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Children with attention-deficit/hyperactivity disorder and autistic features: EEG evidence for comorbid disorders

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ABSTRACT

Attention-deficit/hyperactivity disorder (AD/HD) is the most common psychiatric disorder of childhood, although AD/HD is rarely the only diagnosis given to these children. Within the literature there is some debate as to whether it is valid to diagnose AD/HD with autism as a comorbid disorder, since the present diagnostic systems exclude the diagnosis of both disorders in the same child. The aim of this study was to determine whether electroencephalography (EEG) differences exist between two groups of children diagnosed with AD/HD, one scoring high (AD/HD+) and one scoring low (AD/HD−) on a measure of autism. The EEG was recorded during an eyes-closed resting condition from 19 electrodes, and Fourier transformed to provide absolute and relative power estimates in delta, theta, alpha and beta bands. Compared to age- and sex-matched controls, the AD/HD− group had increased absolute power in all frequency bands, somewhat higher relative theta activity and decreased relative delta. In comparison to the AD/HD− group, patients with autistic features (AD/HD+) had a number of qualitative differences in the beta and theta bands. These results indicate the presence of two comorbid conditions in the AD/HD+ group, which suggests that AD/HD and autism can occur in the same individual.

1. Introduction

Attention-deficit/hyperactivity disorder (AD/HD) is characterised by a persistent pattern of inattention and/or hyperactivity–impulsivity which is maladaptive and inconsistent with developmental level (Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV); APA, 1994). Symptoms of overactivity and inattention are also associated with pervasive developmental disorders (PDD), especially autism and Asperger's syndrome (AS). Both the International Classification of Diseases (ICD)-10 (WHO, 1993) and DSM-IV adopt a strict hierarchical approach to these disorders, excluding a diagnosis of AD/HD if symptoms of inattention and hyperactivity occur during the course of a PDD. However, a substantial body of research has questioned the validity and clinical efficacy of excluding a comorbid diagnosis of AD/HD and PDD (Clark et al., 1999; Frazier et al., 2001; Gillberg and Billstedt, 2000; Goldstein and Schwebach, 2004; Lord, 2000; Yoshida and Uchiyama, 2004), with a growing number of studies reporting children who meet criteria for both disorders. Clinically, this is an important issue, as proper diagnosis is the first step towards effective treatment. To aid this, it is important for diagnostic criteria to accurately identify which disorders do/do not occur together, because forcing a clinician to choose between two diagnoses, when they should choose both, may mean that only one aspect of the patient's problems is being treated.

Clinical studies examining comorbidity in children diagnosed with autism have consistently reported the presence of AD/HD symptoms, sufficient to meet the diagnostic threshold for the disorder, in between 50% (Gadow et al., 2004; Ghaziuddin et al., 1998; Sturm et al., 2004) and 83% (Frazier et al., 2001) of their children. Comorbidity rates of 60% (Goldstein and Schwebach, 2004), 68% (Yoshida and Uchiyama, 2004) and 73% (Wozniak et al., 1997) have also been reported. Those studies which have examined AD/HD symptom subtypes have found that symptoms of inattention are significantly more pronounced than symptoms of hyperactivity (Gadow et al., 2004; Goldstein and Schwebach, 2004; Sturm et al., 2004; Yoshida and Uchiyama, 2004), which is, perhaps, not surprising given that children with autism may be either hyperactive or hypoactive (or, more rarely, normally active). For example, in a retrospective chart study of 101 children diagnosed with 'high functioning' autism (primarily AS) with normal intellectual levels, Sturm et al. (2004) described attention deficits in 95% of the children (rating 67% as exhibiting 'severe deficits'), while hyperactivity was noted in 56% of the children (36% exhibiting 'severe deficits') and 23% were rated with mild to severe hypoactivity. However, Gillberg and Billstedt (2000) have suggested that attention deficits may be universal in autism spectrum disorders.

There is no doubt that the issue of comorbidity of AD/HD and autism is contentious. As noted above, numerous studies have confirmed a significant overlap of symptoms, creating potential problems in clinical diagnosis and treatment (Perry, 1998). A crucial question is whether the inattention and hyperactivity seen in autism spectrum disorders differ qualitatively from the inattention and hyperactivity associated with AD/

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HD. Lord (2000) suggests that there is a qualitative difference, in that, where these symptoms are not 'developmentally inappropriate', their occurrence in autism is a secondary effect of the triad of deficits intrinsic to autism. According to Rutter (2005), there is now an awareness that 'supposedly separate psychiatric conditions [do] co-occur' and what is needed, particularly in relation to the association between autism spectrum disorders and AD/HD, is the broadening of the scientific basis of research in this area.

Electroencephalography (EEG) studies of children with AD/HD have typically found increased theta activity (Satterfield et al., 1972; Mann et al., 1992; Janzen et al., 1995; Clarke et al., 1998, 2001a,b,c, 2007), occurring primarily in the frontal regions (Chabot and Serfontein, 1996; Lazzaro et al., 1998), increased posterior delta (Matousek et al., 1984; Clarke et al., 1998, 2001a,b) and decreased alpha and beta activity (Dykman et al., 1982), also most apparent in the posterior regions (Clarke et al., 1998, 2001a,b; Lazzaro et al., 1998); see Barry et al. (2003) for a review.

In comparison to the AD/HD literature, comparatively few studies of resting state EEG power have been conducted in children with autism. Dawson et al. (1995) examined EEG power at six sites, in a mixed group of low to higher-functioning autistic children and two control groups, a chronological-age-matched group and a language-age-matched group. During EEG recording, subjects viewed 'bubbles cascading from behind a black curtain' situated in front of the child. In comparison with both control groups, the autistic group showed significantly reduced EEG power in the delta, theta and alpha bands. Chabot et al. (2005) reported that autistic children tended to show a decrease in the hemispheric asymmetries of the EEG found in control subjects. Sutton et al. (2005) examined alpha activity in a group of high-functioning autistic children during a mixed eyes open/eyes closed trial. The autistic group exhibited significantly higher alpha power in the centro-parietal regions than controls, and significantly higher left-hemisphere asymmetry mid-frontally (F3/F4) and centrally (C3/C4). Orekhova et al. (2007) found that children with autism had an increase in high beta and gamma activity (24–44 Hz) recorded during a sustained visual attention task. These results were interpreted as indicating that high-frequency EEG activity may contribute to the abnormal development found in this disorder. Stroganova et al. (2007) found that autistic children had a generalised increase in left compared to right hemisphere EEG activity across all bands. This was seen as possibly indicating that autistic children have diminished capacity to generate EEG activity in the right temporal cortex. Coben et al. (2008) compared a group of children with autism to a normal control group. The autism group had global reductions in absolute and relative delta, an increase in both frontal and posterior relative theta, and a reduction in right hemisphere absolute beta activity.

The aim of this study was to determine whether quantitative or qualitative EEG differences exist between children with AD/HD who do or do not exhibit autistic features, in order to determine whether electrophysiological markers exist that support the comorbid diagnosis of both AD/HD and autism in the same child.

2. Methods

2.1. Subjects

Three groups of 60 children, aged between 8 and 13 years, participated in this study. Each group contained 50 boys and 10 girls. The groups consisted of an AD/HD group without autistic features (AD/HD−), an AD/HD group with autistic features (AD/HD+), and a control group. All groups were individually matched on age, using one year age bands, to control for maturational changes in the EEG. The AD/HD− group contained 36 children with the Combined type and 24 with the Inattentive type of AD/HD, and the AD/HD+ group had 44 children with the Combined type and 16 with the Inattentive type of AD/HD. Autistic features were assessed using the autism subscale of the Developmental Behaviour Checklist (DBC; Einfeld and Tonge, 1995). The DBC is a 96-item questionnaire, which assesses behaviour and emotional disturbance in young people with intellectual disabilities. It has robust reliability and validity characteristics (Einfeld and Tonge, 1992, 1996a,b). The questionnaire comes in both parent and teacher forms. The autism subscale consists of a subset of 29 items. The DBC autism subscale has been extensively evaluated and has been found to accurately identify between 80% and 94% of children with some form of pervasive developmental disorder (Brereton et al., 2002; Gray and Tonge, 2008; Witwer and Lacavalier, 2007; Gray et al., 2005). This literature indicates that the measure is a reliable marker of autistic features in the current sample. To be included in the study, subjects in the AD/HD− group had to score below 10 on the autism subscale and subjects in the AD/HD+ group had to score above 23; the clinical threshold on the autism subscale is 17.

The AD/HD groups were drawn from new patients referred to a paediatric practice for a developmental assessment. These subjects had not been assessed previously, had no history of medication use for the disorder, and were tested before being prescribed any medication. The control group consisted of children from local schools and community groups, who responded to newspaper advertisements, or fliers sent home to parents. This study was approved by the combined University of Wollongong and Illawarra Area Health Service Human Research Ethics Committee. In all cases, informed written consent from a parent and written assent from the child were obtained.

Inclusion in the AD/HD groups was based on a clinical assessment by a paediatrician and a psychologist; children were included only if both agreed on the diagnosis. DSM-IV criteria were used and children were included in the AD/HD groups if they met the full diagnostic criteria for the Combined or Inattentive type of AD/HD. The clinical assessment incorporated information from as many sources as were available. These included a history given by a parent or guardian, school reports for a minimum of the past 12 months, reports from other health professionals, and behavioural observations during the assessment. The Child Behavior Checklist (CBCL) and Conners' Rating Scale (Parent Versions) were also administered, and from these, the Conners' DSM-IV Inattentive, Hyperactive–Impulsive and Total subscales, as well as the CBCL Attention Problems subscale, were used to aid in the diagnosis. Children were excluded from the AD/HD groups if they had a disorder of consciousness, a head injury with cerebral symptoms, a history of central nervous system diseases, convulsions or a history of convulsive disorders, paroxysmal headache or tics.

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 central nervous system disease, obvious somatic diseases, convulsions, history of convulsive disorders, paroxysmal headache, enuresis or encopresis after the fourth birthday, tics, stuttering, pavor nocturnes, and conduct disorders. Assessment for inclusion as a control was based on a clinical interview with a parent or guardian similar to that of the AD/HD subjects, utilising the same sources of information.

Children were excluded from all groups if spike wave activity was present in the EEG.

2.2. Procedure

All subjects were tested in a single session lasting approximately 2.5 h. Clinical subjects were first assessed by a paediatrician, where a physical examination was performed and a clinical history taken. Subjects then had a psychometric assessment consisting of a WISC-III, Neale Analysis of Reading and Wide Range Achievement Test-R spelling. After this assessment, subjects had an electrophysiological assessment consisting of an EEG. While subjects were having their assessment, their parent/s completed the Child Behaviour Checklist, Conners' Rating Scale, and the autism subscale of the Developmental Behaviour Checklist.

The EEG was recorded in an eyes-closed resting condition while subjects were seated on a reclining chair. Electrode placement was in accordance with the international 10–20 system, using an electrode cap. The activity in 19 derivations was divided into 9 regions by averaging in each region. These regions were the left frontal (Fp1, F3, F7), midline frontal (Fz), right frontal (Fp2, F4, F8), left central (T3, C3), midline central (Cz), right central (T4, C4), left posterior (T5, P3, O1), midline posterior (Pz) and right posterior (T6, P4, O2). A linked ear reference was used with all EEG electrodes, and reference and ground leads were 9 mm tin disk electrodes. Impedance levels were set at 3–5 kΩ.

The EEG was recorded on a Lexicor NRS-24 using a sampling rate of 256 Hz. A gain of 30,000 was used, with a high pass filter of 0.5 Hz, low pass filter of 64 Hz, and a 50 Hz notch filter. The EEG was analysed using NxLink software. The EEG was visually appraised by an

Table 1
Mean ages and psychometric test scores for the three groups.

	AD/HD+ group	AD/HD− group	Control group
Mean age (years)	9.55	9.49	9.60
Psychometric measures			
Full scale IQ	96.7	96.7	107.4
Spelling age (months)	110.3	112.6	105.4
Reading accuracy (months)	106.4	111.6	141.9
Reading comprehension (months)	104.0	105.4	135.6
DBC autism subscale (raw score)	28.5	6.6	4.2
Conners' DSM-IV Inattentive subscale (*t*-score)	74.0	70.6	54.1
Conners' DSM-IV Hyperactive–Impulsive subscale (*t*-score)	79.9	77.3	48.3
Conners' DSM-IV Total subscale (*t*-score)	79.0	78.4	51.2
CBCL Attention Problems (*t*-score)	74.7	73.8	51.2