

A Narrative Review of Outcomes, Comorbidities, and Alternative Behavioral Interventions in Adolescent and Adult Women with ADHD

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Abstract: Attention deficit hyperactivity disorder (ADHD) is a prevalent neurodevelopmental condition that persists into late adolescence and even adulthood. While a lot of research has addressed the issues of childhood ADHD, manifestation of the condition in adults, particularly females, remains largely obscure. The aim of the present narrative review is to address the sex-specific subtleties of ADHD in adolescent and adult female populations and critically analyze the various intricately complex facets of the associated comorbidities and outcomes, based upon data extracted from scholarly works indexed in online databases (eg, PubMed, Google Scholar, etc). We provide evidences refuting the presumption that ADHD primarily affects men, highlighting the complexity of clinical outcomes and comorbidities, and the consequent misdiagnosis of women as a possible reason. Comprehensive critical assessment of the multiple aspects of psycho-socio-behavioral, cognitive, and other clinical outcomes and comorbidities associated with ADHD in women indicated widespread dysfunctions and atypical characteristics. Furthermore, we also propose the probable utilities of art-based and other unconventional behavioral therapeutic regimens as alternatives and/or additives for the therapy of female ADHD cases to address case- and gender-specific needs and induce an overall improvement in their functioning. While this is not an exhaustive review of the literature, we hope that our points of discussion will generate further interest among scientists, clinicians, and caregivers to address the age and gender specificity of the condition to advance our perspectives of the condition and eventually establish novel therapeutic measures for the same.

Keywords: substance use, borderline personality disorder, sexual victimization, partner violence, academic performance, peer rejection

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by behavioral symptoms of inattentiveness, restlessness, hyperactivity, and impulsivity.¹ It is thought to be one of the most common neurodevelopmental conditions among children and adolescents.² According to the Vth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM), ADHD may be classified into three major subtypes: predominantly inattentive type (ADHD-I), predominantly hyperactive/impulsive type (ADHD-H), and combined symptoms (ADHD-C).³ Although initially thought to be a

neurological condition limited to childhood and adolescence before the age of 12, ADHD symptomatology and associated comorbidities and outcomes have now been confirmed to persist well into adulthood in a sizable number of cases,^{2,4,5} probably due to an intricate interplay of case-specific characteristics, social and familial parameters, and exposure to adverse life events.⁶ Interestingly, persistence of symptomatology into adulthood may be as high as 50% amongst ADHD children.⁷ Furthermore, up to two-thirds of ADHD children may elicit sub-threshold symptoms into adulthood.⁸ Hence, while ADHD has an estimated incidence of 6% in children,⁹ 3–5% of the adolescents and adults may show ADHD-like symptoms.^{7,10–12} Indeed, a recent meta-analytic study using data from multiple geographical regions has estimated an overall global prevalence of ADHD at 7.2% in children and adolescents, and 2.5% in adults.¹³ However, in some select populations, eg, US adults, an even higher incidence rate of over 14% has been reported.¹⁴

Appropriate diagnoses of adult ADHD cases are complicated by the high frequency and severity of comorbidities with overlapping symptoms, such as mood and conduct issues, substance abuse, and learning and sleep dysfunctions.^{15,16} In addition, the core symptoms of impulsivity, hyperactivity, and inattention are expressed in more subtle and diverse ways in adults.⁸ Nevertheless, like in ADHD children, significant psychological, behavioral, academic, family, and social problems are replicated in the adult cases.^{12,17} Although compared to early-onset cases, the severity of core symptoms, particularly externalizing outcomes, are reduced in adulthood ADHD, the former group may have greater manifestation of behavioral and emotional issues as well as other associated comorbidities.¹⁸ Indeed, ADHD during adulthood has significant clinical differences, compared to the manifestation of the condition in childhood, particularly with regard to self-concept and psychosocial issues, including mood disorientation, stress and anger management, and risk-taking behaviors.^{8,19} This is understandable as endocrine, metabolic, and other gendered differentiations, which affect all aspects of an individual's pathophysiology, manifest themselves strongly during adolescence and adulthood.²⁰ Hence, compared to children, adults with ADHD elicit significantly higher concurrences of other mental health conditions, including depression, anxiety, mood and personality, and substance use disorders.¹⁴ In fact, it is estimated that 65–98% of all adult cases diagnosed with ADHD have at least one or another form of comorbid psychiatric condition.²¹ Emotional dysregulation appears to be a primary comorbidity in adult cases, which, because of its high co-occurrence, has been proposed as a differentiating feature of adult vs childhood ADHD condition.²² Further, unemployment, academic underachievement, occupational/financial difficulties and inabilities to sustain long-term partnerships/relationships, and disruptive behavior and criminality are other significant outcomes specific to adult ADHD cases.^{16,23} Adults with ADHD typically exhibit higher cognitive deficiencies and functional deficits, such as issues with information manipulation, organization, and time management.⁵ Because of these differences, diagnosis of adult ADHD cases is difficult and may remain underdiagnosed or misdiagnosed in many instances.²⁴ Remarkably, adult ADHD subjects elicit low self-awareness of their own symptoms and underrepresent impairments related to both hyperactivity/impulsivity and inattentiveness.²⁵

Thus, it is clear that while there has been appreciable progress in understanding the pathophysiology and clinical relevance of ADHD in the adult population in recent years, a complete understanding of the psychopathology, comorbidities, and treatment avenues have been lacking.²⁶ This is especially true for adolescent and adult women, as ADHD was not only thought to be a childhood-limited condition, but also a disorder predominantly affecting males.³ Furthermore, the psycho-socio-behavioral manifestations of ADHD-linked phenotype and comorbidities may have considerably different implications in adolescent and adult female cases of ADHD.²⁷ In addition, pregnancy, childbirth, and postpartum considerations are other aspects of pressing concerns for these subjects. Furthermore, the efficacy of common pharmacotherapeutic regimens in adult cases with ADHD may remain limited, as the pharmacological agents prescribed for controlling ADHD symptoms are actually neuromodulators that inhibit presynaptic reuptake of catecholaminergic neurotransmitters norepinephrine and dopamine.²⁸ In addition to resistance against these agents offered by many adult ADHD cases, their usage may be associated with adverse side effects, particularly in pregnant and lactating women.²⁹ Moreover, since social factors and life events mediate persistence and severity of ADHD symptoms in adults, it is essential to include behavioral paradigms in the therapeutic regimens.⁶

The objective of this narrative review is to critically examine the gendered differences in the manifestation of psycho-socio-behavioral and cognitive outcomes associated with ADHD in adolescent and adult women. We begin our discussion with a brief overview of the potential risk factors influencing the pathophysiology of ADHD. Detailed descriptions of behavioral comorbidities related to sleep and dietary dysfunction, addiction, criminality, academic and occupational underperformance, difficulties in forming social and romantic relationships, and suicidality and self-harm in female

cases of adult ADHD follow. Lastly, we outline the possibilities of implementing some of the most relevant art-based and other non-conventional behavioral therapeutic measures for the benefit of these subjects. For accomplishments of these objectives, we performed extensive searches for pertinent original studies, reviews, books, theses and case reports on scholarly databases such as PubMed, Google Scholar, and EMBASE. A variety of keywords (alone and/or in combination) were used for the retrieval of peer-reviewed scholarly works as per the topics covered in the specific sections.

A Brief Synopsis of Risk Factors Associated with ADHD

ADHD has a complex etiology governed by a plethora of genetic, environmental, and neurological factors, as well as an intricate interplay between them (Figure 1).^{30,31} Familial contribution is a strong factor in ADHD,³² with several genes, including dopamine receptors D4 and D5 (DRD4 and 5), dopamine transporter DAT1, dopamine beta-hydroxylase (DBH), serotonin/5-hydroxytryptamine transporter (5-HTT), serotonin receptor 1 B (HTR1B), and synaptosomal-associated protein 25 (SNAP25), implicated as susceptibility factors.^{33,34} Familial history appears to be a significant modulator of the relationship between abuse during childhood and the development of the clinical outcomes of ADHD. However, in the absence of longitudinal studies, it is difficult to discern the exact directionality of this relationship.³⁵

Additionally, multiple pre-, peri-, and postnatal biological, chemical and environmental risk factors contribute to the pathogenesis of ADHD. For instance, children born via implementation of assisted reproductive technology (ART) may be more susceptible to neurodevelopmental issues, including ADHD.³⁶ Gestational diabetes may also be a predictor of ADHD development, particularly those with a low socioeconomic status.^{37,38} Furthermore, early preterm birth at a gestational age of < 34 weeks has been observed to be associated with the development of ADHD symptoms.³⁹ Interestingly, gestational age appeared to be a stronger associative factor for the development of ADHD symptoms of inattention in girls than in boys. However, the relationship between gestational age and hyperactivity symptoms may be confounded by familial factors.³⁹ Other pre-, peri-, and postnatal factors—such as exposure to drugs and alcohol,

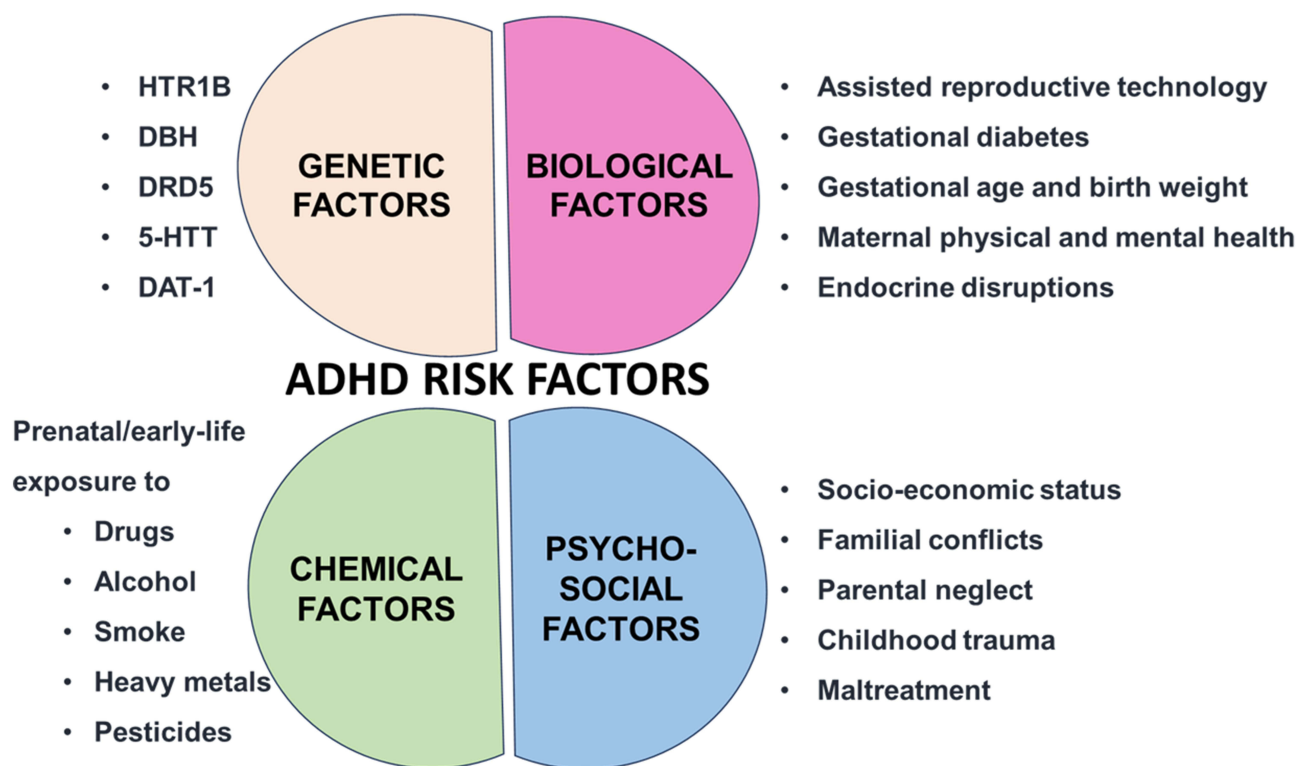


Figure 1 Risk factors associated with ADHD development. A plethora of genetic, neurobiological, environmental, and psycho-social factors, and their interactions determine ADHD pathophysiology.

Abbreviations: DRD4/5, dopamine receptors D4 and 5; DAT1, dopamine transporter; DBH, dopamine beta-hydroxylase; 5-HTT, serotonin/5-hydroxytryptamine transporter; HTR1B, serotonin receptor 1 B.

maternal stress and anxiety, sugar level alterations, high blood pressure, and abnormal birth weights—can all be contributing factors.¹ Maternal smoking is particularly a potent risk factor for development of ADHD,³⁸ however underlying genetic factors rather than smoke exposure per se, might drive this relationship.⁴⁰ Early life chemical exposure to toxicants, such as organophosphate and polychlorinated biphenyl pesticides⁴¹ and mercury,⁴² is also likely to increase the chances of development of ADHD-like phenotypes. Similarly, chemical exposure to endocrine disruptors, such as antiandrogenic phthalates and dichlorophenols, may result in increased ADHD incidence among adolescents.⁴³

Psycho-social issues, for example, associated with maltreatment and abuse, are known to strongly influence ADHD phenotypes.³⁵ Maltreatment, including physical and/or sexual abuse and parental neglect, are also strong predictors of ADHD development,⁴⁴ as these have been reported to result in enhanced impulsivity and inattention, although this may not be true for hyperactivity-related symptoms.⁴⁵ With regard to women, quality of the mother-daughter relationship appears to be a strong mediator of ADHD-related symptoms and other mental health issues in childhood, adolescence, and adulthood.⁴⁶

Gendered Differences in Adolescence and Adulthood ADHD: An Overview

Considering the heterogeneous origins of ADHD, it is hardly surprising that its symptomatic manifestations show considerable variations across culture, age, and gender.^{47,48} In particular, gender appears to significantly influence ADHD symptomatology.⁴⁹ Even in childhood, gender is thought to play a key role in the appearance of subtleties of ADHD outcomes. Thus, ADHD girls may predominantly demonstrate inattentiveness, while boys are more likely to elicit symptoms of hyperactivity and impulsiveness.^{50,51} Such phenotypic subtleties may lead to under-recognition of ADHD in girls, which may be mistaken as attentional and emotional issues.⁵² Further, because female subjects of ADHD often experience depression, anxiety, mood disruptions and other comorbid conditions, and have better coping mechanisms than their male counterparts, core ADHD symptoms may remain misdiagnosed and/or underdiagnosed.^{53,54} Nevertheless, such perceived differences in prevalence of childhood ADHD which is thought to be higher in the male gender, becomes less prominent during adulthood.⁵¹ In fact, data suggests no statistically significant gender differences in the prevalence of adult ADHD.⁵⁵ One factor contributing to this may be the inability to girls to outgrow childhood ADHD symptoms and associated comorbidities.⁵⁶ Interestingly, while the symptoms of hyperactivity and impulsivity decrease with age, inattentive phenotype tends to persist,⁵⁷ which might also explain the diminishment of gendered differences in ADHD prevalence with age. Other reports also suggest that general symptomatology and responses to medications are comparable between adolescents and adults of both genders;^{20,51,58} but see below.

As indicated, because ADHD was historically perceived to be a childhood-limited condition and as a predominantly male disorder,⁵⁹ fewer evaluations of its diagnoses and therapies were directed to the adult female populations.⁶⁰ However, this perspective has been changing rapidly. It is now acknowledged that better understanding of ADHD conditions in adolescent girls and adult women may help in devising better therapeutic regimens, reduce prevalence rates, and positively impact their lives in multiple ways.⁶¹ Indeed, because of the mis-, under- and/or delayed diagnoses of ADHD symptoms in girls and women, they are more likely to elicit increased severity of disease-specific symptoms, as well as associated comorbidities.^{51,59} Concurrently, some outcomes are more pronounced in female ADHD subjects. Thus, women with ADHD elicit greater issues with internalizing symptoms of inattention and lowered self-esteem, while their male counterparts have increased levels of externalizing symptoms of impulsivity, hyperactivity, and aggressive/disruptive behavior.^{8,62} As male ADHD subjects elicit higher levels of externalizing problems, they are likely to be noticed and attended to, compared to females who remain largely ignored. Such inappropriate and delayed diagnostic decisions in female ADHD cases may in turn lead to inappropriate or no treatment measures.⁶³ Further, because of higher incidence of internalizing problems; women with ADHD are more susceptible to acquire depressive and anxious phenotype, and may have poorer coping mechanisms, particularly during adolescence.⁵¹ Even among adults cases of ADHD, women are more vulnerable to develop depressive and anxiety symptoms, compared to their male counterparts.^{59,64} Further, adult women cases of ADHD elicit enhanced prevalence of emotional dysregulation, compared to their male counterparts,⁶⁵ and have greater issues with lowered self-concept and self-esteem.⁵⁹ Concurrently, it has been proposed that females with childhood diagnosis of ADHD tend to retain the symptoms into adulthood, and may elicit more severe psycho-behavioral impairments and even have higher rates of indulging in self-harm.⁶⁶ Further, women with ADHD have been evidenced to have higher risk of committing suicides than their male counterparts.^{67,68} Thus, it appears that higher-order brain functional domains of social interactions, time perception, stress responses and mood manifestations appear to be more severely impaired in adult females with ADHD, compared to their male counterparts. Conversely, women who were diagnosed with

ADHD after an age of 60 years testified to be rejected by peers and faced difficulties at work and in relationships, but found creative ways to cope with the stressing situations, and were more sympathetic towards other individuals with the same diagnoses.^{69,70}

The cognitive and social functions of adult ADHD patients may also be mediated by gender. Intellectual impairments, as assessed by verbal but not overall IQ tests, are more severe in female ADHD subjects than in their male counterparts.⁶² Interestingly, women with ADHD have been reported to have comparatively fewer deficits in working memory and educational functioning.⁴⁹ On the other hand, female cases of ADHD, particularly ADHD-I, have more severe disruptions in academic and social performances and are more likely to be bullied by peers compared to boys with similar phenotypes.⁷¹ In concurrence, female adolescents with a diagnosis of ADHD-I fared worse in negative social preference in relation to internalizing symptoms.⁷² In general, social connectivity may be significantly hampered in adult women with ADHD.⁷³ Both increased anticipation of negative responses from peers and deficient coping mechanisms in presence the of hostile social situations also contribute to social dysfunction in female ADHD cases.⁷⁴

Hence, it appears that, in addition to subtleties in the core symptoms of ADHD, there are appreciable gendered differences in the psycho-socio-behavioral, academic, and cognitive outcomes of the condition, pointing to probable requirements of slightly refined therapeutic measures. In the subsequent sections, we undertake a comprehensive and critical evaluation of the comorbidities (Figure 2) and outcomes (Figure 3) associated with adolescent and adult ADHD cases, with a particular focus on the female gender.

COMORBIDITIES ASSOCIATED WITH ADHD IN WOMEN

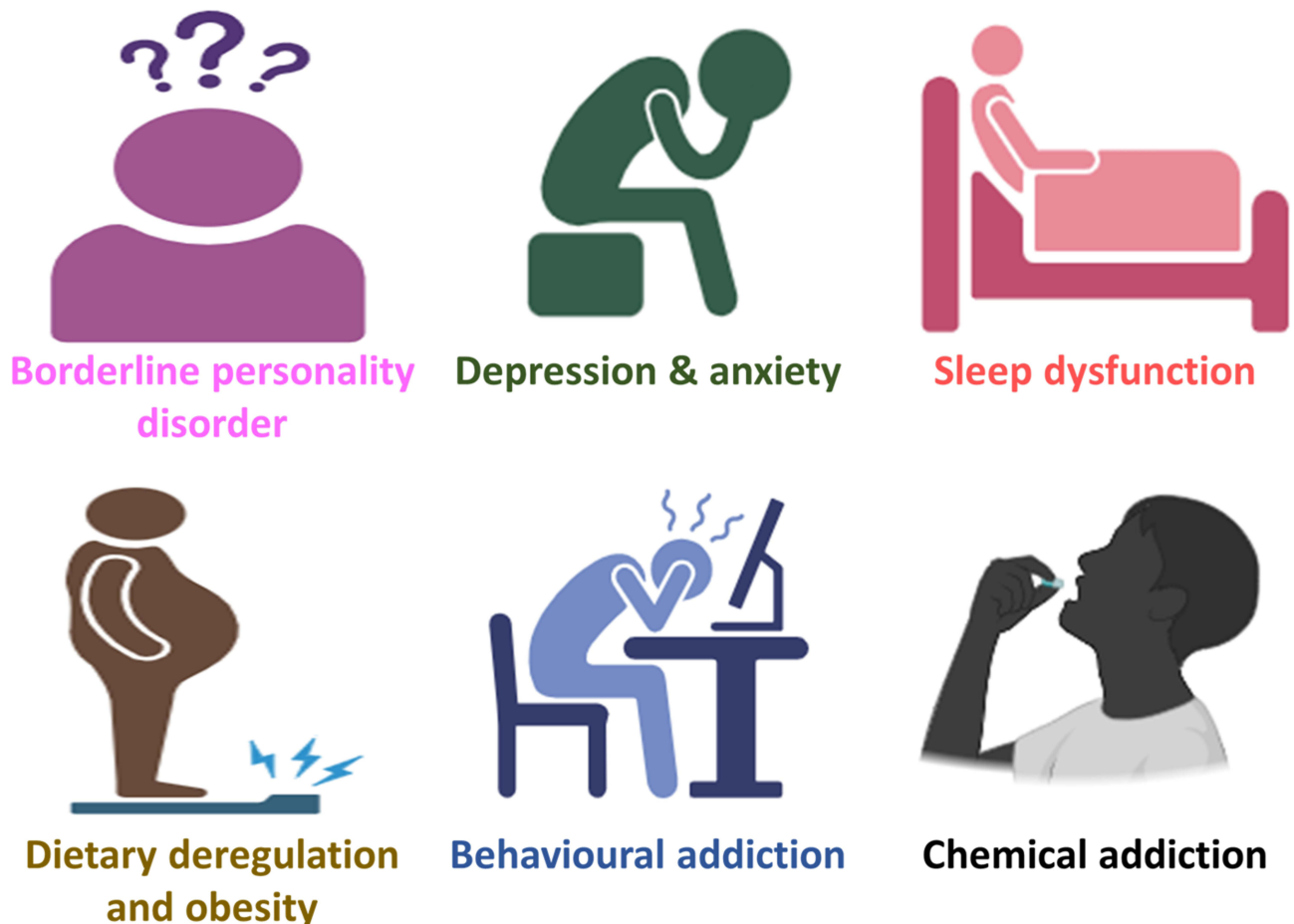


Figure 2 Comorbidities associated with adulthood ADHD. Mental health issues, behavioral deficits, addiction and other physical health concerns may co-exist in subjects with ADHD.

KEY OUTCOMES ASSOCIATED WITH ADHD IN WOMEN

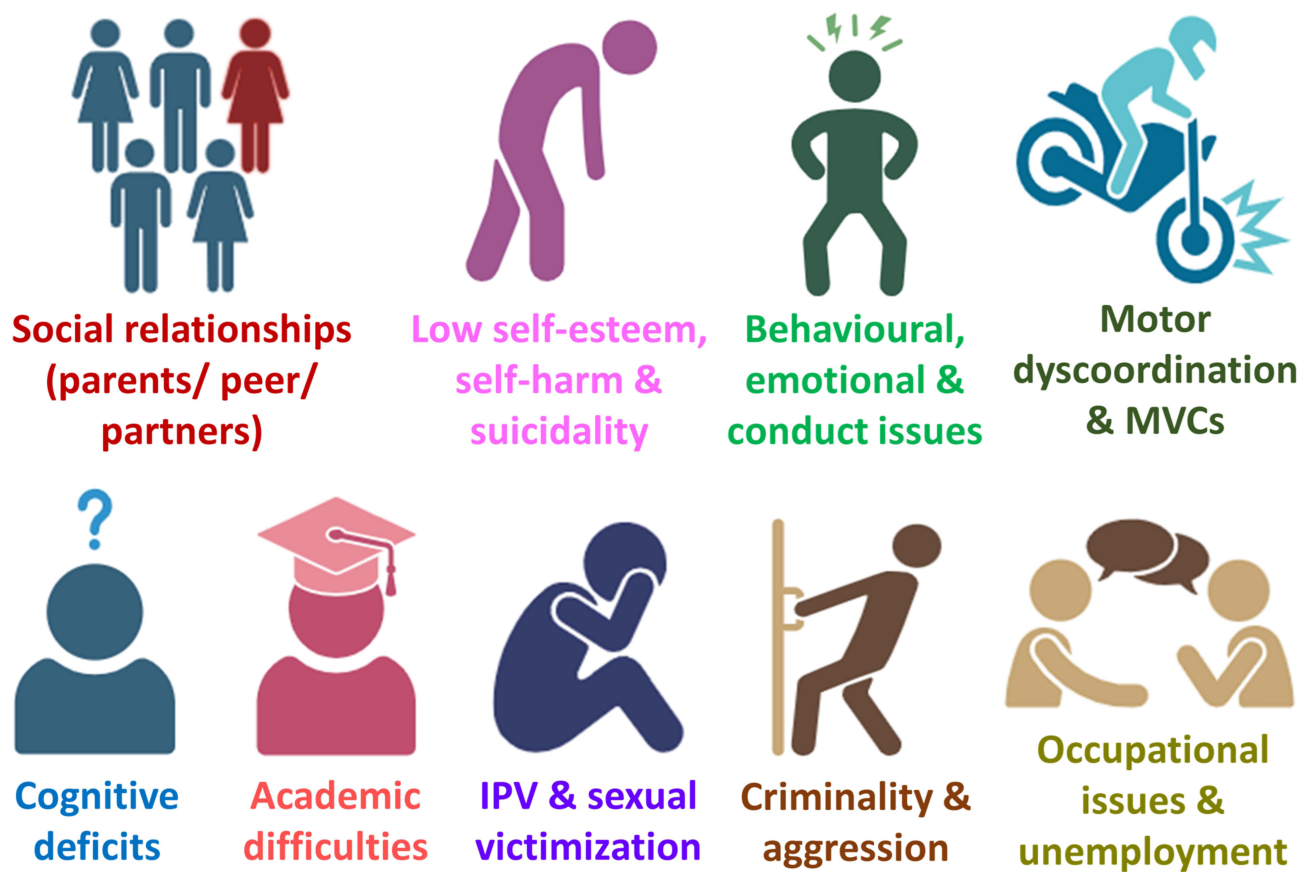


Figure 3 ADHD in adolescent and adult females and some key outcomes. ADHD in women may be associated with significant socio-behavioral, cognitive, and psychological outcomes.

Abbreviation: MVCs: motor vehicle crashes.

Outcomes and Comorbidities in Adolescence and Adulthood ADHD: Focus on the Female Gender

Psychiatric Comorbidities: Depression and Anxiety

Psychiatric comorbidities show significant co-occurrences with ADHD symptomatology, exceedingly higher when compared to other prevalent neurological conditions such as substance use disorder (SUD) and personality disorders.⁷⁵ It is estimated that the incidence of depressive episodes in adult ADHD patients may be as high as 30–60%.²¹ A high proportion of adult women with ADHD also show comorbid depressive and anxiety-like behaviors.⁷⁶ Data from multiple independent studies indicate that, compared to their male counterparts, girls and women with a diagnosis of ADHD-like symptoms have elevated depression and anxiety levels.^{64,65,77,78} Similar findings of gender-based elevations in seasonal depressive symptoms in female ADHD cases were reported by Bijlenga et al.⁷⁹ Interestingly, adult women with ADHD have a complex bidirectional relationship with depressive behavior. While there is a strong association between ADHD symptoms and the age of onset, severity, frequency, and persistence of depressive episodes, ADHD symptoms also serve as predictors of antidepressant usage.⁸⁰ The relationship between ADHD symptomatology and depressive behavior is particularly significant for pregnant women, as it severely impacts both maternal and child health outcomes.⁸¹ Further, female ADHD subjects who have suffered abuse or neglect during adolescence are predisposed to develop psychological issues of anxiety and depression, and are more prone to elicit lowered self-worth and to induce self-harm.⁸² Psychiatric comorbidities in ADHD females may also be moderated by breathing problems during infancy and early gestational

age.⁸³ Interestingly, ADHD girls with comorbid depressive phenotypes have been evidenced to have higher body weights,⁸⁴ an observation that may moderate the relationship between ADHD symptomatology and eating disorders.

Anxiety disorders also have an exceptionally high incidence of ADHD, with a comorbidity rate approaching 25%.⁸⁵ Adult women with ADHD show predominant hyperactivity/impulsivity phenotype, and are more susceptible to developing anxiety issues.⁸⁶ Comorbidity of ADHD and anxiety may result in severe sleep issues,⁸⁷ and attentional deficits.⁸⁸ Comorbidity of ADHD and anxiety disorders is thought to elicit differential phenotypes across ages. Thus, while adolescents with ADHD and anxiety issues show working memory deficits, co-occurrence of the two conditions in adulthood may result in aggravated sleep dysfunctions.⁸⁷ Young adult women with ADHD may be more prone to higher academic examination-related anxiety and cognitive obstruction, in addition to lowered self-esteem.⁸⁹ Lastly, psychiatric comorbidity in adult ADHD patients has been reported to be a significant moderator of enhanced mortality risk, particularly due to unnatural causes such as suicides and unintentional injury.⁹⁰

Borderline Personality Disorder (BPD)

ADHD cases have high incidences of psychiatric comorbidities. Amongst them, BDP is a prominent condition,^{91,92} and shows a comorbidity ranging between 16–38% in adult ADHD subjects.^{93,94} Evidence suggests that the configuration of ADHD symptomatology (inattention, hyperactivity, and/or impulsivity) is closely linked to the appearance of comorbidity of BDP,⁹⁵ probably due to shared genetic and environmental factors, and their interactions.⁹⁶ Other common phenotypic manifestations of the two neurological conditions include substance abuse, lowered self-esteem, and deficient ability to form and maintain social relationships.⁹⁷ In adult women, the most prominent behavioral linkers appear to be executive function deficits and childhood adverse events,⁹⁸ as well as the presence of emotional dysfunction.⁹⁹ Women with BPD may have a high prevalence of ADHD symptoms, both during childhood (45%) and adulthood (16%), with exposure to emotional adversities being one of the significant risk factors. Moreover, the co-occurrence of adulthood ADHD in these cases may be associated with an increased chance of developing Axis I and II mental illnesses.⁹³ Further, it has been reported that ADHD cases with all three symptomatic traits have a greater risk of developing BPD, with impulsivity and emotional dysregulation forming the most prominent underlying factors.^{94,100}

Emotional and Socio-Behavioral Dysregulation

ADHD symptoms in adults are associated with comorbidities of severe emotional and behavioral issues. Diminished reactivity to positive visual stimuli in ADHD adults may be partly responsible for deficits in their motivation/reward systems, culminating as emotional dysregulation.¹⁰¹ Interestingly, emotional dysregulation has been envisioned as one of the primary symptoms differentiating adulthood ADHD from childhood symptomatology.^{22,102,103} Co-occurrence of emotional deficits in ADHD cases is estimated to be significantly higher in adults (34–70%), compared to children (25–40%).¹⁰⁴ Manifestation of emotional issues, however, is dependent on age, with childhood ADHD associated with separation and elimination anxiety, and adolescent cases showing predominant co-occurrence of depression, obsessive-compulsive disorder, bipolar disorder, and social anxiety.⁷⁸ Adulthood ADHD cases also show enhanced risk of developing behavioral comorbidities of conduct and oppositional defiant disorders.¹⁰⁵ Female adults with ADHD diagnoses are particularly vulnerable to emotional dysregulation.¹⁰⁶ This may be mediated by overt aggressive behavior, depressive and anxious phenotype, and eating pathology in female ADHD subjects.^{107,108} Unsurprisingly, conduct issues are mainly predicted by the severity of inattentive phenotype in female ADHD cases.¹⁰⁹

Social deficits with friends, peers, and family are excessively manifested in cases with adulthood persistence of ADHD, compared to remitted individuals, with an odds ratio of 6.26.¹¹⁰ Multiple reports suggest that female subjects with ADHD are more socially impaired and experience greater peer rejection than their neurotypical counterparts.¹¹¹ Moreover, these subjects experience significantly higher victimization and bullying by their peers.¹¹² Interestingly, a study conducted in adolescent ADHD subjects revealed that female subjects showed greater compliance and self-management, and more appropriate peer relationships under single-gender settings than in mixed-gender settings.¹¹³ However, the social behavior of boys with ADHD was exactly opposite to this. Due to the propensity of female ADHD subjects to show socially inappropriate and detrimental behavior, their ability to form favorable peer relationships is considerably diminished.¹¹⁴ In fact, compared to their male counterparts, this appears to be a more severe issue in

preadolescent girls with ADHD.^{71,115} Furthermore, women with ADHD are highly susceptible to social stigmatization and rejection, resulting in severe impacts on their psychological and academic functioning.¹¹⁶ Thus, girls with ADHD have difficulty forming and maintaining friendships, while they are more likely to engage in negative aspects of relationships with their peers, such as conflicts and aggression.¹¹⁷ Heightened moodiness, stubbornness, and anger may be some features of female cases of ADHD¹¹⁸ which are bound to repress their ability to form friendships. The greater inability of ADHD girls to form sustainable friendships is crucial in light of evidence indicating that the presence of friendships may protect them from victimization.¹¹⁹ There is some evidence that, in preadolescent and adolescent girls, there is a significantly higher association of aggressive behavior with ADHD pathology, possibly due to peer disregard. Furthermore, the combined manifestation of the symptoms (ADHD-C) increases this association in comparison to elicitation of only the inattentiveness phenotype,¹²⁰ indicating that girls with ADHD-I are able to better control their aggression and have the ability to express it subtly and in a more acceptable manner. On the other hand, ADHD-I girls are more socially isolated than ADHD-C girls, although the former group faces less peer rejection.¹¹⁵

Quality of Romantic and Sexual Relationships

It appears that the predominance of hyperactivity/impulsivity and inattention symptoms in adults with ADHD leads to differential deficits in romantic relationships.¹²¹ A study conducted by Bruner et al in a sample of college undergraduates revealed that both male and female patients with ADHD-C experienced lower levels of relationship satisfaction, and in women, ADHD symptoms of hyperactivity/impulsivity and inattention contributed significantly to reduced relationship quality.¹²² The persistence of the core symptoms of ADHD into adulthood increases the chances of emotional impulsiveness, which in turn may result in severe impairments in educational and occupational/financial outcomes, and may predispose individuals to driving and criminal offences.¹²³ Emotion dysregulation as a mediator of poor romantic relationships in adult ADHD cases has been confirmed by Bodalski et al in a wide age range of subjects, not just young adults.¹²⁴ Furthermore, they proposed that emotional dysregulation extends beyond simple romantic relationships and can expand to include more general social functioning.

In adolescent women with ADHD, both hyperactivity/impulsiveness and inattention symptoms are negatively associated with the quality of romantic relationships.¹²² Additionally, young females with ADHD show greater levels of stress and hostile relationship conflicts and face more difficulties in regulating their emotions. It is likely that perceiving higher levels of stress in everyday life and increased conflicts in other interpersonal relationships (eg, with parents) contribute to enhanced difficulties in emotion regulation and the formation and maintenance of romantic relationships in young adult females with ADHD.

Interestingly, extended periods of social and romantic isolation and exclusion, lowered self-esteem, emotional distress, and repressed mood may cause adults with ADHD to indulge in hypersexuality, a type of behavioral addiction perceived by the subjects as a coping mechanism to alleviate daily life stress and negative emotions. Indeed, ADHD symptomatology is associated with hypersexuality in both male and female adults.¹²⁵ However, problematic pornography usage, a form of hypersexuality, was dependent on ADHD symptoms only in men, indicating that women may opt for other forms of sexual activity to cope with the low quality of their romantic relationships. Nevertheless, ADHD symptomatology in women is associated with risky sexual behaviors such as indulgence in sex before 15 years of age, sex with a higher number of high-risk sexual partners, and disregard for protective strategies during sex (eg, condom).¹²⁶ Unsurprisingly, the risk of teenage pregnancies is considerably enhanced in girls with ADHD, with an estimated odds ratio of 6.8, as reported in a Swedish sample of pregnant females.¹²⁷ Difficulties in self-regulation pertaining to the use of contraceptives and/or non-availability or non-adherence to sex education and counseling might partly explain these results. Similarly, pregnant girls and women with ADHD diagnoses have been shown to indulge significantly more in risky behaviors of alcoholism, substance use, and smoking and were associated with enhanced obstetric and perinatal oddities.

Sleep Dysregulation

There is strong evidence of an association between sleep dysregulation and ADHD symptomatology in adolescent and adult individuals, with the prevalence of insomnia estimated at 67% in ADHD cases compared to 29% in controls.¹²⁸ Similarly, a recent meta-analytical study estimated the overall prevalence of ADHD in narcolepsy patients to be 25%,

with an exceptionally high odds ratio of 9.6 when healthy subjects were used as controls.¹²⁹ Unsurprisingly, sleep dysfunctions such as insomnia with difficulties initiating and maintaining sleep, obstructive sleep apnea syndrome, restless legs syndrome, periodic limb movement disorder, and sleep-related breathing disorders have been observed to have significantly higher manifestations in the adult ADHD population.^{130–133} The prevalence of delayed sleep phase syndrome (DSPS) is unexpectedly higher in adults with ADHD symptoms, resulting in reduced sleep time, longer latency, and increased nighttime activities.⁷⁹

Excessive sleepiness or hypersomnia during the daytime appears to be a crucial outcome of dysregulated circadian rhythms associated with ADHD symptomatology in adults.¹³⁴ In fact, such sleep dysregulation in adult ADHD subjects is thought to be a key mediator contributing heavily to cognitive, behavioral, psychiatric, emotional, and dietary impairments.¹³⁵ It has been reported that the entire circadian system of adult ADHD cases, including the molecular components, is dysregulated,¹³⁶ resulting in altered daytime functioning and a preferred evening chronotype.¹³⁷

College students with ADHD appear to experience severe sleep-related problems. Unsurprisingly, hyperactivity symptoms were a more robust predictor of decreased sleep duration in students. On the other hand, inattention symptoms in college students with ADHD may be associated with an increased need for higher sleep quality and duration.¹³⁸ Other sleep quality variables such as delayed onset of sleep, sleep quality, and increased daytime sleepiness are known to be associated with adult ADHD, particularly the ADHD-C subtype. In fact, after adjustment for age, 92% of ADHD-C cases reported going to bed late, compared to 57% of ADHD-I cases.¹³⁹ Brevik et al estimated the prevalence of insomnia in adult ADHD-C patients to be 78%, which was significantly higher than that in adults with the ADHD-I subtype (56%).¹²⁸

Eating Disorders and Obesity

Poor dietary intake and eating disorders (eg, binge eating, anorexia nervosa, and bulimia nervosa) are other comorbidities that frequently manifest in adolescent and adult cases of ADHD.¹⁴⁰ Sex appears to be a crucial moderator of the association between ADHD symptomatology and eating disorders. Thus, women with ADHD have a greater prevalence of bulimia nervosa and anorexia nervosa than their male counterparts.¹⁴¹ In fact, women with ADHD might be 3.6 times more at risk of developing eating disorders than neurotypical controls.¹⁴² Multiple factors may influence the incidence of altered eating behaviors in these subjects. Among these, psychiatric comorbidities (depression and anxiety), mood, and emotional dysregulation were the most significant. In general, the impulsivity phenotype is thought to mediate the link between ADHD and eating disorders. In women, severity of altered eating behavior, however, is thought to be primarily dependent on the inattentiveness phenotype, rather than impulsiveness or hyperactivity.¹⁴³ Poor diet may also have a bidirectional relationship with ADHD symptomatology, as adults with ADHD show low frequency of meals, reduced intake of fruits and vegetables, and increased consumption of sweets, and the resultant nutritional deficiency may in turn aggravate disease outcomes.^{55,141}

Obesity is defined as a body mass index (BMI) greater than 30 kg/m², while overweight individuals have a BMI in excess of 25 kg/m² but lesser than 30 kg/m².¹⁴⁴ Several studies have indicated a close relationship between ADHD and the development of the obesity phenotype.^{145,146} Circadian disruptions and consequent abnormal eating habits may contribute to this association.¹⁴⁶ Hormonal control of eating behavior is also thought to be disrupted due to sleep cycle changes in ADHD cases. Patients with ADHD have reduced appetite throughout the day and later binge eating during odd hours.¹⁴⁷ Additionally, the disturbed sleep cycle of ADHD patients can cause tiredness and loss of energy, increasing the consumption of high-calorie food. Inattentiveness and impulsivity, the two most significant attributes of ADHD cases, as well as depressive comorbidity, also contribute to dysregulated eating patterns in ADHD cases.^{141,148,149} Notably, obese individuals have a higher prevalence of ADHD, and pharmacological control of the latter's symptomatology may help in reducing body weights.¹⁵⁰ ADHD co-occurrence in obese subjects is known to aggravate abnormal eating behavior, resulting in excessive binge eating, snack consumption between meals, nighttime eating, and eating in secret.¹⁴⁷

The prevalence of ADHD symptoms in obese adult women is particularly high, with an estimated value of approximately 28%.¹⁵¹ More than 40% of women with childhood ADHD appear to become obese during adulthood, which is significantly higher than the comparison neurotypical control group.¹⁵² A significant contribution of ADHD symptomatology to binge eating and depressive symptoms has been reported in these women.^{151,153} Furthermore, while the presence of the ADHD phenotype may retard treatment measures against obesity in women, anti-ADHD control

measures increase the efficacy of obesity-controlling regimens.¹⁵⁴ In view of the association of ADHD symptomatology with obesity, which is a known risk factor for diabetes, it is hardly surprising that diabetic pathology has been shown to be overexpressed in ADHD adolescents and young adults. In fact, the hazard ratio of developing type II diabetes mellitus in a Taiwanese sample with ADHD compared to normal controls was estimated to be 3 after adjustments for demographic variables and clinical comorbidities.¹⁵⁵

Behavioral Addiction: Gambling Disorder and Internet Addiction

Gambling disorder, or pathological gambling, is a notable form of behavioral addiction that has been shown to be associated with adult ADHD symptomatology.¹⁵⁶ Brandt and Fischer, for instance, investigated a cohort of pathological gamblers and reported that adult ADHD cases elicited enhanced severity of gambling problems.¹⁵⁷ Persistence of ADHD-like symptoms into adulthood results in a higher risk of gambling problems compared to individuals with childhood-limited ADHD symptoms.¹⁵⁸ In fact, the prevalence of ADHD symptoms in adulthood among problem gamblers has been reported to be as high as 20–25%.^{159,160} Cases with comorbidity of gambling disorder and ADHD, compared to non-ADHD cases of pathological gambling, spend more time gambling, elicit a faster progression towards its pathological state, and have a high incidence of comorbid conditions of substance use.¹⁵⁹ Moreover, age appears to be a positive moderator of the relationship between ADHD pathology in adults and gambling severity; however, gender may not be a significant contributor.¹⁶¹

Many studies have shown a strong association between internet addiction and ADHD symptomatology in adolescents and young adults.¹⁶² For instance, a Korean group reported a high incidence of internet addiction in ADHD cases compared to controls.¹⁶³ Similarly, a significant association between ADHD symptomatology and the use of internet-based digital media has been reported in American adolescents.¹⁶⁴ Several factors may predispose ADHD cases to internet addiction, including impaired self-regulation, high boredom, opportunity for multitasking, and desire to achieve immediate (internet-based) rewards. The relationship between internet addiction and ADHD may be determined mainly by inattentiveness and hyperactivity phenotypes but is moderated by other factors such as sleep dysregulation, anxiety, depression, introversion, and substance abuse.^{165–167} While age may not be a factor determining this relationship, gender seems to play a prominent role, with internet addiction being less prevalent in female ADHD subjects.¹⁶² Nonetheless, the presence of ADHD symptoms has been shown to be a significant predictor of internet addiction in female adolescents.¹⁶⁸

Chemical Addiction, Substance Use Disorder (SUD) and Smoking

Multiple lines of evidence have established a high propensity of illicit drug usage amongst adolescent and adult ADHD cases, both during academic life as young adults,¹⁶⁹ and in late adulthood.^{170,171} In fact, persistence of ADHD into adulthood has been shown to be a significant risk factor for marijuana addiction, with an odds ratio of 2.9, relative to remitted cases of childhood ADHD.¹¹⁰ ADHD in female subjects specifically appears to be a predictor of drug abuse.¹⁰⁷ Such an association of chemical addiction (nicotine, cannabis, and cocaine) and adult ADHD has also been confirmed in the Czech population.⁵⁵ In fact, adulthood ADHD may signify an independent risk factor for SUD and other forms of chemical addiction, such as smoking and drinking.¹⁷² Further, compared to controls, ADHD cases may elicit earlier onset and lengthier durations of substance use, enhanced progression of chemical abuse onset to addiction, and greater risk for treatment failures. While it has been estimated that almost half of young adults and adults with ADHD misuse stimulating drugs at some point in their lives,^{84,172} a meta-analytical study estimated the prevalence of comorbid ADHD symptomatology in 23% of all SUD cases.¹⁷³ Similarly, prevalence of cocaine use and cocaine use disorder in adult ADHD cases was estimated to be 26% and 10%, respectively.¹⁷⁴

Several factors may be linked to ADHD and substance abuse. Conduct social (parental and peer) relational and academic issues, which are common comorbidities of adolescent and young adult ADHD cases, are significant moderators of the relationship between ADHD and SUD.¹⁷⁵ ADHD symptomatology may result in severe impairments in academic, occupational, and social functioning, resulting in lowered self-esteem and mood, eventually enhancing the risk of turning to alcohol and/or drugs to cope with adversities. Patients with ADHD may resort to stimulants, perceiving them as medications to control their symptoms and cope with disagreeable daily life incidents. Indeed, among all adults with ADHD, up to 5% may tend to use both prescription stimulants and opioids simultaneously.¹⁷⁰ Enhanced impulsivity,

lack of control, and poor judgment in adult ADHD cases may also present greater chances of experimentation with harmful substances, disregarding long-term consequences.¹⁷² Furthermore, in addition to comorbid mental health and mood conditions, cardiovascular and pulmonary ailments may also increase the risk of concurrent use of opioids and stimulants.¹⁷⁰ Conversely, co-occurrence of ADHD and SUD may result in significant increases in the risk of developing psycho-behavioral conditions, such as depression, anxiety, mood disorders, conduct disorder, antisocial personality disorder, and social phobia.¹⁷⁶

Nicotine addiction is a specific case of chemical addiction that deserves special mention owing to its widespread prevalence worldwide. Meta-analytical assessments identify ADHD as an important risk factor for nicotine dependence.^{177,178} The prevalence of smoking in the adult ADHD population is estimated at 42%, compared to 26% in controls.¹⁷⁹ Women with ADHD symptomatology may be particularly prone to nicotine dependence, likely due to the influence of ovarian hormones.¹⁸⁰ It is possible that the high incidence of smoking among adult ADHD cases is mainly driven by the urge for self-medication using nicotine as a stimulant; however, common genetic and/or environmental elements such as peer pressure, deficient coping mechanisms, and dysfunctional interpersonal relationships may also contribute to this association.^{181,182} Peer interactions (smoker friend, partner, and/or parent) in particular could also play an important role in smoking initiation in ADHD-affected adolescents.¹⁸³ Further, the severity of both inattentiveness and hyperactivity/impulsiveness symptoms has been identified as significant determinants of the likelihood, onset age, and frequency of smoking.¹⁸⁴

Criminality

The association between ADHD pathology and criminality is a serious public health concern. Issues include deliberate fire-setting, property offences, physical misbehavior, and sexual crimes.^{185,186} Interestingly, in addition to being predisposed to engage in disruptive behavior,⁷⁸ adult ADHD subjects are more likely to be victims of criminal acts.¹⁸⁷ Obviously, impulsivity and low self-control are the major mediators of the association between ADHD diagnoses and increased criminal indulgences.¹⁸⁸ Of note, adolescent offenders have a high prevalence rate of ADHD, particularly in the presence of comorbid psychiatric conditions and SUD.^{189,190} In fact, ADHD may be a more significant risk factor for committing violent offences compared to other parameters such as SUD, and ADHD cases account for almost eight times more aggressive behavioral disturbances among incarcerated offenders than other groups.¹⁹¹ The prevalence of ADHD conditions in these prisoners may be as high as 14%. Indeed, data from juvenile detention/correction establishments indicate that almost 12% of boys have ADHD symptoms. In contrast, 18.5% of girls in these centers, but fewer in overall numbers, showed manifestations of ADHD symptomatology.¹⁹² In adults, this proportion may even be higher. For instance, Edvinsson et al reported that a whopping 50% of female prisoners showed ADHD-like behavior.⁵⁸ Along similar lines, prisoners of the female gender have a significantly higher prevalence of ADHD compared to their male counterparts.^{193,194} According to a study by Rösler et al, compared to neurotypical non-ADHD cases, ADHD symptomatology strongly predicts earlier first conviction, substance misuse, and BPD in female offenders.¹⁹⁵ Interestingly, medication-based therapeutic intervention has been reported to reduce the criminality rates of male and female ADHD offenders by 32% and 41% (hazard ratio of 0.59),¹⁹⁶ indicating possible utilities of controlling offensive behavior in adult ADHD subjects by appropriate provision of effective therapies.

Intimate Partner Violence (IPV) and Sexual Victimization

A strong link between childhood and/or adulthood ADHD and IPV has been reported in several studies.¹⁹⁷ The penetration of IPV in the young adult population appears to have a complex relationship with ADHD symptomatology. Overall, the presence of ADHD was reported to be associated with the perpetration of IPV resulting in injury, but it did not predict non-injurious IPV.¹⁹⁸ In contrast, hyperactivity and impulsivity were found to be significant mediators of IPV resulting in injury. Interestingly, although inattentiveness did not predict the enactment of injurious IPV, it was associated with episodes of IPV that did not result in injury. Furthermore, comorbidities of drug and alcohol abuse may serve as significant mediators of the relationship between ADHD symptoms and IPV.¹⁹⁹ Furthermore, ADHD subjects not only have enhanced chances of carrying out acts of IPV and sexual violence episodes, but are also more susceptible to being

victims of such insults.²⁰⁰ College women with ADHD, in particular, are highly susceptible to sexual victimization, with ADHD symptomatology being a significant and robust predictor.²⁰¹

Cognitive Deficits

Several studies have reported that adult patients with ADHD exhibit significantly higher levels of cognitive dysfunction in multiple domains. Altered functional connectivity in cingulo-opercular, sensorimotor, visual, subcortical, striatal, and executive control pathways, compared to neurotypical counterparts, is thought to underlie these deficits.²⁰² Executive function deficits are probably the most widely studied domain of cognitive dysfunction in ADHD adults.^{203,204} Clinical data indicates that ADHD symptoms of inattentiveness as well as hyperactivity/impulsivity are strong correlates and predictors of executive dysfunction.²⁰⁵ Adult individuals with ADHD have diminished visual cortical grey matter areas, which might contribute to their executive attentional deficits.²⁰⁶ Amongst female subjects with a history of childhood ADHD, improvements in executive functions are retarded across age, compared to controls.²⁰⁷ In addition to the obvious negative effects on academic performance, executive dysfunction in ADHD women may also contribute to social dysfunction and psychopathology.²⁰⁸ Additionally, adult ADHD subjects have significantly higher manifestations of problems associated with self-concept, which may aggravate disease symptomatology.²⁰⁹ Further, adults with ADHD have severe deficits in working memory,²¹⁰ which are aggravated by distractions induced by emotionally laden stimuli.²¹¹ Time perception and reproduction are abnormally manifested in adult ADHD cases, and this is independent of IQ, depression, and anxiety levels,²¹² which may contribute to working memory diminishments and executive dysfunctions. Long-term memory, particularly verbal memory, is deficient in adults with ADHD, possibly because of memory acquisition rather than retrieval and incompetency.²¹³ In adults with ADHD, processing facial emotions is the most affected social cognition mechanism.²¹⁴ Emotional processing, but not structural processing, of facial stimuli in adult ADHD subjects has been reported to be significantly deficient compared to age- and gender-matched controls, which may explain the impairments in their social cognition abilities.²¹⁵

Reading Disorders

Reading disorders (RD) involve difficulties in accurately or fluently recognizing words, weak decoding, and spelling disabilities.²¹⁶ The co-occurrence of RD and ADHD is estimated to range from 0.4% to 3.7%.²¹⁷ Clinical studies have shown that RD is seen in 15–45% of children with ADHD.²¹⁸ Children with ADHD and children with only RD show impairments in several shared domains, including time processing, processing speed, concentration, verbal working memory, attention, planning ability, inhibitory control, response inhibition, lexical decision, and visuospatial working memory.²¹⁹ Additionally, children with co-occurring ADHD and RD show a unique symptom of impaired rapid naming of alphanumeric symbols. They also show an increased deficiency in working memory.²²⁰ The most supported theory for the co-occurrence of these disorders is the “multiple deficit model”, which suggests that common genetic factors control a pathophysiological pathway, increasing vulnerability to both disorders.²²¹

College and Academic Experience

High prevalence of ADHD amongst college students, ranging between 2 and 12%, is a matter of substantial concern.^{222,223} Persistence of ADHD symptomatology into adulthood is associated with lowered intelligence quotient scores and impaired academic and professional performances.¹¹⁰ While overall quality of life and personal growth itself are perceived to be compromised in college-age adolescents and young adults diagnosed with ADHD,²²⁴ several other studies have indicated significant negative impact on their academic performances.^{169,225,226} Understandably, college students with ADHD report greater academic performance concerns, which is associated with their inattentive, but not hyperactive/impulsive, phenotype.²²⁷ College students with ADHD are more likely to withdraw from their registered courses and may also exceedingly indulge in risky behavior such as alcoholism and drug abuse.^{222,228} ADHD students also show an increased likelihood of becoming more aggressive under stress and have difficulties in accepting criticism or receiving social support from their peers.²²⁹ Cognitive flexibility, which refers to the ability to shift between two different ideas, think about various ideas simultaneously, or select from multiple approaches, multiple representations of an object, or multiple activities in response to a specific or dynamic situation, may be alternatively manifested in college

students with ADHD compared to their neurotypical counterparts. Kercood et al found that while students with ADHD did not display reduced levels of cognitive flexibility, ADHD symptoms, such as inattention, were still associated with decreased cognitive flexibility. Additionally, ADHD students with higher levels of cognitive flexibility showed reduced confidence in their chosen career paths compared to those with lower cognitive flexibility.²³⁰

Interestingly, the academic performance of female ADHD cases has been shown to be more strongly affected than their male counterparts.⁷¹ Further, adolescent female ADHD subjects who experience peer rejection are more likely to elicit depressed academic performance.¹⁰⁷ As expected, the inattentive phenotype is a robust predictor of academic performance in female ADHD cases.¹⁰⁹ Finally, an interview-based study indicated that female graduate students with ADHD diagnoses, despite maintaining good grades, have difficulty coping with academic pressure, resulting in heightened stress levels and poor overall quality of life.²³¹ Provision of academic and emotional motivation, both by parents and teachers, may be crucial in stimulating resilience in these girls.²³²

Motor Dyscoordination

ADHD symptomatology in children and adolescents has long been known to be associated with deficits in motor coordination.^{233,234} Studies in adults with ADHD have reported similar problems. For instance, by employing the motor function neurological assessment (MFNU) battery, Stray et al observed greater motor problems in adults with ADHD than in the neurotypical reference group. Specifically, they reported severe alterations in motor inhibition and enhanced muscle tone and pain.²³⁵ Interestingly, deficits in neuromotor coordination have been proposed to constitute a differentiating feature of ADHD with regard to other behavioral disorders, such as bipolar disorder.²³⁶ The co-occurrence of insufficiencies in motor coordination and control and fine and gross motor skills in ADHD cases may be driven by the inattentive phenotype alone, with little contribution from hyperactivity-related impairments. Furthermore, the association between ADHD and motor dyscoordination manifests equally in both sexes.²³⁴

Motor Vehicle Crashes (MVCs) and Transportation Accidents

The characteristic symptoms of hyperactivity, impulsivity, and inattention, coupled with deficits in motor, perceptual, and visuospatial executive functions in ADHD cases, can contribute to reckless behaviors while driving, leading to increased MVCs and traffic accidents.^{237,238} In addition, driving offences such as drunk driving and driving without licenses may be exceedingly manifested in adults with ADHD compared to the general population.¹⁸⁷ In recent years, evidence has emerged for the association of ADHD diagnoses with involvement in transportation accidents, which cannot be explained by chance. For instance, Curry et al investigated the association between ADHD-like symptomatology in adolescents and young adults and transportation accidents. They reported a 36% increased risk of newly licensed drivers with ADHD being involved in car accidents compared with subjects without ADHD. This association was not affected by licensing age, gender, or medication.²³⁹ Deficits in driving performance in adolescents with ADHD have also been shown to be independent of gender by Mikami et al.²⁰ However, in contrast to Curry et al, they reported significant effects of medication on hyperactivity/impulsivity and inattention attributes during driving in both sexes. Chang et al also reported a significantly elevated risk of being involved in serious road crashes in both male and female ADHD cases compared with controls. Interestingly, while medication was found to result in a lower risk of being involved in accidents in male subjects, there was no such indication for ADHD cases of the female sex.²⁴⁰ In their follow-up study with a larger sample size, however, they observed beneficial effects of medications in preventing transportation accidents across both sexes and all age groups.²⁴¹ Indeed, other reports also proposed beneficial actions of methylphenidate-based medications in improving the driving abilities of adolescents with ADHD.^{242,243}

Unemployment and Occupational Performance

Evidence indicates that adult ADHD is associated with low educational and occupational attainment and high unemployment,²⁴⁴ and is perceived as a volatile workforce with low achievement in the workplace.²⁴⁵ Compared to control values of 72%, only 22% of adults with ADHD were reported to be under paid employment.²⁴⁶ Dysregulated emotional and social behavior, as well as the presence of comorbid conditions of depression, SUD, and alcoholism, appear to be significant contributors.^{246,247} ADHD adults who are employed may manifest multiple forms of

occupational impairments, such as high absenteeism, low productivity, enhanced irritability and tolerance, lowered self-esteem, and higher susceptibility to accidents and injuries.^{248,249} In fact, the economic burden due to absenteeism/terminations and health care costs incurred due to increased risk of physical injuries as well as the presence of psychiatric comorbidities is prominently higher for ADHD adults.^{250–253} Use of medication may reduce unemployment in middle-aged adults with ADHD, with the duration of intervention showing significant association with lowered incidence of long-term unemployment. Interestingly, the beneficial effects of pharmacological intervention on unemployment in working-age women may be more prominent than in men.²⁵⁴ This gender specificity of the relationship between medication and employment may, however, be influenced by factors such as educational attainment, unemployment rates, and medication adherence and needs to be further explored.

Epilepsy and Seizures

There is some indication that the manifestation of ADHD symptomatology in young children and adolescents is significantly higher in the diseased subjects compared to controls.²⁵⁵ Conversely, ADHD children may be significantly more susceptible to developing epilepsy and show earlier onset and higher frequency and severity of the episodes.²⁵⁶ Further, health-related quality of life may be poorer in epileptic cases with ADHD compared to those without ADHD.²⁵⁷ Interestingly, ADHD-I subtype cases have exceedingly higher risk of developing pediatric epilepsy compared to ADHD-H and ADHD-C cases.^{258,259} With regard to adults, the epidemiological links for co-occurrence of seizures and ADHD are relatively less explored in adults, probably due to the presence of substantial challenges in diagnoses of ADHD in adult epileptic cases.²⁶⁰ Nonetheless, it has been estimated that the adult epilepsy population may have an ADHD incidence of rate between 35–40%,^{261,262} and co-occurrence of ADHD in adult epilepsy cases may be associated with significant cognitive impairment.²⁶³ Interestingly, there appear to be no gender-based differences amongst ADHD cases for the enhanced risk of developing epilepsy.²⁶⁴

Self-Harm, Suicidality and Premature Death

Multiple studies have reported an association between ADHD diagnoses and increased indulgence in suicide attempts, ideations, and plans. In fact, a meta-analytic study has reported an exceptionally high odds ratio of 6.7 for the association of “completed suicides” and ADHD symptomatology.²⁶⁵ Interestingly, female ADHD subjects are at increased risk of developing depressive and suicidal tendencies compared to their male counterparts.^{67,68} Even parasuicidal behavior is much more strongly manifested in adult female ADHD subjects compared to males.²⁶⁶ It has been demonstrated that female subjects diagnosed with the more severe forms of ADHD, including ADHD-C and ADHD-H, are at greater risk of suicidal behavior than those in the ADHD-I category.^{66,267}

Apart from the core ADHD features, several other factors, such as psychiatric comorbidities, social/partner/familial relationship difficulties, financial problems and sense of low achievement, substance misuse, and criminality, may aggravate suicidal tendencies and increase the number of suicidal attempts in ADHD cases.^{266,268,269} Particularly in ADHD women, heightened emotional distress due to lack of friendships and social support may contribute significantly to suicidality.^{267,270} Further, as opposed to males, lowered self-concept and self-esteem appear to be major mediators of the association between ADHD and suicidal ideation in adult women.⁶⁸ Nevertheless, even after accounting for comorbid psychiatric conditions, ADHD subjects elicit significantly increased risks of attempting and completing suicides (odds ratio of 3.6 and 5.9, compared to controls).²⁷¹

Unintentional injuries and suicide attempts resulting in death were significantly enhanced in subjects with ADHD compared with controls. The risk of such deaths is highest within the first five years of diagnosis but remains even after ten years. Additionally, the link between ADHD and premature death is stronger in adulthood than in childhood or adolescence. This could be attributed to the increased severity of ADHD symptomatology as well as the elevated risk of comorbidities in adults. Indeed, co-occurrence of risk factors such as psychiatric and mental issues, mood and conduct disorders, criminality and suicidality, vulnerability to accidents and injuries, and substance misuse in ADHD subjects presumably leads to reduced life expectancy and enhanced chances of premature death.^{90,272} Moreover, subjects with adult diagnoses of ADHD were associated with significantly increased mortality rate ratios compared to those with childhood or adolescent diagnoses of the condition.²⁷² Gender differences were strongly manifested as well, with women

and girls showing higher mortality rate ratios compared to their male counterparts, which may be explained by misdiagnosis/underdiagnosis and the consequent lack of interventions and aggravation of symptoms.²⁷²

Therapeutic Measures in Practice: Issues with Pharmacotherapy

Although novel non-invasive techniques, such as transcranial brain stimulation^{273–275} and mindfulness-based interventions^{276,277} have recently been found to be beneficial in reducing the core symptoms of ADHD subjects, pharmacotherapy remains the most widely used measure to address the disease.²⁷⁸ In general, this results in significant improvements in the core clinical outcomes of ADHD patients of all ages.^{279,280} However, there are significant challenges associated with pharmacotherapy. Non-adherence to pharmacotherapy regimens, which has been reported to be as high as 87%,^{281,282} is a significant issue, particularly for adolescents and adults.²⁸³ However, misuse of both stimulant and non-stimulant ADHD medications is a significant matter of concern,^{284,285} particularly for women with ADHD who are pregnant and/or lactating.²⁸⁶ Furthermore, misuse of anti-ADHD medication in women may be associated with mental health and eating habits.²⁸⁷ This is also true for cases in which ADHD persists into adulthood.²⁸⁸ Tolerability of administered medication may also be a significant issue.²⁸⁹

Additionally, adverse side effects have been reported with pharmacotherapy in patients with ADHD. These include gastrointestinal, cardiovascular, and sleep disturbances.^{13,23,290,291} In particular, adverse cardiovascular side effects resulting in arrhythmia and cardiomyopathy and death in extreme cases have also been reported in adult ADHD subjects under pharmacotherapy.²⁹² In students, long-term stimulant-based ADHD pharmacotherapy may lead to a decline in academic performance.²⁹³ While short-term benefits of anti-ADHD medications are known, less is known regarding their beneficial effects in the long run,²⁹⁴ particularly in adulthood ADHD.^{19,23} Further, because of its short duration of action, pharmacotherapy may not be efficacious enough to ameliorate behavioral comorbidities associated with ADHD, including mental health and emotional/mood issues, criminality, inabilities related to education attainment/employment, substance abuse, and overall quality of life.¹³ Interestingly, while methylphenidate, one of the most widely prescribed medications for cases diagnosed with ADHD, is reported to be effective in children and adolescents,²⁹¹ its utility for adulthood ADHD is contested^{295,296} (see also),²⁹⁷ indicating age should be considered a serious factor for the recommendation of anti-ADHD pharmacotherapeutics.²⁸⁹

Due to these and other disadvantages, although this might be far-fetched, some researchers have even advocated the complete replacement of pharmacotherapy with behavioral interventions.²⁹⁸ Regardless, ADHD therapy, particularly in adults, may require multimodal regimens to address problems associated with all aspects of daily life in these neurodivergent subjects.² Indeed, during the past years, several alternative and/or complementary non-pharmacological measures have been evaluated. Such non-pharmacological therapies have elicited variable effects in ADHD children under school settings.²⁹⁹ Uncertainty of their beneficial effects, probably due to insufficient data, holds true for adult ADHD cases as well.¹³ Nevertheless, other forms of non-pharmacological behavioral and cognitive therapies have been reported to improve overall core clinical, cognitive, and mental health outcomes in adult ADHD individuals.^{277,300} Needless to say, multimodal therapeutic strategies are expected to elicit far more robust improvements in overall outcomes and functioning in ADHD cases.^{23,301} In this regard, we propose evaluations of art-based measures³⁰² as alternatives as well as complementary strategies for the overall improvement of adolescent and adult ADHD cases, including mitigation of any associated comorbidities. Because of the subtle inherent neuroanatomical and neurophysiological differences, art-based and related behavioral therapeutic regimens may be particularly relevant for the female gender.^{303,304}

Can Art-Based and Related Atypical Behavioral Measures Be Inducted in Therapeutic Regimens for the Benefit of Adolescent/Adult ADHD Cases?

The British Association of Art Therapists defined art therapy as a form of psychotherapy for communication and expression.³⁰⁵ The American Art Association has similarly defined art therapy as “an integrated social service and mental wellness line of work that enriches the lives of people, organizations, and families through artistic active creation, applied psychological concepts and creative processes, and human interactions within a psychotherapeutic

relationship".³⁰⁶ Hence, art therapy may be regarded as the application of artistic techniques centered on producing creative expression, increasing concentration and attention, enhancing self-concept, and conveying memories and emotions in order to tackle various psychological issues and improve mental health.³⁰⁷ Varying forms of art-based therapies for improvements in multiple functional parameters, including self-esteem, emotional expression, social skills, and cognitive and academic performances in childhood ADHD cases, have been evaluated, and with good effects.^{308–311} However, while results from several trials have reported beneficial effects of art-based therapeutic regimens in traumatized, depressed, and anxious subjects,^{312,313} their implications for adults diagnosed with ADHD have largely remained obscure. In this section, we propose the use of multiple art-based strategies to improve disease outcomes and associated comorbidities in adolescents and adults with ADHD. Particular focus is given to women with ADHD in whom art therapy-based interventions may result in improved self-concept and expression, social skills, and decision-making, consequently enhancing feelings of empowerment, pride, and trust.³¹⁴

The structural activities of each person's approach to art therapy are unique, as is the provision of therapy. Thus, as opposed to children, where school-based therapies may result in the best results, older individuals may prefer their dwelling places for this purpose.^{315,316} The same applies to the type of activity that may form the basis for art-based interventions in adult ADHD individuals. Play- and toy-play-based therapeutic regimens appear to be the best suited for childhood ADHD.^{317,318} On the other hand, for adults, music-based interventions are probably the most well-known and implemented regimens for therapeutic applications in neurological conditions, including ADHD.³¹⁹ In women with ADHD specifically, music may act as a tool for enhancing self-concept and self-expression.³²⁰ Related paradigms of therapeutic interventions based on dance,^{321,322} and drama³²³ have also yielded promising results in adolescents and may be used for more mature ADHD cases. Dance/movement therapy, which heals mind-body links, in particular seems to be an effective measure to improve multiple outcomes in neurodivergent children, including those with ADHD.³²⁴ In this regard, congregational group dance/movement therapy may be more beneficial in improving social, behavioral, emotional and cognitive outcomes in ADHD adults as similar group, rather than solitary, art-based,³²⁵ and play-related³¹⁸ activities have yielded better results for neurodivergent children. Indeed, appropriate social interactions have been proposed to form a significant basis for alleviating the overall quality of life in ADHD cases.³²⁶ Our view of the enhanced therapeutic effects of social vs solo programs is also supported by evidence of the successful implementation of social activity-based paradigms, such as therapeutic summer treatment programs in children^{327,328} and adolescents.^{113,329} Similarly, dyadic dramatic play involving close contact between ADHD subjects and their caregivers has been demonstrated to elicit beneficial effects on social and behavioral parameters.³³⁰

Another key sphere of movement-based behavioral therapy, although not strictly in the domain of art therapy, which has been shown to be beneficial in alleviating ADHD symptoms and enhancing academic performance in neurodivergent subjects, is martial arts.³³¹ In general, physical activity of different kinds has been shown to stimulate emotional, cognitive, and socio-behavioral outcomes in young ADHD cases.³³² In female adults with ADHD, for instance, Pilates exercise is associated with enhanced sustained attentiveness.³³³ Regarding martial arts-based therapy, a study that evaluated the effects of Tae Kwon Do training on ADHD cases reported that martial arts for 12 months resulted in decreased inattentiveness, hyperactivity, and impulsivity in four out of six subjects.³³⁴ However, further studies with increased sample sizes and in female cases are required to obtain conclusive results.

Apart from the movement-based therapies discussed above, non-conventional nature-based³³⁵ and person-centric expressive³³⁶ domains of art-based therapeutic interventions may also be attempted in adult female ADHD cases. Some pertinent examples include the use of flowers in the therapeutic regimen, since floral artwork has been suggested to be suitable for stress reduction, mood and emotional upliftment, and social skill enhancement in women of different ages.³³⁷ Likewise, food art therapy³³⁸ may be introduced as part of a multimodal approach for female adolescents and adults with ADHD. Similarly, horticulture-based therapeutic programs have yielded good results in enhancing the sociality of Korean children with ADHD.³³⁹ As opposed to all-natural therapeutic strategies, virtual reality-based therapies, which are based on video-generated environments and computer-simulated reality, may also be implemented to induce beneficial outcomes in female ADHD subjects.³⁴⁰ Creative writing³⁴¹ and auto-ethnography³⁴² are other novel alternative therapeutic strategies that may enhance self-concept and uplift mood in women with ADHD. Likewise, clay-based therapies have been reported to be efficient in mitigating clinical symptoms and associated outcomes in children with

ADHD,³⁴³ and may be extended to women. Similarly, while doll-making is primarily considered a therapeutic avenue for children,³⁴⁴ it may also appeal to individuals who have fond childhood memories of companionship with dolls, as they are instruments that may help in self-identification, coping with adverse memories, and enhancing a sense of safety and security.³⁴⁵ A related form of art therapy based on textile use³⁴⁶ may also be considered for women with ADHD. Lastly, “animal-assisted” therapeutic regimens, which are based upon human-animal (eg, horses and dogs) coherence, have also been shown to result in robust beneficial effects on cognitive, emotional, motivational, and social parameters of ADHD subjects,^{347,348} and may be included in the therapeutic regimen for female ADHD subjects of all ages.

In conclusion, we propose that different forms of non-pharmacological behavioral paradigms may be introduced as part of multimodal therapeutic regimens for overall improvement in symptoms and outcomes in women diagnosed with ADHD. However, this should be done in a case-specific manner and in consideration of an individual’s age, culture, and artistic interests. The provision of a multifaceted therapeutic approach will assist women in overcoming ADHD symptoms, improving their mental health conditions, developing positive thinking, reforming self-esteem, enhancing interpersonal skills, improving behavioral skills, excelling in creativity and critical thinking, reducing stress, and improving their overall quality of life.

Conclusion

Manifestation of ADHD symptomatology in adolescent and adult women is considerably different from that in childhood and male subjects. In women, ADHD may be exceedingly associated with several psycho-socio-behavioral dysfunctions, including sleep and dietary deregulations; greater risks of developing depressive behavior, anxiety, and personality issues; cognitive, academic/occupational, and motor dysfunctions; inability to form familial and social relationships; and higher odds of indulging in criminal and addictive behaviors, and self-harm, and suicidality. While the specific issues of ADHD symptomatology in adolescent and adult women are increasingly being recognized, resulting in improved diagnostic and therapeutic avenues, enhanced explorations of their specific needs, outcomes, and issues are still warranted, particularly for specific groups, such as students, the economically weak, and child-bearing women. Similarly, modules of art-based and other behavioral therapeutic regimens must be applied in a case-specific manner to complement and/or replace conventional pharmacotherapeutics. While success stories of resilience of women with ADHD give us hope, we, as researchers and academicians, also need to ensure our contributions to diagnostic and therapeutic advances in the coming years. We hope that our review will form a platform for further research aimed at in-depth evaluations of the sex specificity of diagnoses, symptomatic and comorbid presentations, and therapeutic avenues for ADHD in adult females.

Abbreviations

ADHD, attention deficit hyperactivity disorder; ADHD-C, ADHD with combined symptoms; ADHD-H, ADHD with predominantly hyperactive/impulsive symptoms; ADHD-I, ADHD with predominantly inattentive symptoms; ART, assisted reproductive technology; BMI, body mass index; BPD, borderline personality disorder; DAT1, dopamine transporter; DBH, dopamine beta-hydroxylase; DRD4/5, dopamine receptors D4/D5; DSM, Diagnostic and Statistical Manual of Mental Disorders; HTR1B, serotonin/5-hydroxytryptamine receptor 1 B; 5-HTT, serotonin/5-hydroxytryptamine transporter; IPV, intimate partner violence; MFNU, motor function neurological assessment; MVC, motor vehicle crash; RD, reading disorder; SNAP25, synaptosomal-associated protein 25; SUD, substance use disorder.

Disclosure

The authors report no conflicts of interest in this work.

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