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Why are females less likely to be diagnosed with attention deficit hyperactivity disorder in childhood than males?

Personal View for Lancet Psychiatry

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Summary

Attention deficit hyperactivity disorder (ADHD) is less likely to be diagnosed in females than males, especially in childhood. Even when diagnosed in females, the diagnosis is received typically later than in males, and females are less likely to be prescribed ADHD medication. Given these sex differences in clinical care and treatment for ADHD, it is important to better understand why this is happening, to work towards timely diagnosis in people impacted by ADHD. This essay is a conceptual review, synthesising the literature on this topic. It considers potential biological explanations (e.g. genetic factors), the influence of diagnostic practices (e.g. criteria suitability, diagnostic overshadowing, sexspecific diagnostic thresholds), and socio-cultural explanations (e.g. sex differences in presentation, compensatory behaviours), for these observed sex differences in ADHD clinical practice. The review also outlines future research directions for improving understanding of sex differences in recognition and diagnosis of ADHD.

Introduction

Since attention deficit hyperactivity disorder (ADHD) was first formally defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Classification of Diseases (ICD), it has been observed that males are more likely to meet the diagnostic criteria than females (1,2). In clinical studies of children, the male:female ratio of diagnosis is approximately 4:1, whereas in community/population studies this ratio is closer to 2:1 (2). Given that these studies of community samples comprehensively screen a given population for likely ADHD, this suggests that there is under-recognition of females with ADHD in clinics. Indeed, in a general population sample of children screened for ADHD symptoms and impact, children who met the screening cut-off but had not been diagnosed were more likely to be female, with an odds ratio of 1.83 (3). A systematic review examining factors linked with accessing clinical care found that in children meeting diagnostic criteria for ADHD, female sex was consistently identified as a barrier to timely clinical care, in terms of recognition, evaluation, obtaining a diagnosis, receiving treatment, access and use of specialist health services, and experiencing stigma-related barriers (4). These studies indicate that at least some females who meet diagnostic criteria for ADHD are not being diagnosed clinically.

However, not all population studies take the impact of ADHD symptoms into account and the observed difference between the sex ratios of clinical and community studies could be due to less severely impacted children being under-diagnosed. When measuring ADHD traits in the population, males have consistently higher scores than females, indicating that there are likely true underlying sex differences when measuring ADHD as a dimensional trait (5).

Nevertheless, there is mounting evidence that at least part of the observed sex bias in diagnosis could be explained by under-recognition of ADHD in females, including late or missed diagnosis (6,7). By adulthood, the male:female ratio becomes closer to 2:1 or 1:1 in many samples, including screened population samples (8). This is in line with epidemiological studies observing a later average age at first diagnosis in females (9–12). Not only are females less likely to be diagnosed during childhood, they are also less likely to be prescribed ADHD medication when they are diagnosed, even after accounting for ADHD symptom severity (12–15). This is not unique to ADHD; other neurodevelopmental conditions like autism are also diagnosed less frequently and later in females (16). Indeed, this later age at first diagnosis in females is a more general pattern in healthcare, seen across a vast range of medical conditions (17).

Qualitative studies of women diagnosed with ADHD as adults identify themes of experiences of significant and varied difficulties (i.e. academic, social, psychological functioning, low self-esteem) from early childhood that were not recognised as ADHD, despite prominent ADHD symptoms and engagement with mental health services (18,19). They also identify themes related to a complex journey towards diagnosis, potential reasons for missed ADHD, traumatic experiences that were attributed by participants to lack of childhood diagnosis, and the complex but positive impact of receiving an ADHD diagnosis as adults (18,19).

These emerging qualitative studies highlight the difficulties some females have in getting their underlying ADHD recognised. This complements the quantitative epidemiological studies which provide robust evidence of sex differences in the diagnosis and treatment of individuals with ADHD. The focus of this essay is to consider possible factors and explanations that may be specifically relevant to decreased recognition, referral, and diagnosis of ADHD in females, as well as to outline future research directions in this area. See **Figure 1** for an overview of the way that different factors interact with sex to influence the expression, recognition, and diagnosis of ADHD.

Definitions of sex and gender

Despite the fact that sex and gender are distinct concepts, much of ADHD research, especially when it comes to children and young people, appears to use these concepts interchangeably. Sex or biological sex is typically defined as a binary attribute (i.e. male or female) that is assigned to an individual at birth, though a subgroup of intersex individuals falls outside this binary definition. Gender or gender identity is a socially constructed attribute that reflects an individual's sense of being feminine (e.g. girl or woman), masculine (e.g. boy or man), or an identity that falls outside this binary construct (e.g. non-binary, agender, gender fluid) or changes over time. Unless a study directly incorporates measures of self-reported gender identity or parent-reported child gender expression and behaviour, typically the study only examined the participants' sex assigned at birth. Therefore, the terms male and female will be primarily used throughout this article, particularly in relation to specific genetic and epidemiological studies. Gender will only be used for general statements about how parents and teachers perceive ADHD in children and young people, as well as in relation to studies of gender identity.

Biological factors

ADHD is familial and highly heritable (20). It is plausible that the sex chromosomes could play a role in the increased likelihood of ADHD in males. Indeed, increased levels of ADHD symptoms in carriers of sex chromosome aneuploidies appear to support this (21). However, ADHD is a highly complex and

polygenic condition, with thousands of causal variants scattered throughout the autosomal genome (22), including rare genetic variation such as copy number variants, which are large deletions or duplications of DNA segments (23). Common autosomal variants show a high genetic correlation for ADHD in females and males, indicating shared biology across sex (22,24). According to a polygenic liability threshold model, we would expect that the sex with lower prevalence (i.e. females) would have to have a greater loading of ADHD genetic factors to manifest ADHD. There is some support for this from family studies, which find an increased likelihood of ADHD in siblings of females with ADHD compared to siblings of males with ADHD (24,25). However, there is no strong evidence of such quantitative genetic sex differences at the level of common variants, rare copy number variants, or ultra-rare individual genetic mutations (24,26–28). This suggests that the observed sex differences in population studies may be better explained by other factors (e.g. sex differences in recognition of ADHD depending on the sex of family members with ADHD or other genetic factors). What can be concluded from existing genome-wide studies to date, is that there are no large sex differences in the types of genetic factors implicated in ADHD. Genetic studies of ADHD include relatively few females and further research is needed to better understand potential sex differences in genetic factors.

In terms of other biological factors, studies examining whether hormones or pubertal timing play a role in the observed sex differences are limited. A review of studies investigating the potential link between testosterone levels and ADHD found that studies in humans were limited and inconclusive (29). There is some evidence that variations in estrogen levels may exert a larger influence on mood and wellbeing in females with ADHD compared to those without ADHD (30), but its role in ADHD recognition is unknown. Studies combining males and females, as well as examining females separately, have found no association between ADHD onset and pubertal timing (31,32). It remains to be determined whether pubertal or hormonal sex differences in humans could explain the decreased recognition of ADHD in females.

Diagnostic practice & ADHD symptom types

Suitability of existing diagnostic criteria

The wording of the diagnostic criteria used for ADHD (DSM-5 and ICD-11) has largely remained the same since the publication of the DSM-IV in 1994. The field trials for establishing these diagnostic criteria built on the criteria previously published in the DSM-III and DSM-III-R and were based on a sample including only 21% females (33). As such, the symptom descriptions are likely to be more appropriate for behaviours and difficulties that typically present in males and may be less suitable for identifying ADHD behaviours in females.

Studies of the psychometric properties of ADHD measures suggest that most of the DSM ADHD items show the same measurement properties (i.e. invariance and minimal differential item functioning) by sex during childhood, indicating that these symptoms are measuring the same underlying constructs in males and females (34,35). However, one exception is several of the hyperactive-impulsive items, which have shown remarkably consistent evidence across two studies; the items 'leaves seat in classroom', 'fidgets with hands or feet', and 'runs about or climbs excessively' showed higher endorsement in males and 'talks excessively' and 'interrupts' were more likely to be endorsed in females, despite children having the same level of the latent trait of hyperactivity/impulsivity (36,37). This suggests that hyperactive-impulsive ADHD symptoms may be expressed somewhat differently in males and females.

Indeed, it has been proposed that ADHD may present somewhat differently in females. For example, the symptoms could be less overt and more internal, making detection harder (e.g. daydreaming, restless thoughts, mind-wandering), or more social relationship-oriented, in contrast to the more task-oriented diagnostic criteria; interpersonal items that have been proposed include 'impulsively changing conversation topics' and 'being forgetful or late in social activities' (7,38). Future revisions to diagnostic manuals could benefit from including sex-specific examples for existing symptoms. Measurement scales for screening and assessing ADHD could also benefit from assessing a wider range of ADHD-related behaviours. Qualitative studies of female symptom presentation (38), and also in a more gender diverse sample, would also help to determine whether additional symptoms should be included in the ADHD criteria, better reflecting ADHD in a more diverse sample of young people and adults.

In addition to the symptom descriptions, the ADHD DSM-5 diagnostic criteria also specify that at least 6 symptoms within the inattentive and/or hyperactive-impulsive domain need to be present (with at least 5 symptoms in older adolescents/adults), the symptoms need to be pervasive across multiple settings (typically at home and school for children), several symptoms (usually 3 or more) need to be evident by the age of 12, and symptoms need to cause substantial functional impairment (e.g. at home, in education, with relationships), albeit not limited to prior to age 12. Each of these criteria in turn may have an impact on reducing the likelihood of diagnosis in females.

The diagnosis of ADHD in children and young people typically requires the assessment of symptoms rated by parents/carers and teachers. It is well established that parent and teacher ratings of ADHD show a relatively low degree of correlation (39), which may be owing to situation specificity of symptoms across home and school (40). The degree of correlation between raters may differ by sex; in a population study, parent-teacher ratings were less correlated for females in early adolescence, but more correlated in later adolescence (41). However, it is unclear as to whether the degree of correlation is the same for males and females in a clinical sample. Interestingly, the male:female ratio for ADHD prevalence is higher when parent and teacher ratings agree on ADHD presence (5.3:1; males: 4.2%; females 0.8%) compared to parent-only (2.5:1; males: 14.5%; females 5.7%) or teacher-only (3.3:1; males: 13.8%; females 4.2%) ratings (42). These ratios suggest that males may be more likely to meet the symptom pervasiveness criterion than females. Another population study supports this by finding that females are more likely than males to show 'situational' ADHD, particularly at home (43). Future work needs to further examine this issue and determine whether a different pervasiveness criterion may be more suitable for ADHD assessment in females, provided that ADHD-related impairment is sufficiently high.

Sex differences have also been noted with regards to functional impact of symptoms. In children who met research diagnostic criteria for ADHD after screening in a population study, parents rated females as experiencing less functional impact than males (44). This could explain lower recognition and referral for ADHD in females, given that parents/carers are typically integral to the referral process of their children. Whether females genuinely have less impact from their symptoms or whether they are perceived to have less impact by parents remains to be determined.

A growing body of evidence has begun to reappraise the onset criterion of <12 years for ADHD, with numerous studies now identifying a subgroup of individuals with apparently little evidence of ADHD in early childhood and with symptoms emerging in later adolescence or even adulthood (45–48). Although researchers have called into question whether ADHD is always a childhood onset condition

(45), it seems that even in the absence of recognised ADHD symptoms, individuals in the 'late onset' group are likely to have some early life difficulties (e.g. cognitive difficulties), with similar levels of ADHD genetic factors implicated (48). This late onset group is significantly more likely to be female (46,48), suggesting that females may be less likely to present with early ADHD symptoms (perhaps because of using compensatory or masking strategies) and ADHD symptoms may first emerge or become more impairing later in adolescence (e.g. due to school transition, less support from parents, increasing independence, and potentially hormonal changes starting after menarche increasing both mood and ADHD severity). This could help explain why the observed sex bias in ADHD prevalence narrows by adulthood. Although the decreased male to female ratio in adulthood could plausibly also be influenced by sex differences in persistence or remittance of ADHD symptoms, a meta-analysis found that males are no more likely to show symptom remittance by adulthood than females (49).

While the diagnostic criteria are largely the same for assessing adults (albeit with fewer symptoms required for diagnosis), the transition from childhood to adulthood is associated with a greater reliance on self-reports in the diagnostic process. Young people rely on adults (particularly parents and teachers) to seek referral on their behalf. Thus diagnosis may be delayed until a young adult is able to advocate for themselves and given an opportunity to independently seek support for their difficulties. The evidence from epidemiological studies implies that seeking help for ADHD may be more likely to be the case for females, given the later age at first ADHD diagnosis (9–12).

Diagnostic overshadowing

It has been suggested that under-diagnosis of ADHD in females could be due to primary recognition of mental health difficulties that then overshadow underlying ADHD, or even initial misdiagnosis with other conditions (6,7). Co-occurring mental health difficulties such as anxiety, depression, or self-harm are very common in people with ADHD, particularly females, reflecting the sex difference seen in the general population (2,6,7). Several recent studies support the phenomenon of diagnostic overshadowing and possible initial misdiagnosis in females.

In a study of adults with recurrent depression, there was a notable proportion of females who met diagnostic criteria for ADHD but had never been diagnosed, with indications that they were more likely to show antidepressant treatment resistance (50). In an epidemiological register-based study of individuals clinically diagnosed with ADHD and a co-occurring anxiety disorder, females were more likely than males to have been diagnosed with anxiety before ADHD (11). In a small randomly selected group of young people diagnosed with ADHD, the original reason for referral for females was more likely to be emotional problems, females were more likely to receive non-ADHD medication both prior to and after ADHD diagnosis, and were more likely to have been admitted to psychiatric inpatient care before ADHD diagnosis, compared to males (51). In a large epidemiological study of national healthcare records, females with clinically diagnosed ADHD and co-occurring anxiety, depression, or another mental health condition were more likely than males to be diagnosed with the co-occurring mental health condition prior to their ADHD diagnosis (12). Similarly, in those with ADHD who received antidepressants, females were more likely than males to receive antidepressant medication prior to ADHD diagnosis (12). This study also supported the possibility of misdiagnosis, given that in people who received antidepressants prior to ADHD diagnosis, females were less likely than males to continue to receive antidepressants after ADHD diagnosis (12).

These epidemiological studies are further supported by qualitative studies of the lived experiences of females with ADHD who were diagnosed as adults and given a range of anxiety and mood-related

diagnoses prior to receiving their ADHD diagnosis, which was attributed by some participants as part of the reason their ADHD difficulties were not recognised until they were older (18,19).

Genetic studies also provide consistent evidence of sex differences in which diagnoses young people receive. In children and young people diagnosed with anxiety or depression, females showed a higher level of genetic loading for ADHD and other neurodevelopmental conditions, compared to males with anxiety/depression (11,26,27). These studies indicate that it may be anxiety or depression that manifests and gets recognised in females who are at genetic predisposition to ADHD or other neurodevelopmental conditions.

Overall, there is growing evidence that diagnostic overshadowing from difficulties such as anxiety, mood, and other mental health conditions, could influence the likelihood of timely recognition of ADHD and access to clinical care and treatment in females.

Sex-specific diagnostic thresholds

There is also emerging evidence to indicate that there is a relatively higher threshold for diagnosis in females compared to males. Even when they have high levels of ADHD symptoms, females are less likely to be diagnosed with ADHD and prescribed treatment with ADHD medications, unless they also have prominent hyperactive-impulsive, conduct, emotional, or peer problems (44,52). This implies that ADHD on its own may be insufficient for affected females to be considered for referral, diagnosis, and treatment.

One approach to considering whether a sex-specific threshold for ADHD diagnosis would make an impact is to consider subthreshold individuals. One study of children in the general population identified a prominent subthreshold group of females who had ADHD scores that were 1.5 standard deviations above the female mean score, but below the threshold for diagnosis, whereas they did not find such a subgroup in males (53). This group of females had more functional impact from symptoms than comparison females with lower ADHD scores and less impact than females scoring above the diagnostic threshold, though these groups did not differ on some measures of impact. The study supports the possibility that a sex-specific threshold for ADHD diagnosis could be beneficial for identifying females with ADHD.

Socio-cultural factors

Gendered expectations

Given that parents and teachers are typically the first adults in a young person's life to recognise neurodevelopmental difficulties and seek support on their behalf, they play an instrumental role in the diagnostic process. Due to perceptions and stereotypes surrounding ADHD as a condition occurring more commonly in males, as well as general gendered expectations of children and young people's behaviour, adults may perceive the same behaviours and difficulties differently in young people depending on their perceived gender. Studies providing vignettes describing a child's behaviour, with only the name and pronouns changed to be male or female, have found sex differences, where parents and teachers were less likely to recommend referral for ADHD, learning assistants, and counselling or other treatment for females, believing these to be less effective in females (54,55). However, the evidence is mixed, with others not reporting sex differences in teacher recognition, but rather finding that teachers are less able to identify the inattentive ADHD subtype in children (56). According to a systematic review, in children with additional academic, emotional, or

behavioural difficulties, teachers actually rate females as having more ADHD impairment than males, though they are less likely to recommend interventions for females with ADHD (57). Differences across studies could be owing to improvements in recognition and awareness of ADHD in females over time, although this will likely vary by country and other factors (e.g. teacher age, school socioeconomic level).

The decreased ability of teachers to identify the inattentive subtype (56) supports the possibility that less external presentations of ADHD symptoms are less likely to be recognised by others. This further suggests that self-reported symptoms could be better at capturing more internal or inattentive ADHD presentations, which may be more common in females (7).

Sex differences in ADHD presentation

Sex-specific socialisation and expectations of children and young people may also influence the types of ADHD symptoms that they experience. In addition to the issue that the ADHD symptom criteria may not fully capture the types of symptoms that are experienced by females with ADHD (as discussed earlier), there is also evidence of sex differences in existing symptom criteria.

There is growing recognition that ADHD in females may be more likely to present as the inattentive subtype, rather than the combined or hyperactive-impulsive subtypes (6,7,9,58). Given that these symptoms are less disruptive to others than hyperactive-impulsive behaviours, they may be less visible and less readily recognised, as seen in the teacher vignette study mentioned above (56). This could contribute to under-recognition of female ADHD. However, a meta-analysis of sex differences in symptom severity in children who were recognised and diagnosed with ADHD, found that parent-reported symptoms were similar in males and females, whereas teacher-reported symptoms of both inattentive and hyperactive-impulsive symptoms were higher in males (59). These results could be impacted by the ascertainment of samples included in the meta-analysed studies, for example if individuals with the inattentive subtype were less likely than those with the combined subtype to be included in the studies or there were sex differences in the ADHD subtype within individual studies.

Compensation, masking & scaffolding

A final area of consideration is the possibility that there are sex differences in active (i.e. compensation) and passive (i.e. masking) strategies for coping with ADHD symptoms, as well as external influences (i.e. parental or environmental scaffolding) to support difficulties. This is a rapidly growing area of research in autism, with studies suggesting that autistic people use a variety of strategies to mask or hide their difficulties and actively compensate for or modify their social behaviour to help them fit in socially (60,61). Autistic people with better cognitive abilities are more likely to engage in these behaviours, and females are more likely to use these strategies than males, in samples of children and adults (62). However, it is also becoming clear that the use of such strategies can have a detrimental effect in the longer term, particularly on the mental health of autistic people (63).

There is as yet limited research on this issue in ADHD. The studies examining late onset ADHD have indicated that both internal or individual factors (e.g. verbal ability, reading ability) and external or familial resources (e.g. family income, maternal education) are higher in the later onset group, which is more likely to be female (48). Also, it has been suggested that prosocial behaviours in females may contribute to masking their difficulties and reducing parental/teacher concerns, making diagnosis less likely, though this needs further empirical support (44). It has also been suggested that higher

cognitive ability in people with ADHD may improve abilities to adapt socially and mask underlying ADHD difficulties leading to later onset of difficulties (64), however this is unlikely to explain sex differences. A recent qualitative study identified masking as an important aspect of how people with ADHD interact with 'neurotypical' people without ADHD (65).

Further work is needed to better understand what types of compensation, masking, or scaffolding strategies may be beneficial and reduce likelihood of ADHD impairments and which strategies may mask and reduce likelihood of recognition of existing impairments that may be revealed if scaffolding/masking is not implemented, as well as the degree to which these may differ by sex. We also need to better understand whether certain masking and compensation strategies have negative consequences for individuals, as these can be emotionally difficult to maintain (65). One approach to studying the impact of masking and other strategies is to examine key life transitions or changes in circumstances that are associated with increased demands (e.g. transition from primary to secondary school, leaving school and beginning life as an independent adult, starting a family), as the changing demands of such life experiences are likely to negatively impact an individual's ability to maintain their existing support structures and strategies.

Future directions & clinical implications

Although a true sex difference in ADHD prevalence is likely to exist (2,5), there is also evidence of decreased recognition, referral, and diagnosis of ADHD in females. It is clear that the reasons behind this under-diagnosis in females are complex and multi-faceted. However, many questions remain unanswered. We need to better understand the role of hormones, pubertal timing, and genetics in the manifestation and fluctuation of ADHD symptoms. We need more high-guality studies with sufficiently large samples of females to determine whether our diagnostic criteria are adequate for assessing ADHD in females, whether sex-specific thresholds may be worthwhile, and whether additional revisions to current diagnostic criteria are needed. In particular, we need large-scale population-based epidemiological studies that longitudinally measure the development of ADHD symptoms and associated impairment in multiple settings, that are linked to real-world clinical diagnostic information. Such studies could help tease apart the degree to which ADHD is underdiagnosed in children and what the true sex bias of ADHD is in the population. We also need to learn more about beneficial internal (i.e. compensation) and external (i.e. scaffolding) factors that may help reduce the impact of ADHD, as well as less effective masking strategies and their consequences for individuals. We also need to understand how gender identity influences ADHD expression, recognition, and diagnosis, given that neurodevelopmental conditions like ADHD are associated with greater likelihood of someone identifying as transgender or gender-diverse (66).

The research demonstrates that there is inequality in timely access to clinical care and treatment for females with ADHD. UK clinical recommendations for ADHD do not differ by sex and there is no evidence that treatment with ADHD medication differs for females (7). Studies show that ADHD medication can be highly effective, improving educational and occupational outcomes, as well as reducing the risks of suicide, substance abuse, accidents, and criminality, with no robust sex differences in these effects (67). One challenge is the limited clinical resources for child and adolescent, as well as adult, mental health services, with waiting lists for ADHD assessment being long in the UK and other countries (68).

There are broader societal issues at work. As mentioned previously, later diagnosis in females has been observed across a range of medical conditions (17). In general, diagnostic criteria and medical

knowledge are often based on males, with female patients being labelled as 'atypical' when compared against these male-biased criteria (69). Further, females are more likely than males to experience adverse effects from new drugs (70). It is clear that greater attention, funding, and research is needed for female physical and mental health.

Conclusion

ADHD is frequently missed or diagnosed late in females. Although the jury is still out on whether ADHD truly shows a marked degree of male bias, it is becoming clear that there are multifaceted reasons for ADHD under-diagnosis in females. These broadly include established diagnostic practices and socio-cultural reasons, with less evidence from biological factors. Further work is needed to help improve timely recognition and diagnosis of ADHD in females. Future revisions to ADHD diagnostic criteria should ensure that these criteria are more broadly representative of a gender-diverse population of people with ADHD.

Declaration of interests

The author declares no competing interests.

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