

Neuropsychiatric Differences Between Boys and Girls With ADHD

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Childhood ADHD is a major public health problem, with prevalence estimated to be over 5 million children in the US alone. Of particular concern is the recent increase in diagnosis of the disorder. In 2011, the CDC estimated that nearly 9% of children in the US (1 of 11 children between the ages of 5 and 17) have ADHD; the diagnosis is made in approximately twice as many boys as girls.¹ Moreover, ADHD rarely exists alone. In most children with ADHD (75% to 80%), a second (or even third) psychiatric disorder develops at some point in their lives.²

The changing face of ADHD

While the overall prevalence of ADHD among children and adolescents has increased in the past 10 years, diagnosis among girls appears to have increased more rapidly. In the 1990s, the male to female ratio for ADHD was estimated to be about 9 to 1 in clinical settings and 3 to 1 in the general population.³ More recently, however, a large epidemiological study of 3907 children found that of the 8.7% who met DSM-IV-TR criteria for ADHD, 51% were boys and 49% were girls.⁴ The prevalence of ADHD is reportedly higher in women than in girls, which suggests that ADHD may be underdiagnosed in girls or, alternatively, that the developmental onset of impairing symptoms occurs later in girls than in boys.⁵

The rise in diagnosis of ADHD among girls contributes to the changing face of the disorder. For example, although there are few reported sex differences in problem behavior in infancy and early childhood, sex differences appear to emerge by age 4 years, with boys showing more aggressive and impulsive behaviors.

Two hypotheses have been posited to explain this apparent “remission” of symptoms in young girls. The first is that girls are more likely to channel their problem behavior into internalizing behaviors. In females, ADHD appears to be associated more with anxiety and depression—two-thirds of women with ADHD have comorbid depression.⁶ The second hypothesis is that the change in behavior among girls is a function of more rapid neurobiological, cognitive, motor, and social development.⁷ On one hand, this more rapid rate of development among girls may be protective against the manifestation of some ADHD symptoms in childhood; on the other hand, the onset of pubertal increases in estrogen and subsequent increases in dopamine receptors lead to an acceleration of symptoms in adolescence.⁸

ADHD is nevertheless associated with significant risks for adverse outcomes. Longitudinal studies suggest that individuals with ADHD are far more likely than those without the disorder to

drop out of school, to have few or no friends, to underperform at work, to engage in antisocial activities, and to use tobacco or illicit drugs. Also, youths with ADHD are more likely to experience teen pregnancy and sexually transmitted diseases, to drive too fast and have multiple car accidents, and to experience other psychiatric conditions as adults.⁹

What is already known about ADHD in boys and girls?

- ADHD is a neurodevelopmental disorder in which symptoms begin (most often) in preschool years and persist into adulthood. ADHD is more commonly diagnosed in boys than in girls; however, the rate of diagnosis among girls is rapidly increasing.

What new information does this article provide?

- Boys with ADHD can present with different cognitive and behavioral patterns than girls with ADHD. These differences may be because of the types of comorbid conditions, earlier maturation among girls, and failure to identify the more subtle patterns of symptoms in girls. Despite these factors, girls with ADHD remain at significant psychosocial risk into adulthood.

What are the implications for psychiatric practice?

- Up to 75% of persons with ADHD have at least one other psychiatric disorder, which often makes treatment more challenging. Assessment for and diagnosis of ADHD in girls are more complicated than in boys, because of later onset, more subtle clinical manifestations, and wording in many popular ratings scales that emphasizes behaviors seen more commonly in boys. Children who are young for grade in school tend to be rated as having more symptoms of ADHD than those who are older for grade, leading to greatest rates of ADHD diagnosis among children whose birthday is just before the cutoff for school entry. Given the proposed changes for ADHD diagnostic criteria in DSM-5, it is likely that rates of diagnosis among girls will continue to increase.

The sex paradox posits that the sex in which a given disorder is less prevalent should show greater levels of impairment than the sex in which the disorder is more prevalent.¹⁰ While initial studies suggest that girls with ADHD have better adolescent and adult outcomes than boys with ADHD, more recent findings indicate that girls with ADHD have considerably more functional impairment, including an increased risk of internalizing disorders (eg, depression, suicide), and eating pathology than girls without ADHD.^{3,11,12}

These observations occur despite the fact that with age, symptoms of hyperactivity/impulsivity decline more in girls than in boys.¹³ In fact, a recent study found that by adolescence, only 16% of girls with ADHD showed adequate social adjustment compared with 86% of girls without

ADHD.¹⁴ Another 5-year follow-up of 6- to 17-year-old females with ADHD found that by age 16, ADHD persisted in 71% of the sample.¹⁵ Girls who have a diagnosis of ADHD in childhood continue to show deficits in executive functions as adults, even if their symptoms have remitted to a nondiagnosable level.¹⁶

Early studies that compared neuropsychiatric function in boys who had ADHD with that of girls who had ADHD may have been confounded by group differences in proportion of ADHD subtype, since among school-aged children with ADHD, girls routinely present more often with the inattentive subtype, while boys are more likely to present with the combined subtype.¹³ Not surprisingly, an early meta-analysis that examined sex differences in ADHD found that boys with ADHD had greater levels of hyperactivity symptoms and externalizing behaviors, which were associated with reduced academic skills.¹¹

More recent neuropsychological studies suggest that when samples of boys and girls with ADHD are matched on subtype, girls are often just as impaired as boys, and in some functional areas (eg, planning skills), more impaired than boys.^{16,17} Other studies found that individuals with the subtype less common for their sex (ie, boys with the inattentive subtype and girls with the combined subtype) are at increased risk for cognitive dysfunction.¹⁸

Is assessment biased against girls?

The diagnosis of ADHD in girls is more complicated than in boys because of the later age of onset, more subtle clinical manifestations, and limitations associated with the DSM-IV diagnostic schema and nomenclature.^{8,19} One concern has been that the wording of DSM-IV diagnostic criteria for ADHD and the majority of rating scales are geared toward the manifestation of ADHD in boys. Some have argued that there is a subset of girls who present with symptoms of ADHD and are rated by parents and teachers as having elevated scores when sex-specific norms are used, yet they do not meet DSM-IV criteria for the disorder.²⁰ Parents tend to rate behaviors in boys (ie, inattention, hyperactivity, aggression) as more problematic than behaviors in girls (ie, relational aggression and other “feminine” behaviors).²¹

A Dutch study found that while mothers reported similar levels of disruptive behavior in boys and girls, teachers reported higher levels of concern with attention and aggression among the boys in the same sample.²² Mental health professionals may also display this bias. In a recent study, therapists were presented with 4 diagnostic vignettes: 3 vignettes illustrated some symptoms of ADHD, but not enough to diagnose the disorder according to DSM-IV criteria. Male and female versions of each vignette were created. In the male version of the vignettes, therapists diagnosed ADHD twice as often as they did with the female vignettes. This suggests that therapists do not adhere strictly to DSM-IV criteria, with consequent overdiagnosis of ADHD in boys and underdiagnosis (and undertreatment) in girls.²³

Developmental maturity also appears to play a part in the diagnosis of ADHD, and boys may be at increased risk for diagnosis because of their later development of self-control skills. A recent US study found that the rate of diagnosis of ADHD varied according to the month of the child’s birthday, relative to the cutoff date for entrance into kindergarten. For example, in approximately 8.4% of children born in the month before the cutoff, ADHD was diagnosed, compared with 5.1% of children born in the month after the cutoff.²⁴ Similar findings were also reported in a Canadian study that showed higher rates of diagnosis (relative to sex-matched peers) for both boys and girls born in the month before kindergarten cutoff.²⁵

Sexual dimorphism

There are sex differences in incidence or nature of many CNS-related disorders. Human brains are approximately 8% to 10% larger in males than in females²⁶; however, girls' brains mature earlier and are on a different trajectory. These differences are observed at birth and may be driven by sex chromosome-specific pathways that underlie sexual dimorphism or even by differences in the presence of fetal testosterone.^{27,28} It has been estimated that at birth, girls are 3 weeks ahead of boys in physical maturation and by the time they enter school, girls are approximately 1 year ahead.¹⁰ These findings are highly salient, since different maturation rates appear to be associated with different patterns of cognitive skills (eg, children identified as "late-maturing" performed better than early-maturing children of the same sex on spatial measures).²⁹

A recent meta-analysis identified sex differences in reward sensitivity—women were more sensitive to punishment than men but not more sensitive to reward; men showed higher rates of sensation-seeking than women.³⁰ It has been argued that these patterns of behavior are related and may also have sexually dimorphic phenotypic expression of genes linked to ADHD.³¹

Over the past 15 years, Giedd and colleagues at the NIMH have compiled normative growth curves for the brain. Their work reveals the heterochronous, regionally specific, and sexually dimorphic nature of brain development in which total cerebral volume is reached by age 10.5 in girls and age 14.5 in boys.²⁶

Of particular importance for understanding sex differences in ADHD are the patterns of growth in the frontal lobes and basal ganglia (both known to be anomalous in ADHD). Bush³² found that frontal lobe gray matter volume peaks at around 9.5 years in girls and 10.5 years in boys. The caudate nucleus peaks at 10.5 years in girls and at 14.0 years in boys.

By adulthood, a number of regions of the brain are larger in women than in men (after adjusting for total cerebral volume), including the frontal lobes and hippocampus.³³ Given these observations, when considering neuropsychiatric development in boys and girls in whom ADHD is suspected, it may be best to make determinations of "impairment" on the basis of sex-specific comparisons and to consider the different developmental course of ADHD in males and females.

Early neuroimaging studies of ADHD have identified widespread cortical and subcortical volumetric reductions, including delayed cortical maturation, among school-aged children with ADHD.^{34,35} To date, the generalizability of many published MRI findings in children with ADHD to girls with ADHD has been questioned because most conclusions have been based on samples consisting primarily (or exclusively) of boys, with girls underrepresented in imaging studies of ADHD.¹⁹

A recent meta-analysis of neuroimaging studies in ADHD found that only 20% of participants were female and only 50% of the ADHD samples included females.³⁶ More recent brain mapping studies of ADHD suggest a more subtle pattern of neuroanatomic differences among girls that appears to parallel the earlier reduction in externalizing symptoms.

In a study that compared functional frontal lobe subdivisions in boys and girls with ADHD (aged 8 to 12 years), both boys and girls showed reductions in supplementary motor cortex.

Conversely, boys (but not girls) showed reductions in dorsolateral prefrontal cortex, while girls (but not boys) showed reduced premotor cortex volumes. In both sexes, the differential reductions were associated with different patterns of executive dysfunction, but boys showed more relative problems with inhibitory control.³⁷

In a study that assessed basal ganglia volume and shape in boys and girls with ADHD (aged 8 to 13 years) and age-matched controls, compared with controls, boys with ADHD showed compression in several regions, including the left anterior and right ventral putamen, the bilateral mid-body of the caudate, and the left dorsolateral and right ventromedial head of the caudate.³⁸ However, no differences were observed in girls with ADHD compared with controls.

The neuropsychiatric signature of ADHD in girls

The research literature has only begun to identify a signature pattern of brain anomalies and behavioral deficits associated with ADHD in girls, in part because girls “age-out” of many symptoms earlier than boys. For example, motor development follows an earlier-maturing developmental course in girls than in boys. The developmental status of the motor system in 144 typically developing children (72 boys and 72 girls, aged 7 to 14 years) was examined by Larson and colleagues.³⁹ They found significant sex effects for atypical subtle signs (involuntary movements) and motor speed. In all cases, girls showed fewer subtle signs and were faster and more proficient than boys. Moreover, by age 7 years, many of the motor skills assessed reached “adult” level in girls, but not in boys.

A pattern of prolonged motor dysfunction emerges in boys, but not in girls, with ADHD. In a study that examined age-related reduction in motor subtle signs (overflow, dysrhythmia) in 268 children aged 7 to 14 years, boys with ADHD had more overflow and dysrhythmia than controls, while girls with ADHD did not differ from controls. Also, during this age range, girls with ADHD showed significant reduction in overflow (associated) movements, while boys showed little change during this period. This suggests that the frontal-striatal and cerebellar brain systems implicated in motor overflow and dysrhythmia mature earlier in girls.⁴⁰

In a study that examined executive functions in school-aged children with ADHD, O’Brien and colleagues¹⁷ found that both boys and girls showed similar patterns of deficit on tasks involving response preparation and working memory; however, they manifested different patterns of executive dysfunction. On tasks related to response inhibition, boys were more impaired; on tasks related to strategic planning, girls were more impaired.

Summary

The well-established sexual dimorphism in human neurobiological development extends to the patterns of behavior observed along the developmental course of ADHD. Current research suggests that the prevalence of ADHD among females is approaching that of males. Given the proposed changes in the ADHD diagnostic criteria for DSM-5 (which will raise the required age of onset of symptoms from 7 to 12), it is likely that the rate of diagnosis among girls will continue to increase. Cross-sectional research that compared boys and girls with ADHD has yielded inconsistent findings, because adolescent girls are at a different point in their development than boys of the same age.¹⁹

More recent longitudinal studies highlight the pattern of adolescent and adult risks associated with ADHD in females and bring to focus the importance of making clinical judgments in

assessment and treatment of ADHD on the basis of sex-specific comparisons. Continued work examining the sex differences in expression of ADHD from early childhood (ie, preschoolers) through adulthood is encouraged.⁴¹

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