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ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN PERIMENOPAUSAL WOMEN: THE IMPACT OF HORMONAL CHANGES ON SYMPTOM SEVERITY AND CLINICAL IMPLICATIONS – A LITERATURE REVIEW

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ABSTRACT

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) is increasingly recognized as a lifelong condition; however, the impact of the menopausal transition on its symptomatic trajectory remains significantly under-researched. In females, ADHD is frequently masked by compensatory mechanisms until midlife, leading to diagnostic delays. This review examines the neurobiological and clinical intersection between fluctuating ovarian steroids and ADHD pathophysiology.
Methods: A narrative synthesis of 20 selected scientific sources was conducted, incorporating neuroendocrinological reviews, clinical cohort studies, neuroimaging data, and qualitative research.
Results: Evidence indicates a "double whammy" effect from the convergence of neurodevelopmental dopamine deficiency and perimenopausal estrogen withdrawal. 17β-estradiol acts as a critical neuromodulator of dopaminergic and serotonergic systems, exerting neuroprotective effects on the prefrontal cortex. Its decline during perimenopause unmasks previously latent ADHD symptoms, exacerbating executive dysfunction ("brain fog"), inattention, and emotional dysregulation. Women with hormone-related mood disorders such as PMDD exhibit heightened vulnerability. Additionally, "diagnostic overshadowing" frequently occurs, whereby ADHD symptoms are misattributed to menopausal depression or anxiety. The analysis highlights the efficacy of lisdexamfetamine in mitigating cognitive deficits in this demographic.
Conclusions: The menopausal transition represents a period of significant clinical vulnerability for women with ADHD. Optimizing outcomes requires individualized, interdisciplinary strategies integrating stimulant pharmacotherapy with Hormone Replacement Therapy (HRT) and gender-sensitive psychoeducation. Future longitudinal research is essential to establish standardized clinical guidelines.

KEYWORDS

Attention-Deficit/Hyperactivity Disorder (ADHD); Women; Perimenopause; 17β-estradiol; Dopamine

CITATION

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Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a multifaceted neurodevelopmental condition defined by enduring patterns of inattention, hyperactivity, and impulsivity that substantially impair an individual's functioning across multiple life domains. For decades, ADHD was predominantly conceptualized as a male-centered disorder, a bias that determined diagnostic criteria and led to the systematic under-recognition of the condition in females. Contemporary expert consensus statements indicate that this under-recognition of ADHD in females is largely driven by referral biases, as well as by their distinct symptom profiles and psychiatric comorbidities (Young et al., 2020). Although the gap in diagnostic rates between genders is gradually narrowing, women are still significantly more likely to receive a diagnosis only in adulthood. Frequently, this occurs in the fourth or fifth decade of life, following years of misdiagnosis or the eventual breakdown of long-established, high-effort compensatory strategies.

This diagnostic delay is not merely a clinical oversight; it reflects a deeper deficit in understanding the sex-specific manifestations of ADHD and its complex relationship with female endocrine physiology. In contrast to the relatively stable hormonal environment in males, females undergo a series of profound endocrine transitions throughout the lifespan - beginning with menarche, continuing through menstrual cycle fluctuations, pregnancy, and the postpartum period, and culminating in the menopausal transition. Contemporary neuroscience increasingly indicates that sex hormones, particularly estradiol, function as potent neuroregulators. A neuroendocrinological perspective suggests that the differential vulnerability of males and females to neurodevelopmental and emotional disorders may be closely linked to the influence of hormones on the organization of neurobiological systems across different stages of development (Martel et al., 2009).

By modulating dopamine receptor density and the activity of enzymes involved in neurotransmitter degradation, these steroids influence the dopaminergic and noradrenergic systems - pathways central to the pathophysiology of ADHD. Consequently, fluctuations in steroid hormone levels directly impact executive capacities, including concentration, goal-directed planning, and inhibitory control.

The perimenopausal period, defined as the transition leading up to the final menstrual period, represents a "window of vulnerability" and a critical turning point in the clinical trajectory of ADHD. During this stage, erratic and precipitous declines in 17β-estradiol levels can drastically exacerbate core ADHD symptoms, creating a "perfect coincidence" of neurodevelopmental and hormonal challenges. Perimenopausal women frequently report a marked escalation in executive dysfunction, memory lapses, and emotional dysregulation, which often coexist with hallmark menopausal symptoms such as vasomotor instability and sleep disturbances.

The clinical significance of this intersection is profound. The withdrawal of estrogen may act as a catalyst for symptoms that previously remained below the threshold of clinical detection, potentially triggering the first overt manifestation of ADHD-like impairment. Conversely, in women diagnosed earlier in life, these hormonal shifts often diminish the efficacy of established coping mechanisms and pharmacological interventions. The overlap between core ADHD symptoms and the "brain fog" typically associated with menopause leads to diagnostic overshadowing, where ADHD symptoms are misattributed to menopause-related cognitive decline or vice-versa. Despite growing clinical awareness, there remains a distinct lack of longitudinal data and standardized guidelines for managing ADHD during the menopausal transition, which prevents many women from receiving adequate medical support during this vulnerable period.

The research problem of this paper focuses on the following question: How does the decline in estrogen levels affect the cognitive architecture of women with ADHD during perimenopause? This literature review aims to synthesize current evidence regarding the impact of hormonal changes on ADHD symptom severity in midlife. It explores the neurobiological mechanisms through which estrogen withdrawal influences executive function, examines the diagnostic challenges inherent in this life stage, and discusses the clinical implications for treatment. Understanding the interaction between sex steroids and neurotransmission allows for more precise therapeutic design, including the evaluation of the roles of stimulant medications and Hormone Replacement Therapy (HRT). By identifying existing knowledge gaps, this paper seeks to bridge the divide between psychiatry and gynecology, advocating for a lifespan-oriented, gender-sensitive approach to ADHD management.

Methodology

The present literature review was conducted to synthesize current scientific knowledge regarding the intersection of Attention-Deficit/Hyperactivity Disorder (ADHD) and the perimenopausal transition in women. Given the emerging nature of this field, a thematic synthesis approach was employed to integrate findings from neurobiological, clinical, and qualitative studies.

A comprehensive search of electronic databases, including PubMed, PsycINFO, Embase, and Scopus, was performed. The search was limited to peer-reviewed articles published between 2009 and 2026 to ensure the inclusion of the most recent advancements in neuroendocrinology and adult ADHD research. Publications from high-impact, peer-reviewed journals, including *Journal of Attention Disorders*, *Frontiers in Neuroscience*, and *Journal of Psychiatric Research*, were incorporated, ensuring scientific rigor of the conclusions presented. The search terms utilized a combination of Medical Subject Headings (MeSH) and free-text keywords, including: "ADHD", "Attention-Deficit/Hyperactivity Disorder", "women", "females", "perimenopause", "menopause", "estrogen", "17β-estradiol", "hormonal fluctuations", and "executive function".

To maintain a high level of clinical relevance and scientific rigor, the following inclusion criteria were applied:

Population: Adult females (assigned female at birth) with either a formal diagnosis of ADHD or clinically significant ADHD symptoms.

Hormonal Focus: Studies investigating the impact of endogenous hormonal shifts (menstrual cycle, perimenopause) or exogenous hormonal interventions (HRT/MHT) on ADHD symptoms.

Outcome Measures: Changes in symptom severity (ASRS, DIVA), cognitive functioning (executive function, working memory), and quality of life.

Study Type: Systematic reviews, meta-analyses, expert consensus statements, observational cohort studies, and qualitative interviews.

Exclusion criteria included studies focusing solely on childhood ADHD without a lifespan perspective, animal models (unless used for fundamental neurobiological mechanisms of dopamine-estrogen interaction), and non-peer-reviewed "grey literature."

A total of 20 key sources were selected for deep analysis. These sources were categorized into three primary thematic domains:

1. Neurobiological Mechanisms: Focused on the interaction between estradiol and the dopaminergic/serotonergic systems (e.g., Bendis et al., 2024; Barth et al., 2015).

2. Clinical Epidemiology and Symptom Presentation: Examining the exacerbation of symptoms during hormonal lows and the perimenopausal transition (e.g., Osianlis et al., 2026; Jakobsdóttir Smári et al., 2025).

3. Pharmacological and Therapeutic Interventions: Evaluating the efficacy of stimulants (e.g., Shanmugan et al., 2017) and female-specific psychosocial supports (de Jong et al., 2024). This analysis builds upon recent evidence syntheses, including systematic reviews examining the direct associations between ADHD symptoms and sex hormone fluctuations in females (Osianlis et al., 2025). Data extraction focused on identifying recurring clinical patterns, the physiological basis of "brain fog" versus ADHD inattention, and the presence of diagnostic overshadowing. This synthesis adopts an interdisciplinary perspective, integrating insights from psychiatry, endocrinology, and clinical psychology and also provides the basis for the results and discussion sections of this review.

Results

Neurobiological Underpinnings of ADHD

Analysis of the accumulated evidence, including cohort studies, systematic reviews, imaging studies, and qualitative analyses, allows for the development of a comprehensive picture of the functioning of women with ADHD, taking into account hormonal changes. The results indicate a close, bidirectional relationship between the hypothalamic-pituitary-ovarian axis and dopaminergic and noradrenergic neurotransmission. ADHD is inextricably linked to dysregulation of catecholaminergic systems, particularly the dopaminergic (DA) and noradrenergic (NE) pathways in the prefrontal cortex (PFC) and striatum. The clinical expression of ADHD in women is strongly modulated by the action of ovarian steroids, primarily 17β-estradiol (E2).

Estradiol as a neurosteroid modulating dopaminergic transmission

As evidenced by the research synthesis presented by Bendis et al. (2024) and Barth et al. (2015), 17β-estradiol (E2) extends well beyond its traditionally ascribed role as a sex hormone, functioning instead as a critical neuromodulator with broad influence over the functional architecture of the brain. Dopamine - a neurotransmitter centrally involved in reward processing, mood regulation, planning, motor response initiation, and the control of goal-directed behavior - is subject to multidirectional estrogenic influence encompassing its synthesis, release, and metabolic turnover.

At the molecular level, two complementary mechanisms through which E2 acts upon the dopaminergic system can be distinguished. Via the genomic pathway, estradiol upregulates the expression of tyrosine hydroxylase - the rate-limiting enzyme in the conversion of tyrosine to dopamine - thereby augmenting the overall availability of this neurotransmitter. Concurrently, through a non-genomic mechanism, E2 acts as an inhibitor of catechol-O-methyltransferase (COMT) within the prefrontal cortex (PFC). This is of particular clinical relevance in women with ADHD, who frequently carry the Val158Met polymorphism of the COMT gene, which confers an altered rate of dopamine catabolism. Additionally, estradiol downregulates the density of dopamine transporters (DAT), effectively prolonging dopamine's presence in the synaptic cleft and enhancing its biological availability. Neuroimaging data further indicate that elevated E2 levels correlate with increased D2 receptor availability in the striatum, potentially amplifying the efficiency of dopaminergic transmission along mesolimbic pathways.

A further dimension of estradiol's neurobiological action concerns its capacity to promote neuroplasticity. Del Río et al. (2018) demonstrated that E2 fosters synaptogenesis and increases dendritic spine density in the hippocampus and PFC. During periods of physiological estrogen decline - such as the luteal phase of the menstrual cycle or the perimenopausal transition - a functional attenuation of these synaptic connections ensues, manifesting in women with ADHD as a pronounced deterioration in working memory and executive performance.

Perimenopause as a state of relative hypodopaminergia

The irregular and progressive decline in E2 concentrations during perimenopause gives rise to a condition referred to as relative hypodopaminergia. In women with ADHD, whose dopaminergic systems already exhibit chronic dysregulation at baseline, estrogenic withdrawal serves as an additional decompensating factor, further deepening pre-existing deficits. This mechanism accounts for the clinical observations suggesting that during phases of elevated E2 - such as the follicular phase of the menstrual cycle or the premenopausal period - cognitive symptoms of ADHD may be partially masked or maintained at the threshold of compensation. Conversely, the perimenopausal decline in estrogen unmasks or substantially exacerbates difficulties with sustained attention, impulse control, and emotional regulation.

Effects on the prefrontal cortex and executive functions

The prefrontal cortex, which constitutes the neuroanatomical substrate of executive functions - encompassing working memory, inhibitory control, and cognitive flexibility - is densely populated with both subtypes of estrogen receptors (ERα and ERβ). As Shanmugan et al. (2017) emphasize, adequate E2 concentrations are a prerequisite for the optimal tuning of PFC neurons, maintaining dopamine and norepinephrine levels within the range necessary for efficient cognitive performance.

Under conditions of estrogen deficiency characteristic of the menopausal transition, this delicate equilibrium is disrupted. A reduced signal-to-noise ratio within PFC circuitry translates into subjectively experienced cognitive clouding - commonly described as "brain fog" - as well as objectively measurable declines in working memory capacity. Martel et al. (2009), and subsequently Kooij and de Jong (2025), emphasize that these phenomena are not merely epiphenomena of brain aging, but rather represent the expression of a specific interaction in which diminished estrogen levels "unmask" a latent neurodevelopmental vulnerability - present since early life, yet compensated for decades by a favorable hormonal milieu.

Beyond dopamine: serotonin and glutamate

Bendis et al. (2024) emphasize that dopamine plays a key role in ADHD, but E2 also influences the serotonergic and glutamatergic systems. Estradiol promotes the survival of serotonergic neurons and increases binding to the 5-HT1 receptor. Consequently, the decline in E2 levels during perimenopause contributes not only to the cognitive symptoms of ADHD but also to emotional dysregulation and irritability. These symptoms often co-occur during this transitional period. This "reciprocal interaction" between neurotransmitter systems explains why ADHD in perimenopause is often associated with a high burden of mood-related comorbidities.

The impact of hormonal fluctuations on the trajectory of ADHD symptoms in women: from the menstrual cycle to the perimenopausal transition

Symptom dynamics during the reproductive years and psychiatric comorbidity

Understanding the variability in ADHD symptom severity among female patients necessitates an examination of their longitudinal neuroendocrine history. Prospective studies indicate a robust correlation between the phase of the menstrual cycle and profiles of cognitive and emotional functioning. In fact, the variability of sex hormone status throughout the menstrual cycle may offer a critical explanation for the historically conflicting results of studies evaluating cognitive functions in females with ADHD (Haimov-Kochman & Berger, 2014). Roberts et al. (2018) demonstrated that during the early follicular and late luteal phases - which are characterized by the lowest estradiol (E2) concentrations - there is a statistically significant increase in inattention and impulsivity. Crucially, the exacerbation of the clinical picture correlates not only with hypoestrogenism but particularly with states wherein low E2 is accompanied by elevated concentrations of progesterone (P4) or testosterone.

It is postulated that allopregnanolone (a primary metabolite of progesterone) modulates GABAergic neurotransmission, which in women with ADHD may paradoxically induce a sensation of dysphoric slowing and "brain fog." An additional moderator of hormonal reactivity is the baseline personality profile; patients exhibiting high levels of the "sensation seeking" trait react significantly more abruptly to neurosteroid fluctuations (Roberts et al., 2018). As Wynchank et al. (2025) note, cyclical decompensations resulting from hormonal shifts are frequently misdiagnosed as bipolar II disorder, whereas the underlying etiology is the endocrine modulation of primary attention deficits.

Evidence of this population's neurobiological hypersensitivity to sex steroid dynamics is further substantiated by the drastically elevated comorbidity of hormone-dependent disorders. According to Dorani et al. (2021) and Eng et al. (2024), the prevalence of Premenstrual Dysphoric Disorder (PMDD) in women with ADHD reaches 45–46%, a rate nearly ten times higher than that observed in the neurotypical population (3–8%). A similar trajectory applies to postpartum depression (PPD), diagnosed in 40.6% of the studied cohort (Dorani et al., 2021). This pronounced reactivity to precipitous drops in 17β-estradiol during the luteal phase or the puerperium serves as a reliable clinical model and a predictor of symptom severity during the subsequent menopausal transition.

The "Double Whammy" framework and the perimenopausal transition

From a clinical standpoint, the perimenopausal period constitutes the most critical stage in the life span of a woman with ADHD. The mechanistic underpinnings of this phenomenon are elucidated by the "Double Whammy" paradigm, conceptualized by Eng et al. (2024). This framework posits that female patients with ADHD are subject to a cumulative burden of two distinct types of hormonal influences:

1. Organizational Effects: Arising from the impact of prenatal and pubertal hormones on early brain architecture, thereby establishing the neurobiological foundations of ADHD.

2. Activational Effects: Associated with the ongoing fluctuations of circulating ovarian hormones that continuously modulate real-time symptom expression.

During the perimenopausal transition, the activational factor reaches its apex. The withdrawal of the neuroprotective and pro-dopaminergic effects of estradiol is superimposed upon the aging processes of a brain already operating under conditions of neurodevelopmental dopaminergic dysregulation. This is robustly reflected in epidemiological data. A large-scale cohort study conducted by Jakobsdóttir Smári et al. (2025) revealed that the risk of severe psychological distress during perimenopause is 81% higher (OR = 1.81; 95% CI: 1.45–2.27) in patients with ADHD compared to control subjects. Notably, the clinical presentation in this cohort is disproportionately concentrated on neuropsychiatric deficits rather than typical somatic manifestations (e.g., vasomotor symptoms). Notably, 62% of patients with ADHD rated perimenopausal concentration disturbances as extremely disruptive. These findings align seamlessly with the analysis by Chapman et al. (2025), which demonstrated a strong correlation between the severity of ADHD symptoms (assessed via ASRS) and a significant decline in menopausal quality of life (MENQoL), particularly regarding occupational functioning.

Cognitive decompensation and diagnostic challenges

The progressive decline in estradiol concentrations ultimately precipitates the collapse of "masking"-advanced, highly cognitively taxing compensatory strategies that have enabled many women with ADHD to maintain high levels of social and occupational functioning for decades (Chapman et al., 2025; Eng et al., 2024). This phenomenon introduces profound diagnostic challenges. It necessitates meticulous differentiation between standard menopausal "brain fog" and an abrupt exacerbation of underlying ADHD traits. Although both phenomena manifest as deficits in sustained attention and working memory, in women with ADHD, the menopausal hormone withdrawal strikes neural networks that are already fundamentally compromised (Antoniou et al., 2021; Shanmugan et al., 2017).

This is corroborated by recent survey research (Osianlis et al., 2026), in which perimenopausal women reported the highest lifetime severity of inattentive symptoms across all hormonal life stages. Consequently, female patients in the 45–55 age bracket frequently present to psychiatric clinics for the first time, erroneously interpreting their cognitive decline as early-onset dementia. In contemporary clinical practice, these presentations most commonly represent the manifestation of a previously undiagnosed neuroatypical system (ADHD) that has been radically "unmasked" by perimenopausal endocrine restructuring.

Pharmacotherapy in the context of menopause: the LDX breakthrough

Among the most clinically significant findings in the reviewed literature are the studies by C. Neill Epperson (2015, 2017) investigating the use of lisdexamfetamine (LDX) in menopausal women.

Efficacy of LDX: The 2015 trial demonstrated that LDX administration in menopausal women - including those without a prior ADHD diagnosis but presenting with newly emergent executive function deficits - resulted in a 41% reduction in symptom severity as measured by the Barkley Deficits in Executive Functioning Scale (BDEFS).

fMRI and MRS Findings (Shanmugan et al., 2017):

1. Dorsal anterior cingulate cortex (dACC) activation: Neuroimaging data indicated that LDX enhances activation of the dorsal anterior cingulate cortex during tasks requiring cognitive control. The dACC constitutes a critical node within the executive control network and has been shown to be particularly vulnerable to hypoestrogenic states.

2. Neurochemical profile: Magnetic resonance spectroscopy (MRS) revealed that LDX modulates the glutamate-to-creatine ratio in the prefrontal cortex (PFC). This finding suggests that stimulant medications may compensate for the loss of estrogenic support for glutamatergic and dopaminergic neurotransmission.

Therapeutic implications

Collectively, these findings indicate that ADHD pharmacotherapy may represent a viable therapeutic alternative or adjunct to hormone replacement therapy (HRT) in menopausal women experiencing cognitive dysfunction commonly referred to as "brain fog."

Hormone Replacement Therapy (HRT) and ADHD

The evidence regarding the effects of HRT on ADHD symptomatology remains inconclusive, as emphasized by Wynchank et al. (2025) and Antoniou et al. (2021).

Selective efficacy: HRT demonstrates considerable effectiveness in ameliorating vasomotor and anxiety-related symptoms; however, its impact on ADHD-specific executive functions - including planning and response inhibition - is frequently insufficient in the absence of concomitant psychostimulant therapy.

Progestogen type: Emerging evidence suggests that synthetic progestogens used in HRT formulations may exacerbate cognitive dysfunction in women with ADHD, whereas micronized progesterone appears to be better tolerated and associated with a more favorable neurocognitive profile.

Synergistic effects: The most favorable clinical outcomes - encompassing improvements in both quality of life and occupational performance - have been observed in patients receiving combination therapy, consisting of hormonal stabilization via estradiol (E2) alongside individually titrated doses of psychostimulant agents (methylphenidate or LDX).

Discussion

The analysis of the collected research material - encompassing 20 heterogeneous publications ranging from systematic reviews and neuroendocrinological studies to large-scale cohort investigations and qualitative interviews - sheds new light on the subject of attention-deficit/hyperactivity disorder in women. The findings presented in the preceding section unequivocally indicate that menopause does not constitute merely a physiological stage marking the cessation of the reproductive years, but rather a critical neuroendocrine period that profoundly disrupts the cognitive and emotional architecture of women with ADHD. A thorough discussion of these findings necessitates a multidimensional approach, integrating neurobiological paradigms, diagnostic and therapeutic challenges, and the broader psychosocial context.

A paradigm shift: ADHD as a dynamic, hormone-dependent disorder

Historically, ADHD has been conceptualized as a static neurodevelopmental disorder, diagnosed predominantly in school-age boys and characterized by hyperactivity and impulsivity. The accumulated body of scientific evidence, however, compels a fundamental reconceptualization of this framework. In women, symptom presentation more frequently assumes an internalized form - encompassing inattention and emotional dysregulation - and, crucially, exhibits considerable dynamism across the life course, closely correlated with fluctuations in sex hormone concentrations.

Hormones such as 17β-estradiol and progesterone function as potent neurosteroids within the central nervous system. Estradiol modulates the neurotransmitter systems central to the pathophysiology of ADHD: the dopaminergic, serotonergic, and glutamatergic pathways. It increases dopamine receptor density and inhibits enzymatic dopamine degradation in the prefrontal cortex (PFC). From this perspective, the reproductive years - characterized by relatively elevated estrogen concentrations, particularly during the follicular phase - may represent for women with ADHD a form of natural, endogenous "pharmacotherapy," attenuating baseline dopaminergic deficits.

Menopause, and the perimenopausal phase in particular, abruptly disrupts this equilibrium. The decline in estradiol, compounded by chaotic hormonal fluctuations, destabilizes dopaminergic and serotonergic pathways. The result is the "unmasking" of ADHD symptoms that may have been effectively compensated for - or maintained at subclinical levels - for decades. Understanding this mechanism is of fundamental importance for contemporary psychiatry, as it demonstrates that the intensification of ADHD symptoms in women aged 40–60 does not reflect the de novo acquisition of the disorder, but rather its neuroendocrine decompensation.

Disentangling "brain fog": diagnostic challenges and the risk of misdiagnosis

One of the most pressing clinical challenges to emerge from the reviewed literature is the phenomenon of symptom overlap. The menopausal transition is associated with the occurrence of "brain fog," characterized by short-term memory impairment, difficulties with sustained concentration, fatigue, and mood dysregulation. In patients with ADHD, these symptoms affect precisely the same cognitive domains already compromised by the disorder itself.

Research conducted by Chapman et al. (2025) and Jakobsdóttir Smári et al. (2025) yields particularly valuable, if nuanced, insights in this regard. The study by Jakobsdóttir Smári demonstrated that women with ADHD face a statistically significantly elevated risk of experiencing severe perimenopausal symptoms across both psychological and somatic domains (as assessed via the PHQ-15 and MRS questionnaires). Chapman et al., meanwhile, observed that following the application of rigorous statistical correction (FDR), an ADHD diagnosis per se did not independently predict a worse objective vasomotor symptom burden relative to control

subjects. Critically, however, Chapman identifies a salient phenomenon at the level of subjective attribution: women with ADHD may differentially attribute their symptoms, ascribing memory and concentration difficulties to their ADHD rather than to menopausal processes.

This difference in symptom attribution carries profound implications for clinical practice. A gynaecologist consulted by a patient presenting with concentration difficulties may attribute these exclusively to menopause and initiate hormone replacement therapy (HRT), thereby overlooking an underlying ADHD diagnosis. Conversely, a psychiatrist may erroneously interpret an exacerbation of inattention and irritability as the onset of treatment-resistant depression or an anxiety disorder, disregarding the endocrinological substrate. This fragmentation of medical care means that middle-aged women with ADHD frequently navigate the healthcare system without receiving adequate support.

The "Double Whammy" phenomenon in its psychosocial and biological context

The qualitative analyses provided by Bürger et al. (2024) and de Jong et al. (2024) illuminate the fact that biology represents only one dimension of the problem. The "Double Whammy" framework aptly characterizes the situation confronting middle-aged women. On one hand, they experience a decline in neurological capacity attributable to estradiol withdrawal; on the other, the 45–55 age range coincides, in Western societies, with a frequent apex of life demands. These women occupy senior professional positions while simultaneously caring for adolescent children and ageing parents.

For a woman with ADHD who has spent her entire life employing exhausting masking strategies and relying on rigid structure and routine to function at a level comparable to neurotypical peers, any erosion of cognitive resources constitutes a catastrophic disruption. Qualitative interviews reveal that patients in this life phase experience profound burnout, extreme shame, and a precipitous decline in self-esteem. The loss of control over even routine daily responsibilities is described as deeply distressing. Many patients who received an ADHD diagnosis only in midlife characterize this moment as simultaneously liberating - in that it provided an explanation for why they are neither "lazy" nor "unintelligent" - and as a period of grief for the decades lived without appropriate support.

Pharmacotherapy in the era of hormonal transition: dilemmas and emerging standards

Any discussion of therapeutic interventions must engage with the landmark studies on psychostimulant use during the perimenopausal period. Research by Epperson (2015) and Shanmugan (2017) demonstrated that lisdexamfetamine (LDX) can effectively improve executive functioning in middle-aged women. The significance of these findings is twofold: they establish the neurobiological basis of cognitive difficulties and identify specific neural circuits - including the dorsolateral prefrontal cortex (DLPFC) and the anterior cingulate cortex - in which stimulant medications compensate for hormonal deficits. Notably, LDX was found to reduce glutamate (Glx) levels in the DLPFC, which become pathologically elevated in the context of estrogen withdrawal.

An important clinical implication emerging from research on dose adjustment across the menstrual cycle (de Jong et al., 2024) is the concept of flexible pharmacotherapy. These investigators demonstrated that increasing psychostimulant doses during the luteal phase - when estrogen concentrations decline - reduces both ADHD symptoms and mood fluctuations. Extrapolating this finding to the menopausal context, psychiatrists should consider reviewing and potentially adjusting medication doses in women entering perimenopause. A standard, fixed dose that has proven effective over ten years may prove wholly inadequate at the age of fifty.

The role of hormone replacement therapy (HRT/MHT) also warrants consideration. Although estrogens possess well-documented neuroprotective properties, evidence suggests that HRT alone may be insufficient to fully reverse executive deficits in patients with ADHD. The progestogen component of HRT presents an additional challenge: synthetic progestogens may further impair mood and cognitive function. The optimal therapeutic approach therefore appears to involve synergistic collaboration between a gynaecologist - responsible for establishing an appropriate HRT regimen, ideally incorporating transdermal estradiol and micronized progesterone - and a psychiatrist tasked with optimising stimulant dosing.

The significance of comorbid conditions: PMDD, postpartum depression, and menopause

A discussion of menopause requires situating it within the broader context of a lifespan approach to women's health. The study by Dorani et al. (2021) documented strikingly elevated prevalence rates of premenstrual dysphoric disorder (PMDD) (45.5%) and postpartum depression (PPD) (40.6%) among women with ADHD relative to the general population. This points to the existence of a distinct phenotype within the ADHD population - a so-called "neurosteroid fluctuation hypersensitivity" phenotype.

This association carries fundamental implications for menopausal care. A history of severe postpartum psychiatric crises or poor tolerance of the luteal phase prior to menopause should serve as a "red flag" for

clinicians, indicating a substantially elevated probability of abrupt decompensation during the perimenopausal transition. As the evidence demonstrates, menopause is not an isolated event but rather the final and most prolonged stage along the continuum of hormonal challenges in a woman's life. Furthermore, the most recent genomic and epidemiological analyses suggest that women with ADHD may enter menopause earlier than their neurotypical counterparts. Early menopause entails prolonged exposure to low estrogen concentrations, which in turn increases the risk of cardiovascular disease (CVD), osteoporosis, and dementia.

Limitations of the existing evidence base and knowledge gaps

Notwithstanding the seminal contributions of the reviewed publications, their limitations must be objectively acknowledged. The substantial majority of survey-based studies rely on cross-sectional designs. The absence of long-term longitudinal research tracking the same patients from early adulthood through pregnancy to post-menopause impedes the formulation of robust causal inferences regarding the evolution of symptoms over time.

Second, a considerable proportion of the data is derived from self-report instruments - including scales such as the ASRS and WHQ - which may be susceptible to recall bias. Neuroimaging and qualitative studies are additionally characterized by small sample sizes, limiting the generalizability of findings. A further notable deficiency is the lack of ethnic and socioeconomic diversity within the studied populations - a significant concern given that the experience of menopause and access to ADHD diagnosis vary considerably across cultural and material contexts.

Recommendations for future research and clinical practice

The foregoing discussion permits the delineation of clear directions for the advancement of both science and clinical medicine in the context of ADHD in women at midlife and beyond.

First, integrated clinical assessment: psychiatric diagnostic tools must be supplemented with endocrinological modules. Enquiries regarding menstrual history, pregnancy outcomes, postpartum depression, and current menopausal status should constitute a standard component of the evaluation of every adult female patient.

Second, longitudinal studies incorporating objective biomarkers: there is an urgent need for research combining daily hormonal assays from blood or saliva samples with neuropsychological task performance and fMRI data, enabling precise mapping of "windows of vulnerability" in women.

Third, pharmacotherapeutic optimisation: large-scale clinical trials investigating the safety and efficacy of combining various HRT formulations - including transdermal estrogens - with stimulant medications (methylphenidate, amphetamines) in women aged 45 and above are critically needed.

Fourth, medical education: training of primary care physicians and gynaecologists in the atypical clinical presentation of ADHD is essential to reduce the incidence of diagnostic errors and the prolonged suffering they engender.

The end of the reproductive years need not constitute a sentence of permanent dysfunction for women with ADHD. Advances at the intersection of endocrinology and psychiatry offer genuine hope for the development of individualised treatment protocols capable of restoring to these patients a meaningful degree of control over their health and daily functioning during the menopausal transition and beyond.

Conclusions

Based on the analysis of 20 peer-reviewed publications, clear conclusions may be drawn regarding the impact of menopause on ADHD in women. The menopausal transition constitutes a period of elevated risk for clinical instability in patients with ADHD. The principal findings of the present review are as follows.

First, confirmation of a biological association: a robust correlation exists between the decline in estradiol concentrations and the deterioration of executive functions, reflecting the established role of estrogens in the modulation of the dopaminergic system.

Second, symptom specificity: women with ADHD experience the menopausal transition with greater severity, reporting heightened psychological and somatic symptom burden, which underscores the necessity of intensified medical care during this period.

Third, treatment efficacy: stimulant medications - lisdexamfetamine in particular - demonstrate considerable effectiveness in ameliorating menopause-associated cognitive deficits, establishing them as a clinically significant therapeutic option alongside, or as an alternative to, hormone replacement therapy (HRT).

Fourth, an imperative for medical education: there is an urgent need for the systematic training of clinicians in the recognition of ADHD in adult women, with the aim of reducing diagnostic delays and facilitating timely access to appropriate support.

Future Research Directions

Long-term prospective studies tracking women with ADHD throughout the perimenopausal period - correlating daily hormonal levels with the severity of cognitive symptoms - are critically needed. A further priority is the systematic investigation of pharmacokinetic and pharmacodynamic interactions between stimulant medications and various HRT formulations, with the goal of establishing safe and efficacious combined treatment protocols. Finally, future research should focus on the development of female-specific diagnostic instruments that explicitly incorporate hormonal fluctuations as a clinically salient contextual variable.

REFERENCES

1. Antoniou, E., Rigas, N., Orovou, E., Papatrechas, A., & Sarella, A. (2021). ADHD symptoms in females of childhood, adolescent, reproductive and menopause period. *Materia Socio-Medica, 33*(2), 114–118. https://doi.org/10.5455/msm.2021.33.114-118
2. Barth, C., Villringer, A., & Sacher, J. (2015). Sex hormones affect neurotransmitters and shape the adult female brain during hormonal transition periods. *Frontiers in Neuroscience, 9*, Article 37. https://doi.org/10.3389/fnins.2015.00037
3. Bendis, P. C., Zimmerman, S., Onisiforou, A., Zanos, P., & Georgiou, P. (2024). The impact of estradiol on serotonin, glutamate, and dopamine systems. *Frontiers in Neuroscience, 18*, Article 1348551. https://doi.org/10.3389/fnins.2024.1348551
4. Bürger, I., Erlandsson, K., & Borneskog, C. (2024). Perceived associations between the menstrual cycle and attention deficit hyperactivity disorder (ADHD): A qualitative interview study exploring lived experiences. *Sexual & Reproductive Healthcare, 40*, Article 100975. https://doi.org/10.1016/j.srhc.2024.100975
5. Chapman, L., Gupta, K., Hunter, M. S., & Dommett, E. J. (2025). Examining the link between ADHD symptoms and menopausal experiences. *Journal of Attention Disorders, 29*(14), 1263–1277. https://doi.org/10.1177/10870547251355006
6. de Jong, M., Wynchank, D. S. M. R., Michielsen, M., Beekman, A. T. F., & Kooij, J. J. S. (2024). A female-specific treatment group for ADHD—Description of the programme and qualitative analysis of first experiences. *Journal of Clinical Medicine, 13*(7), Article 2106. https://doi.org/10.3390/jcm13072106
7. Del Río, J. P., Alliende, M. I., Molina, N., Serrano, F. G., Molina, S., & Vigil, P. (2018). Steroid hormones and their action in women's brains: The importance of hormonal balance. *Frontiers in Public Health, 6*, Article 141. https://doi.org/10.3389/fpubh.2018.00141
8. Dorani, F., Bijlenga, D., Beekman, A. T. F., van Someren, E. J. W., & Kooij, J. J. S. (2021). Prevalence of hormone-related mood disorder symptoms in women with ADHD. *Journal of Psychiatric Research, 133*, 10–15. https://doi.org/10.1016/j.jpsychires.2020.12.005
9. Eng, A. G., Nirjar, U., Elkins, A. R., Sizemore, Y. J., Monticello, K. N., Petersen, M. K., Miller, S. A., Barone, J., Eisenlohr-Moul, T. A., & Martel, M. M. (2024). Attention-deficit/hyperactivity disorder and the menstrual cycle: Theory and evidence. *Hormones and Behavior, 158*, Article 105466. https://doi.org/10.1016/j.yhbeh.2023.105466
10. Epperson, C. N., Shanmugan, S., Kim, D. R., Mathews, S., Czarkowski, K. A., Bradley, J., Appleby, D. H., Iannelli, C., Sammel, M. D., & Brown, T. E. (2015). New onset executive function difficulties at menopause: A possible role for lisdexamfetamine. *Psychopharmacology, 232*(16), 3091–3100. https://doi.org/10.1007/s00213-015-3953-7
11. Haimov-Kochman, R., & Berger, I. (2014). Cognitive functions of regularly cycling women may differ throughout the month, depending on sex hormone status: A possible explanation to conflicting results of studies of ADHD in females. *Frontiers in Human Neuroscience, 8*, Article 191. https://doi.org/10.3389/fnhum.2014.00191
12. Jakobsdóttir Smári, U., Valdimarsdottir, U. A., Wynchank, D., de Jong, M., Aspelund, T., Hauksdottir, A., Thordardottir, E. B., Tomasson, G., Jakobsdottir, J., Lu, D., Nevriana, A., Larsson, H., Kooij, S., & Zoega, H. (2025). Perimenopausal symptoms in women with and without ADHD: A population-based cohort study. *European Psychiatry, 68*(1), Article e133. https://doi.org/10.1192/j.eurpsy.2025.10101
13. Kooij, J. J. S., & de Jong, M. (2025). Research advances and future directions in female ADHD: The lifelong interplay of hormonal fluctuations with mood, cognition, and disease. *Frontiers in Global Women's Health, 6*, Article 1613628. https://doi.org/10.3389/fgwh.2025.1613628
14. Martel, M. M., Klump, K., Nigg, J. T., Breedlove, S. M., & Sisk, C. L. (2009). Potential hormonal mechanisms of attention-deficit/hyperactivity disorder and major depressive disorder: A new perspective. *Hormones and Behavior, 55*(4), 465–479. https://doi.org/10.1016/j.yhbeh.2009.02.004
15. Osianlis, E., Thomas, E. H. X., Jenkins, L. M., & Gurvich, C. (2025). ADHD and sex hormones in females: A systematic review. *Journal of Attention Disorders, 29*(9), 706–723. https://doi.org/10.1177/10870547251332319
16. Osianlis, E., Thomas, E. H. X., Li, Q., Bellgrove, M., May, T., Chapman, D., Kulkarni, J., & Gurvich, C. (2026). ADHD in females: Survey findings on symptoms across hormonal life stages. *Journal of Psychiatric Research, 193*, 208–215. https://doi.org/10.1016/j.jpsychires.2025.11.035

17. Roberts, B., Eisenlohr-Moul, T., & Martel, M. M. (2018). Reproductive steroids and ADHD symptoms across the menstrual cycle. *Psychoneuroendocrinology, 88*, 105–114. https://doi.org/10.1016/j.psyneuen.2017.11.015
18. Shanmugan, S., Loughead, J., Nanga, R. P. R., Elliott, M., Hariharan, H., Appleby, D., Kim, D., Ruparel, K., Reddy, R., Brown, T. E., & Epperson, C. N. (2017). Lisdexamfetamine effects on executive activation and neurochemistry in menopausal women with executive function difficulties. *Neuropsychopharmacology, 42*(2), 437–445. https://doi.org/10.1038/npp.2016.162
19. Wynchank, D., Sutrisno, R. M. G. T. M. F., van Andel, E., & Kooij, J. J. S. (2025). Menstrual cycle-related hormonal fluctuations in ADHD: Effect on cognitive functioning—A narrative review. *Journal of Clinical Medicine, 15*(1), Article 121. https://doi.org/10.3390/jcm15010121
20. Young, S., Adamo, N., Ásgeirsdóttir, B. B., Branney, P., Beckett, M., Colley, W., Cubbin, S., Deeley, Q., Farrag, E., Gudjonsson, G., Hill, P., Hollingdale, J., Kilic, O., Lloyd, T., Mason, P., Paliokosta, E., Perecherla, S., Sedgwick, J., Skirrow, C., ... Woodhouse, E. (2020). Females with ADHD: An expert consensus statement taking a lifespan approach providing guidance for the identification and treatment of attention-deficit/hyperactivity disorder in girls and women. *BMC Psychiatry, 20*(1), Article 404. https://doi.org/10.1186/s12888-020-02707-9