EEG coherence in children with attention-deficit/hyperactivity disorder: Differences between good and poor responders to methylphenidate

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A B S T R A C T
This retrospective study investigated differences in regional derivations of EEG coherence between good and poor responders to methylphenidate (MPH) in children (aged 8–12 years) with the combined type of attention-deficit/hyperactivity disorder (AD/HD). Participants included groups of good and poor male MPH responders and an aged-matched group of male controls. An eyes-closed, resting electroencephalogram (EEG) was recorded from 21 electrode sites. Coherence was calculated from eight intrahemispheric and eight interhemispheric electrode pairs, for the delta, theta, alpha and beta frequency bands. Compared with controls, the AD/HD participants had enhanced laterality over short-medium inter-electrode distances, and elevated frontal interhemispheric coherences, in the theta band. Good MPH responders had higher intrahemispheric coherences than poor MPH responders over short-medium and long inter-electrode distances in the beta band. Enhanced laterality at short-medium inter–electrode distances suggests that the AD/HD children may have a developmental lag in short-axonal connections in the left hemisphere. Elevated frontal interhemispheric theta coherence consistently indicates some frontal dysfunction in AD/HD. The beta coherence differences found between good and poor MPH responders could indicate that good MPH responders have some type of structural dysfunction associated with cortical connections involved in attention/arousal.

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1. Introduction

Attention-deficit/hyperactivity disorder (AD/HD) is a debilitating and persistent childhood developmental condition. The disorder is characterised by behaviourally inappropriate symptoms of inattention, hyperactivity and impulsivity (Pelham et al., 1992), and is believed to affect 4–6% of school children (American Psychiatric Association, 1994). Without effective and appropriate treatment, AD/HD can interfere with normal functioning, and increase the risk of developing psychiatric and social pathologies later in life (Barkley, 1997; Mannuzza et al., 1993).

Methylphenidate (MPH), a psychostimulant, is the leading treatment option for AD/HD. In Australia there has been an 8.5-fold increase in the consumption of licit psychostimulants between 1994 and 2000 (Berbatis et al., 2002). Psychostimulants such as MPH increase the arousal level of the central nervous system (CNS) by stimulating the release and inhibiting the reuptake of the dopamine and noreadrenaline neurotransmitters (Biederman and Spencer, 1999; Durston, 2003). Behaviourally, MPH exerts its therapeutic effect by increasing attention while simultaneously decreasing impulsivity and gross motor activity (Swanson et al., 1995; Yıldız et al., 2007). Although up to 90% of children with AD/HD have a positive response to psychostimulants (American Academy of Child and Adolescent Psychiatry, 2002), they have not been extensively researched through cortical measures such as electroencephalogram (EEG) coherence.

Coherence between an electrode pair for a particular band is defined as the cross-spectral power between the sites, normalised by dividing the square root of the product of the power at each site in the time domain between two signals in a given frequency band (Shaw, 1981). This EEG measure is thought to describe the degree of connection between structures underlying each of the pair of recording electrodes (Clarke et al., 2005; Ruchkin, 2005). High coherence between any two EEG signals is interpreted as indicating strong connection between cortical areas (Fein et al., 1988).

Normal cortical development involves periods of cell proliferation and pruning. This is understood to result in systematic (but not necessarily linear) fluctuations in EEG coherence (Barry et al., 2004; Thatcher et al., 1987). Thatcher’s two-compartment model of corticocortical associations theorises that short and long neuronal fibres contribute differently to EEG coherence as a function of inter-electrode...
distance. Long-distance coherence increases with the development of long axonal connections; in contrast, coherence at shorter inter-electrode distances decreases with development, due to increases in complexity and competition of interactions within dense cell populations (Thatcher et al., 1986). There has been research support for this model within children with AD/HD (Barry et al., 2006, 2007; Clarke et al., 2005, 2007). One implication from this work is that coherences from electrode pairs separated by long and short distance are not meaningfully combined, and should be analysed separately.

In relation to AD/HD populations, Montagu (1975) found that hyperkinetic children had significantly higher intrahemispheric coherences compared to normal controls. Chabot et al. (1996) and Chabot and Serfontein (1996) found increased intrahemispheric and interhemispheric coherences in the frontal and central cortical regions of children with attention disorders. Barry et al. (2002) reported that children with AD/HD had elevated intrahemispheric coherences at short-medium inter-electrode distances in the delta, theta and alpha bands. These results indicate reduced cortical specialisation of short-axonal connections in AD/HD. Barry et al. (2002) also found that AD/HD children had reduced intrahemispheric coherences at longer inter-electrode distances in the alpha band. This indicates that AD/HD children have less developed long axonal connections compared to controls. The study also found that frontal interhemispheric coherences in AD/HD children were greater in delta and theta bands, but lower in beta. Barry et al. (2002) suggested that there are significant frontal differences between AD/HD and normal children in cortical specialisation in both slow wave (delta and theta) and beta activity.

Despite the popularity of MPH in the treatment of AD/HD, and the wide availability of studies on cortical abnormalities in AD/HD, there have been few enquiries into differences between good and poor MPH responders. Although most children with AD/HD receive significant benefits from psychostimulants, not all who respond to one type of psychostimulant will respond to another (Arnold, 2000). This highlights questions as to why some children respond positively to these medications and others do not, and if there are identifiable electrophysiological differences between these children. Clarke et al. (2002) investigated EEG differences between good and poor MPH responders in 40 children with the Combined type of AD/HD. The results from Clarke et al. (2002) show significant differences between good and poor psychostimulant responders. Clarke et al. (2002) concluded that the EEG profiles of good psychostimulant responders were more abnormal than (and qualitatively different from) the poor psychostimulant responders.

Continuous performance tasks (CPTs) are commonly used as a clinic-based measure of acute medication effects in children (Riccio et al., 2001). Since its origins with Rosvold et al. (1956), the CPT has developed into a measure of attention and impulsivity. The A–X variant of the CPT is currently the most widely used (Riccio et al., 2001). The A–X variant requires the subject to watch a continuous stream of random targets and non-targets. The subject is asked to respond only when a target (X) follows a specified non-target (A). Typically, counts of commission errors (response to an X not preceded by an A), or false positives, and omission errors (failure to respond to an X following an A), or false negatives, are recorded. The CPT has been described as a sensitive measure of sustained attention (or inattention in AD/HD children) and to some degree, a measure of impulsivity (Swanson, 1985), two of the core cognitive deficiencies in AD/HD. Riccio et al. (2001) reviewed studies that used CPTs to measure the effects of psychostimulants (most popular being MPH) in AD/HD children. Results found that MPH had a positive effect on CPT results, with increased correct hits, decreased commission and omission errors (Riccio et al., 2001). The CPT is an excellent clinical tool to provide an objective measure of medication effects and concentration with good face validity (Benedict et al., 1994). However, to date, EEG coherence differences have not been explored between good and poor medication responders. The aim of this study is to clarify interactions between AD/HD, the brain and psychostimulants. This retrospective study is linked to Clarke et al. (2002) and examined differences in regional derivations of intrahemispheric and interhemispheric coherences between good and poor MPH responders in children (aged 8–12 years) with the combined subtype of AD/HD.

2. Methods

2.1. Participants

Three groups of children all aged 8–12 years (M = 10.1 years, S.D. = 1.4), participated in this study. There were 18 boys in each of the AD/HD good-responder group (AD/HDg) and the control group, and 17 boys in the AD/HD poor-responder group (AD/HDp). These male subjects were initially examined in an EEG power study by Clarke et al. (2002).

All participants had a full-scale Wechsler Intelligence Scale for Children (WISC–III) IQ score of 85 or higher. The AD/HD children were selected from new patients referred to a paediatric practice for an AD/HD assessment. The AD/HD participants had not been diagnosed as having the disorder previously, had no history of medication use for any psychological disorder, and their paediatric, psycho-educational and electrophysiological assessments were completed before testing or prescription of any medication. Control participants were medication free at the time of the study.

Inclusion in the AD/HD groups was based on the clinical assessments and agreement of diagnoses by a paediatrician and a psychologist. Children were included in the two AD/HD groups if they met the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) diagnostic criteria for AD/HD Combined type (APA, 1994). Clinical interviews incorporated information from as many sources as were available. These included a history given by parent(s)/guardian(s), school reports from previous 12 months, reports from any other health professionals, and behavioural observations. Children were excluded if they had a history of a problematic prenatal, perinatal or neonatal period, a disorder of consciousness, a head injury resulting in cerebral symptoms, a history of central nervous system (CNS) diseases, convulsions or a history of convulsive disorders, paroxysmal headache, or tics.

Participants in the control group were recruited via local schools and community groups. Inclusion in the control group was based on: an uneventful prenatal, perinatal and neonatal period; no disorders of consciousness, head injury with cerebral symptoms, history of a CNS disease, obvious somatic diseases, convulsions, history of convulsive disorders, paroxysmal headaches, enuresis or encopresis after the fourth year of life, stuttering, pavor nocturnus or excessive nail-biting, obvious mental diseases, conduct disorders, and no deviation from normal mental and physical developments. Assessment for inclusion as a control participant was based on a clinical interview with parent(s)/guardian(s) similar to that of the AD/HD participants (described above), utilising the same sources of information.

All participants were right-handed and-footed. Handedness was assessed by ascertainment of the hand used for writing, catching and throwing a ball, holding a bat, and the foot used to kick a ball. Participants were excluded if spike wave activity was evident in their EEG.

2.2. Procedure

The parent(s)/guardian(s) of all participants gave their informed consent prior to the release of any clinical records or testing. Ethics approval for this study was obtained from the combined Illawarra Area Health/University of Wollongong Human Research Ethics Committee. All AD/HD participants were assessed and received standard medical care at the paediatric practice of RM and MS.

Participants were tested in two sessions, together lasting approximately 3.5 h. First, a paediatrician obtained a clinical history and conducted a physical examination. Participants then had psychometric assessments consisting of the WISC-III, the Wechsler Analysis of Reading and the Wide Range Achievement Test-R spelling test (WRAT). Participants then had an electrophysiological assessment consisting of evoked potentials (not reported here) followed by an eyes-closed resting EEG, recorded while seated in a reclining chair. AD/HD participants then had a break for approximately 2 h before returning for medication testing.

An electrode cap ensured that electrode placement was in accordance with the International 10–20 system. A single electrooculograph (EOG) electrode was referenced to the Fpz electrode and placed beside the participant’s right eye, and a ground lead was placed on the left cheek. A linked ear reference was used for all EEG sites and impedance levels were below 5 kΩ. The reference and ground leads were 9 cm apart, with tin electrodes. The EEG was recorded and analysed on a Cadwell Spectrum 32, software version 4.22 (Cadwell Laboratories Inc., Kennewick, WA, USA), using test type EEG, montage Q-EEG. A standard 21 channel monopolar cap, with linked-ears reference, was used in this study. The sensitivity was set at 150 μV per cm, with a high frequency filter set at 70 Hz, a notch filter set at 50 Hz and a low frequency filter set at 0.53 Hz. The sampling rate of the EEG was set at 200 Hz and the Fourier transformation used 2.56 s epochs.

Thirty 2.56 s epochs were selected from the live EEG trace and stored to disk. Epoch rejections were based on both computer and visual selection. Computer rejection levels were set using a template recorded at the beginning of each EEG session and all
subsequent epochs were compared to this. The EOG rejection level was set at 50 μV. An EEG technician visually evaluated every epoch for acceptance or rejection. The 30 selected epochs were reduced to 24 epochs (−1 min) for Fourier analysis by a second technician.

The recorded EEG was analysed in four frequency bands: delta (1.5–3.5 Hz), theta (3.5–7.5 Hz), alpha (7.5–12.5 Hz), and beta (12.5–25 Hz). For each frequency band, coherence estimates were calculated from eight intrahemispheric (FP1–F3, FP2–F4, T3–T5, T4–T6, C3–P3, C4–P4, F3–O1, and F4–O2) and eight interhemispheric (FP1–FP2, F7–F8, F3–F4, C3–C4, T3–T4, T5–T6, P3–P4 and O1–O2) electrode pairs.

The medication test consisted of the Vigilance Task of the Gordon Diagnostic System (Gordon, 1986). Participants viewed a series of sequentially displayed numbers and had to respond (with a button press) to a target number that followed another target number. Numbers were presented for 200 ms with an 800 ms inter-stimulus interval. Each test consisted of three identical blocks, which contained 180 stimuli in each block. Within each block, there were 15 random presentations of the paired target stimuli. The total number of correct responses and commission errors were recorded. Following Novartis medication guidelines (Novartis Australia, n.d.), the AD/HD participant lasted for about 1 h prior to receiving a 10 mg oral dose of MPH (Ritalin, Novartis Pharmaceuticals) and was rested 1 h later to ensure absorption (Kim et al., 1999). The second vigilance task was similar to the first, but used different target numbers. Percentage changes in correct responses and commission errors were calculated. Participants were included in the AD/HD group if they had an increase in correct responses and a decrease in commission errors — a good response. Participants in the AD/HD group also showed behavioral improvements as reported by their parent(s)/guardian(s), at their first follow-up clinical appointment (6 months after the initial assessment). Inclusion in the AD/HD group was based on: no change or a decrease in correct responses and an increase in commission errors — a poor response.

2.3. Statistical analysis

We followed our previous analytic strategy (Barry et al., 2002, 2004, 2005a, 2006, 2007; Clarke et al., 2005, 2007, 2008; Dupuy et al., 2008) with the present data to allow ready comparison of group similarities and differences across studies. Prior to analysis, all coherences were transformed for reporting. The skew of the data was then assessed to confirm normality required by analyses of variance (ANOVA were used. The transformed data was within the limits for this test and the following analysis conducted. The 16 sets of coherences were grouped for analysis into regions of interest. Each test consisted of three identical blocks, which contained 180 intrahemispheric coherences (for short-medium and long inter-electrode distances), and three for interhemispheric coherences (for different cortical regions). For each region of interest, ANOVAs were used to examine the effects of group upon coherences in each frequency band. The ANOVAs were completed on the computer software package SPSS (version 15.0). In the first test group, a planned comparison compared the patient groups with the control group (to establish differences between AD/HD and controls). The second group test compared the AD/HD group and the AD/HD group.

As shown in Fig. 1C, the AD/HD group had elevated frontal interhemispheric coherences in the delta (F = 4.70, P = 0.05) and theta bands (F = 16.59, P < 0.001).

2.3. AD/HDg versus AD/HDp

As shown in Fig. 1A, over short-medium inter-electrode distances, the AD/HD group had greater intrahemispheric coherence over short-medium inter-electrode distances in the delta band (F = 4.72, P = 0.05) (see Fig. 1A). The AD/HD group also showed enhanced (L< R) laterality in the theta band over short-medium inter-electrode distances (F = 15.14, P < 0.001). The AD/HD group had reduced (L< R) laterality in the beta band (F = 5.21, P < 0.05).

As shown in Fig. 1C, the AD/HD group had elevated frontal interhemispheric coherences in the delta (F = 4.70, P = 0.05) and theta bands (F = 16.59, P < 0.001).

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Delta</th>
<th>Theta</th>
<th>Alpha</th>
<th>Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fp1–F3</td>
<td>0.75 (0.18)</td>
<td>0.77 (0.17)</td>
<td>0.78 (0.19)</td>
<td>0.79 (0.16)</td>
</tr>
<tr>
<td>Fp2–F4</td>
<td>0.74 (0.16)</td>
<td>0.79 (0.25)</td>
<td>0.79 (0.14)</td>
<td>0.79 (0.16)</td>
</tr>
<tr>
<td>T3–T5</td>
<td>0.57 (0.12)</td>
<td>0.59 (0.18)</td>
<td>0.54 (0.22)</td>
<td>0.60 (0.12)</td>
</tr>
<tr>
<td>T4–T6</td>
<td>0.55 (0.15)</td>
<td>0.58 (0.18)</td>
<td>0.54 (0.20)</td>
<td>0.58 (0.15)</td>
</tr>
<tr>
<td>C3–C4</td>
<td>0.78 (0.09)</td>
<td>0.75 (0.15)</td>
<td>0.75 (0.19)</td>
<td>0.80 (0.08)</td>
</tr>
<tr>
<td>P3–P4</td>
<td>0.77 (0.13)</td>
<td>0.70 (0.20)</td>
<td>0.70 (0.14)</td>
<td>0.74 (0.10)</td>
</tr>
<tr>
<td>O1–O2</td>
<td>0.78 (0.19)</td>
<td>0.72 (0.18)</td>
<td>0.72 (0.18)</td>
<td>0.76 (0.14)</td>
</tr>
</tbody>
</table>

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There were no laterality differences in intrahemispheric coherences at either short-medium or long inter-electrode distances, and no differences in interhemispheric coherences.

3.3. Correlations

A significant inverse relationship was found between the short-medium intrahemispheric coherences in the delta frequency band and the commission errors. Increased commission errors were correlated with reduced short-medium intrahemispheric coherences in the delta band ($r = -0.42$, two-tailed $P < 0.05$).

Two significant inverse relationships were found between coherences in the delta and theta bands and the full-scale WISC-III IQ scores. Increased full-scale WISC-III IQ scores were correlated with reduced frontal interhemispheric delta coherence ($r = -0.34$, two-tailed $P < 0.05$) and reduced frontal interhemispheric theta coherence ($r = -0.28$, two-tailed $P < 0.005$). Also, a significant positive relationship was found with increased full-scale WISC-III IQ scores correlated with elevated long-distance intrahemispheric alpha coherence ($r = 0.34$, two-tailed $P < 0.05$).

Two significant inverse relationships were found between scores on the WRAT spelling scores and theta coherences. Increased WRAT spelling scores were correlated with reduced short-medium intrahemispheric theta coherence ($r = -0.44$, two-tailed $P < 0.001$) and reduced frontal interhemispheric theta coherence ($r = -0.36$, two-tailed $P < 0.01$).

The reading accuracy scores on the Neale Analysis of Reading was negatively correlated with frontal interhemispheric theta coherence ($r = -0.42$, two-tailed $P < 0.005$) and positively correlated with short-medium intrahemispheric beta coherence ($r = 0.28$).

3.4. Sensitivity and specificity

A sensitivity (true positive) of 0.72 and specificity (true negative) of 0.89 was obtained between the AD/HD (both good and poor responders) and control subjects, using short-medium intrahemispheric beta coherence, temporal theta, alpha and beta coherence and central/parietal/occipital beta coherence. A sensitivity of 0.83 and a specificity of 0.82 were obtained between the good and poor responders, using frontal theta, and alpha and central/parietal/occipital beta coherence.

4. Discussion

This retrospective study investigated regional derivations of coherence in 8–12-year-old children with the combined type of AD/HD. Compared with controls, the AD/HD children (regardless of medication response) had increased laterality over short-medium inter-electrode distances in the theta band. Enhanced short-medium intrahemispheric coherences in the left hemisphere have been reported consistently among children with AD/HD (Barry et al., 2006, 2007; Clarke et al., 2005, 2007). According to Thatcher’s model (Thatcher et al., 1986), coherence values over short-medium cortical distances should reduce through refinement and normal development of short-axonal connections. The current result suggests that the short-medium neuronal connections in the left hemisphere are not as developed as in the right hemisphere in AD/HD.

In the present study, children with AD/HD showed elevated frontal interhemispheric coherences in the theta band. This result matches previous EEG coherence studies (Chabot et al., 1996; Chabot and Serfontein, 1996), which found that children with attention disorders had marked frontal and posterior hypercoherence. Barry et al. (2002) found that AD/HD children had increased frontal coherences in the
delta and theta bands. Both boys with AD/HD (Barry et al., 2005a,b,c) and girls with AD/HD (Barry et al., 2006) had increased frontal interhemispheric coherences in the theta band. Barry et al. (2007) also found that children with AD/HD had elevated frontal interhemispheric coherences in the slow wave (delta and theta) bands. Male medication responders (Clarke et al., 2005) also had increased pre-medication frontal interhemispheric coherences in the delta and theta bands, compared with controls. Imaging studies have found evidence of structural abnormalities in the frontal lobes of children with AD/HD. Recent magnetic resonance imaging (MRI) (Briber et al., 2007) and magnetoencephalography (MEG) (Weinbruch et al., 2005) studies have found children with AD/HD to have structural fronto-striatal abnormalities. Mostofsky et al. (2002) found that boys with AD/HD had significantly smaller frontal lobe tissue absolute volume compared to age- and sex-matched controls. The results of the past and present coherence studies, and current imaging studies, suggest that children with AD/HD have identifiable structural frontal lobe abnormalities, and this may help in the future identification of AD/HD.

The current study found that AD/HD children who respond positively to MPH had elevated intrahemispheric coherences over both short-medium and long inter-electrode distances in the beta band (see Fig. 1A and 1B). Clarke et al. (2007) found that children with AD/HD had increased short-medium intrahemispheric coherences in the beta band compared to controls. Barry et al. (2005a,b,c) found that boys with combined type AD/HD had higher short-medium intrahemispheric beta coherences than boys with Inattentive type AD/HD. A similar near-significant result was found in girls with AD/HD Combined type — higher short-medium intrahemispheric beta coherences than girls with AD/HD Inattentive type (Barry et al., 2006). These previous studies, together with the present results, suggest that increased intrahemispheric beta coherences may be specific to the Combined type of AD/HD. However, although previous studies have reported coherence differences in the beta band between either AD/HD and controls (Clarke et al., 2007) or AD/HD Combined type cf. AD/HD Inattentive type (Barry et al., 2005a,b,c, 2006), the present result was found within a sample of AD/HD Combined type; between good and poor MPH responders.

Stimulants, such as MPH, inhibit the reuptake of dopamine and it may be that this function acts differently between good and poor MPH responders. Winsberg and Comings (1999) found that the Dopamine Transporter Gene (DAT1) had significant differences between identified good and poor MPH responders among a sample of African-American children with AD/HD. The current study found significant differences between good and poor MPH responders across several cortical areas, and this may help identify consistent cortical profiles between the two responding types.

The current study found that commission errors recorded from the A–X variant of the Vigilance task of the Gordon Diagnostic System were negatively correlated with short-medium intrahemispheric coherence values in the delta band. Commission errors, or false positives, are taken to indicate impulsivity in AD/HD children (Gordon, 1991). According to Thatcher et al. (1986), reduced short-medium intrahemispheric coherence indicates increases in complexity and cortical cell development. The current results suggest that impulsivity (as measured by commission errors) is significantly correlated with short-medium neuronal development and specialisation. It may be that increased impulsivity is associated with abnormal short-medium neuronal development. Further research may help link specific AD/HD behaviours with EEG coherence values and clarify this result.

Several significant two-tailed correlations were found between coherence and the performance tests (the full-scale WISC-III IQ score, the WRAT spelling score and the reading accuracy and comprehension scores from the Neale Analysis of Reading). There was a negative correlation with elevated frontal interhemispheric delta and theta coherences linked with reduced full-scale WISC-III IQ scores. There was a positive correlation with full-scale Wechsler Adult Intelligence Scale (WAIS)-III IQ scores and long intrahemispheric alpha coherences. Increased spelling scores (WRAT) were associated with reduced short-medium intrahemispheric and frontal interhemispheric theta coherences. While the accuracy scores from the Neale Analysis of Reading were negatively correlated with frontal interhemispheric theta coherence and positively correlated with short-medium intrahemispheric beta coherence. The comprehension scores from the Neale Analysis of Reading were negatively correlated with frontal interhemispheric theta coherences. Previous studies have investigated EEG coherence between children with various levels of reading and writing abilities (Barry, et al., 2009; Chabot and Serfontein, 1996; Chabot et al., 1996; Marosi et al., 1995, 1997). These studies investigated differences between children differing on levels of learning ability. Marosi et al. (1995) found that poor reading–writing performance was associated with elevated coherences in the delta, theta and beta bands and reduced coherence in the alpha band. Although, the current results did not differentiate between groups, the direction of the relationship between coherence and the performance tests matches the results from previous studies; negative relationships within coherences in the delta, theta and beta bands and positive relationship with alpha coherences. These preliminary findings aid in research directions for EEG coherence investigations in children with AD/HD and learning disorders.

The sensitivity (true positive) and specificity (true negative) of coherence values were also calculated between the combined AD/HD groups and control and between the two clinical groups. Frontal interhemispheric theta and alpha and central/parietal/occipital interhemispheric beta coherences were best at differentiating between the AD/HD groups and the controls. Temporal interhemispheric theta, central/parietal/occipital interhemispheric theta, temporal alpha, short-medium intrahemispheric beta and central/parietal/occipital interhemispheric beta coherence were factors that loaded best at differentiating the good MPH responders from the poor MPH responders. These results show good differentiation between AD/HD participants and controls. Due to the small sample size, these results are limited and no direct conclusions can be made about the use of coherence as a diagnostic tool. However, these results are promising and provide good indications for future research.

Placebos, or inert substances, can be used in drug research to help separate the real effects of ‘active’ drugs from the subjective effects of taking a pill (Andreassi and Mahwah, 2000). A lack of a placebo condition may have limited this study. However, this study analysed pre-treatment (or pre-medicated) EEG coherence activity in AD/HD children. The researchers consider that placebos are unlikely to influence pre-medication EEG activity and therefore they were not used in this study. This study investigated the EEG coherence profiles between good and poor MPH responders in children with the Combined type of AD/HD. The AD/HD participants showed consistent coherence differences compared with controls, notably increased interhemispheric frontal theta coherences and enhanced left intrahemispheric coherences. It is possible that increased frontal theta coherence could be used in the objective identification of AD/HD. The differences between the good and poor MPH responders are unique and puzzling. It is possible that the results illustrate some cortical structural aspects associated with attention or arousal. However, without a deeper understanding of coherence differences within specific bands, conclusions can only be speculative. It is clear that the electrophysiology of AD/HD is complex and multifaceted, and that no simple model can provide a comprehensive explanation of the disorder.

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