMN) amplitude, greater symptom severity, impaired attention profiles, and a broader spectrum of executive function deficits compared to controls (Hsieh *et al*., 2021).

While EEG/ERP-based neuroalgorithms represent a promising approach for identifying ADHD-related neuropathways, the diagnostic sensitivity is inadequate for clinical diagnosis (Müller *et al*., 2019). Compared with matched healthy controls, the Event Related Potential (ERP) and the TMS Evoked Potentials (TEPs) components in ADHD during Stop Signal Task were found to be significantly attenuated (Hadas *et al*., 2021). A decrease in amplitudes and an increase in latencies of Event Related Potentials (ERPs) were shown in individuals with ADHD in several positive and negative deflections (Münger *et al*., 2021). ADHD appears to be associated not only with a delayed neuro-developmental trajectory, but also with an early onset age-related neurophysiological decline in some areas of the brain (Kakuszi *et al*, 2020). A study comparing ADHD to normal controls shows decreases in concentration of glutamate, N-Acetyl Aspartate, and Choline in individuals with ADHD (Hai *et al*., 2020). In ADHD, a greater total overflow and interhemispheric somatomotor network connectivity can also be observed compared to typically developing individuals (Chen *et al*, 2021). In ADHD, a reduction of functional connectivity (FC) of the dorsal default-mode network (DMN), precuneus-post salience network (SN), and ventral DMN-post SN was shown (Wang *et al*., 2021). A trend difference in fractional anisotropy (FA) of individuals with ADHD compared to controls between right inferior frontal gyrus (IFG) and right posterior cingulate, posterior cingulate to right anterior cingulate, and left posterior cingulate to left middle temporal gyrus can also be integrated into future biomarker research (Tremblay *et al*., 2020). A reduction of both functional connectivity and global network efficiency was also found in ADHD, alongside altered nodal efficiency, such as an increase in the dorsal and visual attention networks and a reduction in default and somatomotor networks, compared to healthy controls (Wang *et al*., 2020).

Past studies have reported a greater concentration of *Bifidobacterium* in children with ADHD. However, this is in contrast with another study stating that after micronutrient intervention, the level of *Bifidobacterium* is decreased (Sukmajaya *et al.*, 2021). A study of total white blood cells in individuals with ADHD reveals that MiR-140-3p, miR-27a-3p, miR-101-3p, let-7g-5p, miR-30e-5p, miR-486-5p, miR-1515-5p, and miR-126-5p were found to be decreased after a series of methylphenidate treatment (Wang *et al*., 2022). Recent studies have further demonstrated that ADHD is linked to alterations in dopamine receptor systems, particularly those involving the D1 through D5 receptor (Rabitho & Setiawati, 2024). A journal by Nobukawa stated that a greater pupil diameter with lower complexity and symmetry was observed in individuals with ADHD (Nobukawa *et al*., 2021). However, a study by Das and Khanna stated that lower dilation speeds and pupil size were observed in ADHD positive subjects (Das & Khanna, 2021). This aligns with a study by Wainstein stating that a decreased pupil diameter during a spatial working memory task was found in ADHD, with a correlation with subjects' performance and reaction time variability (Chen *et al*., 2023).

4. Coping Mechanisms in ADHD

Coping mechanisms refer to the behavior and thoughts used when faced with external and internal stressful situations. Coping can affect one's adherence to therapeutic regimens and overall condition development, particularly when lifestyle modification is made. In conditions where a non-pharmacological approach affects condition progression, coping serves as a determinant of symptom severity. The impact of coping styles is experienced not only by patients but also by the physicians and nurses involved in their treatment. Hence, recognizing one's coping mechanisms is essential in determining the most appropriate manner of engagement to establish a strong and effective doctor-patient relationship. The importance of assessing both one's distress level and coping responses is essential as individuals who employ maladaptive strategies tend to interpret their physician's behavior as distant or insufficiently supportive and may hinder therapeutic alliance (Algorani & Gupta, 2023). Coping mechanisms can be categorized into adaptive and maladaptive strategies. Adaptive coping strategies refer to the positive and effective approaches to managing stress. Several forms of adaptive coping strategies include problem solving, social support, and cognitive restructuring. On the other hand, maladaptive coping strategies refer to the ineffective ways to handle stressful situations that are able to give short-term relief but lead to further complications in the long run. Forms of maladaptive coping strategies include avoidance, substance abuse, and rumination (Joseph, 2025).

Individuals diagnosed with ADHD mostly implemented maladaptive coping strategies rather than adaptive coping strategies. Adults with ADHD were more likely to use avoidance and escape strategies (Barra *et al.,* 2021). Impairments in emotional regulation and inhibitory control are frequently associated with the emergence of maladaptive coping tendencies like avoidance, denial, or self-blame (Effendy & Setiawati, 2025). A past study stated that compared to controls, adults with ADHD employ more maladaptive attachment and coping outcomes (Al-Yagon *et al*., 2020). Individuals with high symptoms of ADHD have an increased level of maladaptive coping strategies and a decreased quality of life (Abdelmalak & Vávrová, 2025). However, greater ADHD symptoms were negatively correlated to self-awareness of emotional dysregulation (Ben-Dor Cohen *et al*., 2023).

5. Family well-being in ADHD

The quality of family relationships, which includes supportive behaviors such as providing love, advice, and care, as well as sources of strain such as arguments, criticism, and excessive responsibilities, may affect well-being through social, behavioral, and physiological pathways. Family members can influence one another's behaviors through social control and by offering guidance, promoting healthier behaviors, and better use of healthcare services. However, tension or stress within these relationships may also prompt individuals to adopt behaviors that undermine their health as a way of coping with that stress (Thomas *et al.,* 2017). Parenting approaches are strongly associated with children's likelihood of developing ADHD (Setyanisa *et al.*, 2022). Urging parents to adopt positive changes may inadvertently produce adverse effects, as such an approach can strengthen the link between negative parenting practices and the development of maladaptive coping responses (Pearce & Kiel, 2025). Family functioning and well-being can also be enhanced by managing the symptoms and emotional dysregulation of children with ADHD (Setiawati *et al*., 2024).

Caring for a child with ADHD has been associated with increased emotional strain among caregivers or family members. However, the use of effective coping strategies has been shown to support and improve caregivers' or family members' psychological well-being (Nadi Sakhvidi *et al.*, 2024). Past studies have stated that family member with ADHD was found to have notable negative effects on parents' or caregivers' sleep patterns, amount of time spent resting, life satisfaction, overall health-related life satisfaction, and psychological well-being. However, these effects were not uniformly consistent across control groups (Peasgood *et al.*, 2020). This aligns with a study by Bhide et al., stating that families of children with ADHD and subthreshold ADHD indicate consistently low or deteriorating family functioning (Bhide *et al.*, 2023). Moreover, mothers of children with ADHD often show anxiety, fatigue, and frustration, as they are regularly being blamed for their child's challenging behavior. This can lead to their child's poor academic performance and social rejection (Setiawati *et al.*, 2018). However, this is opposed by past study, stating that most mothers were reported to experience either minimal strain or an absence of burden altogether (de Lorient *et al.*, 2025).

ADHD imposes substantial demands on caregivers, affecting them economically, socially, and emotionally. Observational research on children with ADHD and their parents has exhibited conflicted parent-child interactions and maladaptive parenting. Daily activities, including completing homework or bedtime routines, might be challenging in families of children with ADHD. Moreover, parents of children with ADHD are at an increased risk of experiencing marital difficulties (Peñuelas-Calvo *et al.*, 2020). A pattern between several factors related to parenting and ADHD symptoms has been shown to have a significant association. Lower quality of parent and child interactions, maltreatment, parental divorce or single parenting, and greater child media exposure were linked with a greater probability of ADHD (Claussen *et al.*, 2022).

6. Discussion and Future Directions

The evidence summarized in this study reinforces that ADHD is a complex neurodevelopmental disorder influenced by both genetic and environmental contributors, as supported by findings on neurophysiological, neuroimaging, neurochemical, and molecular alterations (Hai et al., 2020; Chen et al., 2021; Wang et al., 2021). Although varied markers, including ERP alterations, functional connectivity reductions, neurotransmitter distinctions, and miRNA expression changes, have been associated with ADHD, the diagnostic sensitivity of these psychobiological markers remains limited (Müller et al., 2019; Hadas et al., 2021). This indicates the need for a multi-level diagnostic framework for ADHD rather than relying on a single biomarker. Consistent with past research, individuals with ADHD frequently demonstrate maladaptive coping strategies like avoidance and escape behaviors that may contribute to overall reductions in functioning and quality of life (Barra et al., 2021; Abdelmalak & Vávrová, 2025). This pattern extends to caregivers and family systems, where heightened stress, strained interactions, and psychological burden are well-documented (Nadi Sakhvidi et al., 2024; Peasgood et al., 2020). Successful intervention strategies for ADHD combine multiple approaches, including cognitive-behavioral techniques, sensory activities, cognitive exercise, and strategies based on spiritual or value principles. Parenting practices like mindful engagement, emotional regulation coaching, and parental resilience are also important to provide a strong foundation for intervention outcomes. This highlights the need for an active collaboration among families, educational, and professionals to ensure the comprehensive support of individuals with ADHD (Yakin *et al.*, 2025).

7. Conclusion

Attention Deficit Hyperactivity Disorder (ADHD) is a hyperkinetic disorder involving disturbances in activity and attention that arises from a complex interplay of genetic and environmental factors, reflected through diverse psychobiological markers spanning neurophysiology, neuroimaging, neurochemistry, and molecular profiles. Individuals with ADHD commonly exhibit maladaptive coping strategies, contributing to heightened emotional dysregulation and reduced quality of life. These coping patterns, together with the behavioral challenges associated with ADHD, significantly influence overall family functioning and well-being. Families often experience elevated stress, strained interactions, and disruptions in daily routines; however, effective coping mechanisms within the family can mitigate psychological burden and improve relational stability. Strengthening adaptive coping skills and supporting family-level resilience may therefore represent essential pathways for improving outcomes in individuals with ADHD as well as their families and caretakers.

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