EEG Correlates of Attention Deficit Hyperactivity Disorder in Females: Unique Manifestations, Early Detection, and Treatment Targets

Dr. Steven Rondeau BCN (EEG), QEEG-DC | December 2021

1. Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental condition characterized by hyperactivity, greater impulsivity and poor attention [1]. Epidemiological data indicate that ADHD symptoms are noticeable in **only 3-5% of school children.** For the most part, symptoms start manifesting in childhood and continue to affect behavior well into adulthood [1].

The prevalence of ADHD in boys is 2- to 9-fold higher than in girls when clinical samples are considered, and 2- to 3-fold higher in epidemiologic samples [2]. Interestingly, while ADHD prevalence seems to be more equally distributed among adult persons [3], adult women diagnosed with ADHD tend to be older than men with a comparable diagnosis [4]. In addition to the lower rates of diagnosis, girls and women with ADHD are less likely to be treated when compared with boys and men [5]. Therefore, it is important to understand whether the data on adult ADHD prevalence are incorrect or if ADHD symptoms are generally missed in girls.

Multiple factors are thought to contribute to the low rates of ADHD diagnosis in girls, including the predominant symptoms displayed **(internalizing rather than externalizing behavior)** and the subtype most represented in this population **(inattentive rather than hyperactive)** [6]. Also, comorbid affective disorders [7, 8], which may more directly affect internalizing, obsessive-compulsive disorder often accompanied by perfectionistic behaviors [9], could play a role in masking or at least mitigating ADHD symptoms in girls and consequently delay diagnosis. Other factors might include the **tendency for relational (covert) than overt aggression** [10] and also the **less common episodes of physical aggression** in girls with ADHD, when compared with boys [11]. The need for referral by others (parents and teachers) for treatment [12] and the fact that referrals are made more often for boys than for girls [13] should also be considered. **Girls with ADHD often exhibit symptoms of inattention, hyper-talkativeness and emotional reactivity**, which are often ignored by family or teachers, and affect referral/treatment rates [14-16]. In particular, inattention is typically under reported by teachers because it rarely affects the overall classroom performance, especially when schoolwork is regularly completed in spite of the attention challenges.

Also, because symptom severity can increase the likelihood of referral [12], girls may be less likely to receive a formal diagnosis and receive treatment if concern is not raised by either teachers or parents/guardians. Interestingly, a study that explored the underdiagnosis of ADHD in girls confirmed that mothers felt that DSM-IV criteria for the disorder did not reflect the behavior displayed by their daughters [17].

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In another study, girls who were overlooked by their teachers were instead referred for an assessment by their parents [13], perhaps because while parents compared their daughters with other girls of the same age, teachers were more likely to compare the girls with the boys in the same class. This has been confirmed by a more recent study that explored disruptiveness as a factor for referrals of girls [13] , suggesting that teachers may dismiss the less obvious signs of ADHD in this population. As a result of unequal prevalence ratios, referral biases and flawed diagnostic standards, girls are often not appropriately evaluated and adequately treated by mental health professionals [12]. In this context, more research needs to investigate and unveil the relationship between behavioral disturbances and altered brain function in females with ADHD [6, 15, 17, 18].

There are three main types of ADHD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), and distinction of these three types is based on the symptoms that more clearly stand out [1]:

1) Predominantly inattentive
2) Predominantly hyperactive-impulsive
3) Combined type

There is common agreement that children with ADHD exhibit EEG abnormalities. Specifically, it is well known that this population typically displays **elevated frontal theta** [19, 20], **increased posterior delta** [21, 22], and **reduced alpha/beta** in general [21, 23, 24]. However, most of these findings were obtained from male or mixed-sex samples, where females were only minimally represented. For example, Clarke et al. [21] found qualitative EEG differences between the combined and inattentive types in a cohort were females were only minimally represented (64 boys and 16 girls) and while other research in comparable samples of males and females has been carried out [24], more data is needed to establish a link between behavioral abnormalities and non-normative EEG in this population. On the other hand, if girls are not referred to clinics as much as boys, then it is possible that those who are referred for an assessment may display **more severe symptoms of the disorder** [6, 15] and that the girls recruited at research studies represent only a small portion of the whole population of girls with ADHD. Hence, it is important to consider that the neurophysiological anomalies detected in studies with only girls might offer only a partial perspective on the overall female ADHD population, as they might mainly represent the profile of girls displaying more severe/socially impacting behavioral symptoms.

2. EEG abnormalities in females with ADHD

2.1 Power anomalies

Studies with ADHD girls suggest an overall hypoarousal profile and similar EEG profiles regardless of the ADHD subtype considered [25]. For example, a study with ninety girls investigating EEG differences between the inattentive and the combined types found that the two groups had **greater absolute delta, theta and total power across the scalp**, when compared with age-matched controls. In particular, the increased absolute theta and total power were greater along the midline, where reduced absolute beta activity was also found. When compared with controls, the girls with ADHD had **reduced relative delta and beta activity, but increased relative theta activity across the scalp.** Reduced **relative delta, alpha and beta power in the midline central regions** was also found in the ADHD groups, suggesting equal activity across the scalp. However, in line with previous research [25], the study found no global EEG differences between the two subtypes investigated and recent findings suggest that although the hypoarousal profile is in line with the ADHD literature, it does not reflect the arousal levels of the central nervous system (CNS) in this population. In this context, Barry et al. [26] found no correlation between the theta/beta profile and electrodermal activity, a well established marker of CNS arousal. Instead, **the theta/beta profile has been suggested to underpin deficits in attentional processing** [26], although further research is needed to confirm this.

An important question is why global EEG differences have been shown in boys between ADHD subtypes, but not in ADHD girls. Of relevance, is that ADHD diagnoses heavily rely on referrals, and if teachers or family do not perceive girls to be problematic and/or exhibiting ADHD-like behaviors, these are less likely to be assessed and/or treated. Evidence suggests that teachers may perceive boys to be more disruptive and to exhibit more ADHD-type behaviors than girls [14]. Therefore, only girls who are identified as being highly disruptive might be more likely to be referred to a mental health specialist, which could explain why female ADHD clinical groups exhibit low levels of EEG global differences.

2.2 Coherence anomalies

Inter-hemispheric coherences have been shown to be higher in the frontal and central cortical regions of children with attention disorders [19, 27]. Also, children with ADHD may display greater delta/theta and lower beta inter-hemispheric coherence in the frontal regions. However, while both boys and girls with ADHD show atypical cortico-cortical connectivity [28] frontally and temporally, girls may also display enhanced laterality in the delta and theta bands for short-medium intra-hemispheric coherences [28, 29]. Interestingly, Clarke et al. [30] interpreted frontal delta and theta coherence increases as indicative of some form of **frontal lobe dysfunction.** Frontal lobe deficits have been linked to executive function impairments in ADHD [31-33], which **could underpin symptoms of inattention, hyperactivity and greater impulsivity** [31, 32].

2.2.3 Effects of psychostimulants on coherence

Importantly, **no significant effects of cognitive stimulants have been detected on coherence in girls with ADHD** [34]. Stimulant medications such as methylphenidate and dexamphetamine generally normalize EEG power anomalies in children with ADHD [35, 36] and similar results have been observed in a study with only girls [37].

Clarke et al. [37] have suggested that while EEG power reflects stimulant-sensitive activity in a range of frequency bands, cortical coherence reflects EEG coupling between topographically separate brain regions. Hence, the EEG power changes and the lack of corresponding changes in EEG coherence in girls with ADHD might support the notion that the two measures (power and coherence) reflect different aspects of brain activity. In particular, while EEG power more directly reflects differential cortical activity, coherence can instead provide information on brain structure [30]. In this context, the evaluation of before/after effects of stimulants on EEG power and coherence could offer important insights on the resulting behavioral changes in both boys and girls with ADHD, and might also unveil selective targets for alternative interventions in patients where medication fails to normalize both power and coherence.

3. Clinical Correlations

In clinical care, we have observed several consistent themes in females with documented qEEG patterns suggesting an ADHD diagnosis and yet presenting with a vast range of less typical symptoms:

1) Depression [38, 39]
2) Social isolation and avoidance [38, 40]
3) Screen addiction [41]
4) Social media or relational obsessive behaviors [42, 43]
5) Rebellious and oppositional behaviors [44]
6) Poor response to medication (for symptoms that are not directly related to ADHD) [45]
7) Substance use disorders [46]

Clinicians can use these indicators as a guide when presented with female patients whose diagnosis is seemingly elusive, or when treatment response has been poor. Many times, symptoms will begin as minor concerns for academic settings such as struggles with homework or chores, not listening or forgetfulness, gravitation towards lying or “naughty behaviors”. While seemingly innocent in grade school children, these symptoms are often missed until poor academic performance displayed at later stages of the curricular development becomes a reason of concern [47]. Hence, clinical correlation along with distinct qEEG findings can provide an invaluable guide to formulating accurate diagnoses and choosing appropriate treatments, while avoiding the trial and error approach most often used in standard mental health care.

Conclusions

Symptoms of ADHD in girls are often under reported by school teachers and family, mainly because of their rare effects on social functioning. While physical aggression is less commonly observed in girls with ADHD, inattention, hyper-talkativeness and emotional reactivity may instead be displayed more often in this population. Studies employing EEG have consistently found increased theta and decreased beta activity across the scalp, which is usually linked to reduced cognitive performance, greater impulsiveness and lower resilience. Also, similarly to what has been found in boys, increased inter-hemispheric and lateralized coherence has been shown in girls with ADHD. While the link between behavioral symptoms and EEG anomalies in girls needs to be established in large scale studies, EEG offers the opportunity to evaluate psychophysiological imbalances that could inform interventions and hence improve clinical outcomes.

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