Psychopharmacology (2002) 164:277–284
DOI 10.1007/s00213-002-1205-0

ORIGINAL INVESTIGATION

Adam R. Clarke · Robert J. Barry · Dominique Bond · Rory McCarthy · Mark Selikowitz

Effects of stimulant medications on the EEG of children with attention-deficit/hyperactivity disorder

Received: 20 December 2001 / Accepted: 8 July 2002 / Published online: 11 September 2002

Abstract *Rationale:* Stimulant medications are the most commonly used treatments for attention deficit/hyperactivity disorder (ADHD) in North America and Australia, although it is still not entirely known how these medications work. *Objectives:* This study aimed to investigate the effects of stimulant medications on the EEG of children with the Combined subtype of ADHD. *Method:* An initial EEG was recorded during an eyes-closed resting condition and Fourier transformed to provide absolute and relative power estimates for the delta, theta, alpha and beta bands. Theta/alpha and theta/beta ratios were also calculated. Subjects were placed on a 6-month trial of a stimulant and a second EEG was recorded at the end of the trial. *Results:* The ADHD group had significantly greater absolute delta and theta, less posterior absolute beta, more relative theta, and less relative alpha than the control group, which is typical of EEG studies of children with ADHD. The use of stimulant medications resulted in normalisation of the EEG, primarily evident in changes in the theta and beta bands. *Conclusions:* These results suggest that stimulants act to increase cortical arousal in children with ADHD, normalising their brain activity.

Keywords Attention deficit/hyperactivity disorder · Children · EEG · Stimulants · Medication

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a persistent problem that may change with development from preschool through adulthood. It interferes with many areas of normal development and functioning in a child's life, and if untreated, it predisposes the child to psychiatric and social pathology in later life. Prevalence rates vary according to the population that is sampled, the diagnostic criteria, and diagnostic instruments that are used. However, studies place the prevalence rate at between about 4% (Pelham et al. 1992) and 6% (Lindgren et al. 1990), with the DSM-IV (APA 1994) estimating the prevalence of ADHD in the general population at approximately 3–5% of school-age children.

For over 50 years, ADHD has been treated with stimulant medications such as methylphenidate and dexamphetamine. In North America, stimulants are widely used for the treatment of ADHD, with clinical guidelines recommending an initial trial of medication (Swanson et al. 1998). Numerous controlled trials (Wilens and Biederman 1992) and clinical and empirical reports (Swanson et al. 1993) have established that about 80% of patients have clinically significant benefits from medication, with medication increasing attention, and decreasing impulsivity and gross motor activity. Despite this long-standing use of stimulants in ADHD, the precise effects on brain functioning remain unclear.

EEG studies have found that children with ADHD have increased theta activity (Satterfield et al. 1972, 1973a, 1973b; Janzen et al. 1995; Clarke et al. 1998, 2001b, 2001c) which occurs primarily in the frontal regions (Mann et al. 1992; Chabot and Serfontein 1996; Lazzaro et al. 1998), increased posterior delta (Matousek et al. 1984; Clarke et al. 1998, 2001b, 2001c) and decreased alpha and beta activity (Dykman et al. 1982; Callaway et al. 1983), also most apparent in the posterior regions (Mann et al. 1992; Clarke et al. 1998, 2001b, 2001c; Lazzaro et al. 1998), compared to children without ADHD. This profile has been seen as supportive of both a central nervous system (CNS) maturational lag (Mann et al. 1992), and cortical hypoarousal (Satterfield and Cantwell 1974).

In an attempt to understand better the action of stimulant medications on children with ADHD, a number

A.R. Clarke (✉) · R.J. Barry · D. Bond
Brain and Behaviour Research Institute,
and Department of Psychology, University of Wollongong,
Wollongong 2522, Australia
e-mail: adam_clarke@uow.edu.au
Tel.: +61-2-42215775
Fax: +61-2-42214914

R. McCarthy · M. Selikowitz
Private Pediatric Practice, Level 3/9 Bligh Street, Sydney, Australia

of researchers have investigated changes in the EEG due to the administration of a stimulant. Chabot et al. (1999) found that 56.9% of a sample of children with ADHD showed normalisation of the EEG after the administration of a stimulant, while 33.8% remained unchanged and 9.3% showed an increase in EEG abnormality. Swartwood et al. (1998) and Lubar et al. (1999) investigated the effects of methylphenidate in 23 boys with ADHD. Results from these studies failed to identify any global changes in the EEG due to medication. From this, it was concluded that methylphenidate may affect the brainstem and other subcortical areas rather than cortical functioning. In a preliminary report, Loo et al. (1999) found that, after administration of methylphenidate, good responders had decreased theta and alpha, and increased beta activity in the frontal regions, while poor responders showed the opposite EEG changes. The limitation of this study was that only 10 ADHD subjects were used, pointing to the need for further replication.

The aim of this study was to investigate further the effects of stimulant medications on the EEG of children with ADHD.

Materials and methods

Subjects

Fifty boys with a DSM-IV diagnosis of ADHD Combined type and 40 control boys participated in this study. All children were between the ages of 8 and 13 years. Subjects had a full-scale WISC-III IQ score of 85 or higher. The ADHD group was drawn from new patients presenting at a pediatric practice for an assessment for ADHD. The ADHD patients either had not been diagnosed as having ADHD previously and had no history of medication use for the disorder, or had previously been assessed by another clinician and treated with medication but were medication-free for a minimum of five half-lives at the initial assessment. The control group consisted of children from local schools and community groups who were medication-free.

Inclusion in the ADHD group was based on a clinical assessment by a pediatrician and a psychologist; children were included only where both agreed on the diagnosis. DSM-IV criteria were used and children were included only if they met the full diagnostic criteria for the ADHD Combined type. Clinical interviews incorporated information from as many sources as were available. These included a history given by a parent or guardian, school reports for the past 12 months, reports from any other health professionals and behavioural observations during the assessment. Children were excluded from the ADHD group if they had a history of a problematic prenatal, perinatal or neonatal period, a disorder of consciousness, a head injury with cerebral symptoms, a history of CNS diseases, convulsions or a history of convulsive disorders, paroxysmal headache or tics. Subjects were also excluded if they met DSM criteria for conduct or oppositional defiant disorder, a depressive or anxiety disorder, Asperger's or Tourette's syndrome.

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 CNS diseases, obvious somatic diseases, convulsions, history of convulsive disorders, paroxysmal headache, enuresis or encopresis after the fourth birthday, tics, stuttering, pavor nocturnes or excessive nailbiting, psychiatric condition listed in the DSM-IV, and no deviation with regard to physical development. Assessment for inclusion as a control was based on a clinical interview with a parent or guardian similar to that of the ADHD subjects, utilising the same sources of information.

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

Procedure

All subjects had an initial assessment that lasted approximately 2.5 h. Subjects were first assessed by a pediatrician, 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 evoked potentials followed by an EEG. The ADHD subjects then had a lunch break for approximately 2 h and returned for medication testing.

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 produced by Electrocap International. The activity in 21 derivations was divided into nine regions by averaging in each region. These regions were the left frontal (Fp1, F3, F7), midline frontal (Fpz, 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, Oz) and right posterior (T6, P4, O2). A single electro-oculogram (EOG) electrode referenced to Fpz was placed beside the right eye and a ground lead was placed on the left cheek. A linked-ear reference was used with all EEG derivations. Reference and ground leads were 9 mm tin disk electrodes, and impedance levels were set at less than 5 kohm.

The EEG was recorded and Fourier transformed by a Cadwell Spectrum 32, software version 4.22, using test type EEG, montage Q-EEG. The sensitivity was set at 150 μV/cm, low frequency filter 0.53 Hz, high frequency filter 70 Hz and 50 Hz notch filter. The sampling rate of the EEG was 200 Hz and the Fourier transformation used 2.5-s epochs.

Thirty 2.5-s epochs were selected from the live trace and stored to floppy disk. Epoch rejection was based on both visual and computer selection. Computer reject levels were set using a template recorded at the beginning of the session and all subsequent epochs were compared to this. The EOG rejection was set at 50 μV. The technician also visually appraised every epoch and decided to accept or reject it. These were further reduced to 24 epochs (1 min) for Fourier analysis by a second technician. The EEG was analyzed 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 both absolute and relative power, as well as the total power of the EEG (1.5–25 Hz). Theta/alpha and theta/beta ratio coefficients were also calculated by dividing the power of the slower frequency band by the power of the faster frequency band.

The medication test consisted of the Vigilance Task of the Gordon Diagnostic System (Gordon 1986). Subjects viewed a series of digits which were sequentially displayed, and had to respond to a target number, which followed another target number, by pressing a button. The total number of correct responses and commission errors were recorded and the child was given 10 mg methylphenidate or 5 mg dexamphetamine. The patient was then retested 1 h after the initial test using a second vigilance task which used different target numbers. Percentage changes in correct responses and commission errors were calculated, and subjects were prescribed the test medication if they had a decrease in commission errors with no decrease in correct responses. Subjects were retested on another medication at the earliest convenience of the parents if the above criteria were not met. Once a medication was selected, the children were placed on a trial of the medication lasting approximately 6 months. At the end of the trial, a follow-up assessment was conducted, which consisted of a repeat assessment, including reading, spelling, evoked potentials and an EEG. At this assessment, the child had taken their prescribed dose of methylphenidate or dexamphetamine 1 h prior to testing.

Statistical analysis

Three independent analyses of variance was performed examining the effects of region, group, and medication effect for each band in absolute and relative power, the total power, and ratio coefficients. The effects of region were examined in two orthogonal three-level repeated-measures factors. The first of these was a sagittal factor within which planned contrasts compared the frontal region with the posterior region, and their mean with the central region. The second factor was laterality, within which planned contrasts compared activity in the left hemisphere with that in the right hemisphere, and their mean with the midline region. These single degree of freedom *F*-tests allow optimal clarification of site effects within the regions studied and obviate problems arising from asymmetry of the variance-covariance matrix often found with repeated-measures analyses of physiological data, and hence do not require Greenhouse-Geiser type adjustments. Further, as all these contrasts are planned, and there are no more of them than the degrees of freedom for effect, no Bonferroni-type adjustment to α is required (Tabachnick and Fidell 1989). The first group analysis compared the patient group at the initial assessment without medication (ADHDoff) with the control group to establish ADHD differences from normals. A repeated measures analysis compared the patient group at the first assessment on medication (ADHDon) with their initial assessment to investigate medication effects. The three-group design allowed a final analysis to be carried out without affecting the family-wise error rate (Howell 1998). This compared the ADHDon group with the control group to determine the degree of normalisation. Only between-group effects and interactions are reported here for space reasons.

Results

A summary of significant results is shown in Table 1.

ADHDoff versus control subjects

All *F*-tests reported in this section had *df*=1,88. Globally, the ADHDoff group had significantly greater absolute theta (F=18.84, P<0.001), more relative theta (F=37.29, P<0.001), less relative alpha (F=11.30, P<0.001), and higher theta/alpha (F=26.31, P<0.001) and theta/beta (F=22.60, P<0.001) ratios than the controls (Fig. 1). Group differences were greater in the posterior regions than the frontal regions for relative alpha (F=3.98, P<0.05), and greater in the frontal regions than the posterior regions for the theta/alpha ratio (F=8.90, P<0.01). The ADHDoff group had greater power than the control group in the posterior regions, and less power in the frontal regions for relative delta (F=14.00, P<0.001), and this profile was reversed in absolute beta (F=8.66, P<0.01). In relative alpha (F=7.68, P<0.01) and theta (F=4.29, P<0.05), the difference between the mean of the frontal and posterior regions, and the central regions, was less in the ADHDoff group than the control group.

Laterally (Fig. 2), the difference in power between the midline and the two hemispheres was greater in the ADHDoff group than the control group for absolute theta (F=6.42, P<0.05), and the theta/alpha (F=4.69, P<0.05) and theta/beta (F=4.51, P<0.05) ratios. This difference in power between the midline and the two hemispheres was greater in the frontal regions than the posterior regions, in the ADHDoff group compared to the control group, for total power (F=7.20, P<0.01), absolute delta (F=7.41, P<0.01), absolute theta (F=17.80, P<0.001), relative theta (F=5.94, P<0.05), and the theta/alpha (F=21.12, P<0.001) and theta/beta (F=15.75, P<0.001) ratios. Maximal group

Table 1 Summary of significant comparisons between groups. *vs* versus, *F* frontal, *P* posterior, *C* central, *L* left hemisphere, *R* right hemisphere, *M* midline

Comparison	Absolute power					Relative power				Ratios	
	Total	Delta	Theta	Alpha	Beta	Delta	Theta	Alpha	Beta	Theta/Alpha	Theta/Beta
ADHD off vs control											
Main effect			***				***	***		***	***
Main effect×F vs P					**	***		*		**	
Main effect×F/P vs C							*	**			
Main effect×L/R vs M			*							*	*
Main effect×F vs P×L vs R					*						
Main effect×F vs P×L/R vs M	**	**	***				*			***	***
Main effect×F/P vs C×L/R vs M	**		**	*		*					
ADHD off vs ADHD on											
Main effect			*				*		*	*	**
Main effect×F vs P×L vs R								*		*	
Main effect×F vs P×L/R vs M		*	**							*	
Main effect×F/P vs C×L/R vs M							*				
ADHD on vs control											
Main effect			*				***	***		***	**
Main effect×F vs P					*	*		*		*	
Main effect×F vs P×L vs R	*			*	*						
Main effect×F vs P×L/R vs M											**
Main effect×F/P vs C×L/R vs M						**					*

*P<0.05, **P<0.01, ***P<0.001

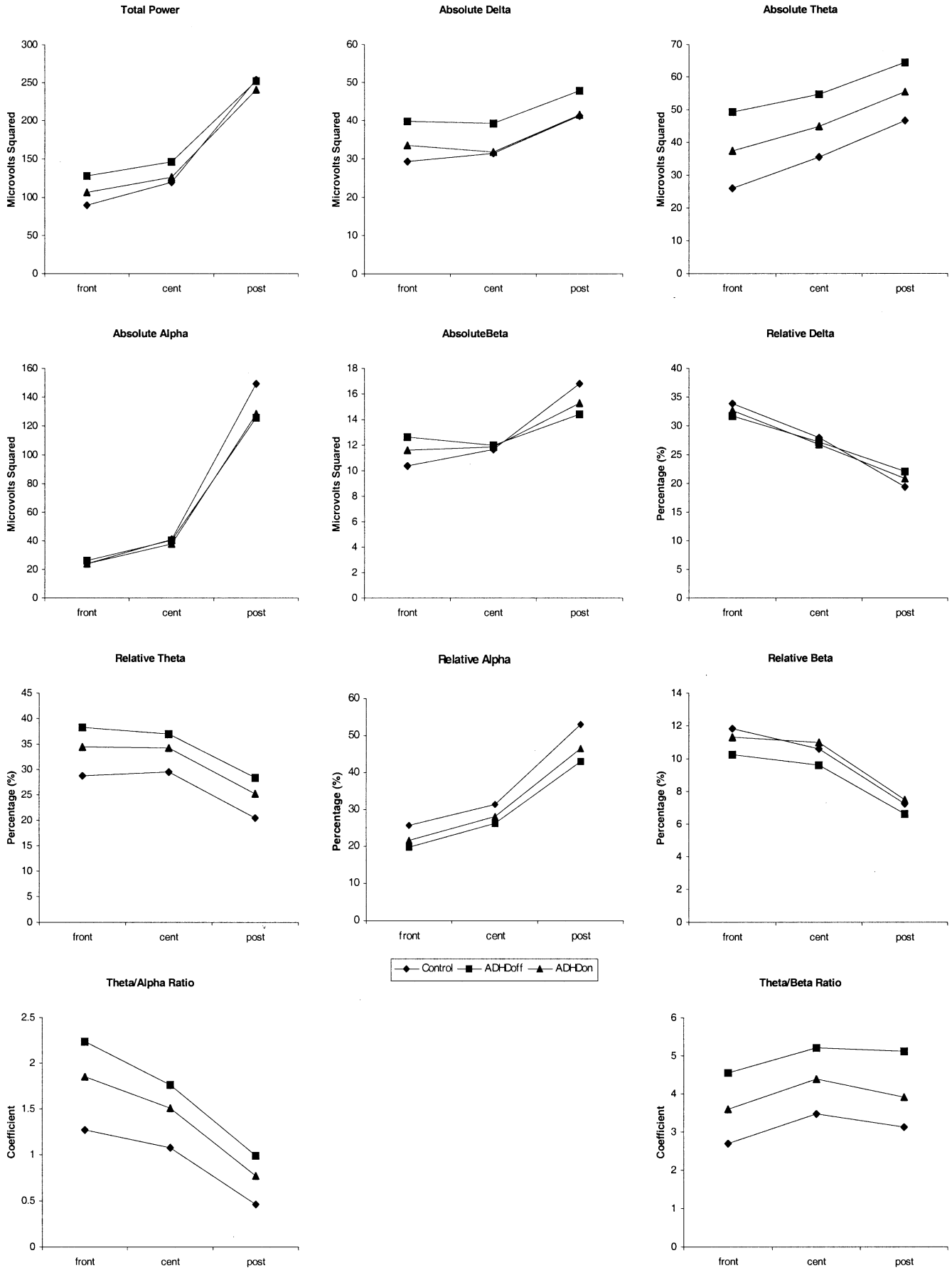

Fig. 1 Power distribution and ratio coefficients as a function of scalp region, from frontal to posterior regions, for the control group and the ADHD group off medication and after a 6-month trial on stimulants

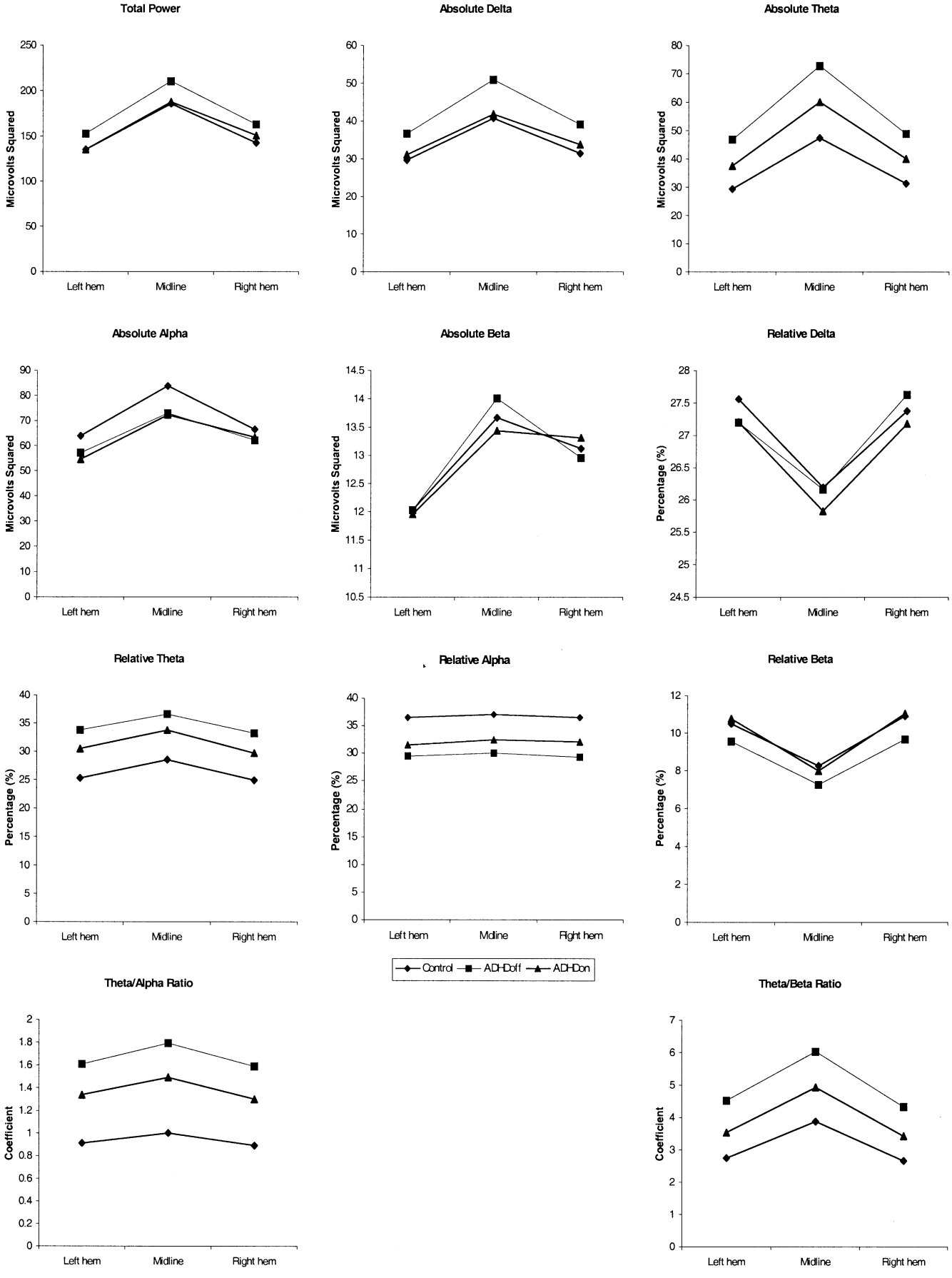

Fig. 2 Power distribution and ratio coefficients as a function of scalp region, lateral section from left to right hemisphere, for the control group and the ADHD group off and on stimulant medications

differences between the midline and the two hemispheres occurred at the central regions for total power (F=7.73, P<0.01), absolute theta (F=6.34, P<0.01), absolute alpha (F=5.50, P<0.05), and relative delta (F=4.81, P<0.05). In absolute beta (F=5.62, P<0.05), the ADHDoff group had a greater asymmetry of beta power in the posterior regions compared to the frontal regions, but this was reversed in the control group, with the asymmetry being greater in the frontal regions.

EEG changes with medication in the ADHD group

All F-tests reported in this section had df=1,49. Significant reductions in absolute theta (F=5.65, P<0.05), relative theta (F=5.13, P<0.05), the theta/alpha (F=4.13, P<0.05) and theta/beta (F=6.00, P<0.01) ratios, and an increase in relative beta (F=4.15, P<0.05) were found with medication use (see Fig. 1). The frontal enhancement of midline power compared to the two hemispheres reduced with medication in absolute delta (F=4.47, P<0.05), absolute theta (F=8.95, P<0.01), and the theta/alpha ratio (F=6.42, P<0.05). Medication produced its greatest reduction in relative theta at the vertex (midline>hemispheres, central>frontal/posterior regions (F=4.73, P<0.05). The comparison of the two hemispheres in the frontal and posterior regions indicated a significant right posterior increase in relative alpha (F=5.80, P<0.05), and a right posterior reduction in the theta/alpha ratio (F=5.97, P<0.05) with medication.

ADHDon versus control subjects

F-Tests reported in this section had df=1,88. The ADHDon group continued to demonstrate more absolute theta (F=5.00, P<0.05), more relative theta (F=16.82, P<0.001), less relative alpha (F=12.05, P<0.001), and higher theta/alpha (F=12.05, P<0.001) and theta/beta (F=7.45, P<0.01) ratios than the control subjects (Fig. 1). Group differences remained greater in the posterior regions than the frontal regions for relative alpha (F=5.59, P<0.05), and greater in the frontal regions than the posterior regions for the theta/alpha ratio (F=5.59, P<0.05). In absolute beta, the ADHDon group still had more frontal power than the control group and less power in the posterior regions (F=4.00, P<0.05). In relative delta, this frontal/posterior difference remained reversed, with the ADHDon group having more posterior power and less frontal power (F=5.67, P<0.05).

In the ADHDon group compared to the control group, the difference in theta/beta ratio between the midline and the two hemispheres remained greater in the frontal regions than the posterior regions (F=8.35, P<0.01), but became maximal at the central regions (F=4.89, P<0.05). This indicated that the decrease in the theta/beta ratio at the midline was greatest in the frontal regions. The central enhancement of relative delta, for the comparison of the midline and the two hemispheres, remained significant (F=8.15, P<0.01).

In total power (F=5.06, P<0.05), and absolute alpha (F=6.58, P<0.05) and beta (F=6.58, P<0.05), the ADHDon group retained a greater power asymmetry in the posterior regions than in the frontal regions, compared with the control group, with the enhancement of power being greatest in the right posterior region.

Changes at the individual level

As changes in the EEG due to medication were primarily found in the theta and beta bands, relative theta and beta was reviewed in each subject. For the purposes of calculating individual change, subjects were split into a young group (8-, 9- and 10-year-olds) and an older group (11, 12 and 13) to minimise the effects on results of maturational changes in the EEG. Means and standard deviations were calculated from control subjects within these groups, and results from the clinical sample were assessed within these parameters.

When off medication, 78% of the total ADHD sample had relative theta more than 1 SD above the mean of control subjects, and 64% were more than 2 SD above the mean. When on medication, 28% of those who were 2 SD above the mean remained 2 SD above, 25% normalised to between 1 and 2 SD above the mean, and the remaining 47% normalised to within 1 SD of the control mean. Of those subjects who were initially 1 SD above the mean, 71% showed a reduction in theta to less than 1 SD from the control mean. Within the 22% of unmedicated ADHD subjects who were initially within 1 SD of the control levels, 87% showed an increase in relative theta due to medication.

In relative beta, 8% of the unmedicated ADHD boys had deficiencies of beta greater than 2 SD below the controls, 30% were between 1 and 2 SD down, 48% had normal beta levels, and 14% had excess beta activity more than 1 SD above controls. With medication, 75% of subjects initially more than 2 SD down increased beta activity by 1 SD, and 25% completely normalised. Normalisation occurred in 80% of subjects originally down 1 SD. Beta levels in subjects with normal off-medication beta mainly remained normal (58%), or increased by at least 1 SD (33%). Eighty-five percent of subjects with excess beta when off medication showed normalisation when on medication.

Discussion

EEG studies of children with ADHD have generally found an increase in theta activity, primarily in the frontal areas (Capute et al. 1968; Wikler et al. 1970; Satterfield et al. 1973b; Clarke et al. 1998, 2001b, 2001c), decreased alpha and beta activity (Mann et al. 1992; Clarke et al. 1998, 2001b, 2001c; Lazzaro et al. 1998), and an increase in the theta/alpha (Clarke et al. 2001b, 2001c) and theta/

beta ratios (Lubar 1991; Janzen et al. 1995; Clarke et al. 1998, 2001b, 2001c) compared to normal children. In the present study, the ADHD group had significantly greater absolute delta and theta, less posterior absolute beta, more relative theta, less relative alpha, and higher theta/alpha and theta/beta ratios. These results indicate that the children with ADHD in this study have EEG profiles that are typical of those reported in other studies.

EEG studies of the effects of stimulant medication have been fairly inconsistent. Swartwood et al. (1998) and Lubar et al. (1999) did not find any global changes in the EEG due to medication. Chabot et al. (1998) found that just over half of their sample showed normalisation of the EEG after the administration of a stimulant, whereas Loo et al. (1999) found, with methylphenidate, that only good responders demonstrated normalisation of the EEG.

This study found that stimulant medications produced changes in the EEG towards normalisation, with reductions in absolute and relative theta, the theta/alpha and theta/beta ratios, and an increase in relative beta. In the normal maturation of children, a strong complementary change between the theta and alpha bands has been found, with alpha activity increasing with age as theta decreases (Benninger et al. 1984, Clarke et al. 2001a). The fact that most children with ADHD have increased theta and decreased alpha activity in their EEG has supported the proposition that these children have a maturational lag in CNS development (e.g. Mann et al. 1992). While the present results from the unmedicated EEGs do not necessarily contradict this model, the changes in the EEG due to medication do not indicate that stimulants act on components associated with the maturational status of the brain. The theta/alpha ratio did reduce with medication, but in the absence of an increase in absolute or relative alpha, the reduction in the ratio appears due to change in the theta band only, which negates a maturational-lag explanation of the effects of stimulants.

A second model of ADHD proposes that these children are cortically hypoaroused. This appears to involve hypofunctionality of catecholaminergic pathways projecting to prefrontal cortical areas (Todd and Botteron 2001). Neuroimaging studies have found structural changes in both basal ganglia structures and the prefrontal lobes (Castellanos et al. 1996; Filipek et al. 1997). However, it is not clear whether the problems seen in ADHD result from decreased activity in these pathways or less responsivity of the targets of these paths. In EEG studies, changes in cortical arousal should be reflected in the theta and beta bands (Lubar 1991). During resting conditions, the dominant activity in the EEG is in the theta and alpha bands. When arousal is increased, activity reduces in the theta band and shifts towards the beta band. With the administration of a stimulant in the present study, the primary changes in the EEG were in the theta and beta bands, with a decrease in theta and an increase in beta activity. Global changes in delta and alpha were not found. These results suggest that stimulant medications are acting to increase cortical arousal. In the small doses used to treat these children, the medications are simply acting to stimulate an underaroused cortex.

While normalisation of the EEG was evident, complete normalisation was not found except for the elevation of midline power in absolute delta and theta, and the theta/alpha ratio. This was primarily due to substantial variability within the sample, as was indicated by the review of individual subjects. Chabot et al. (1998) used a methodology very similar to that used in this study, and found that only 56.9% of their sample showed normalisation of the EEG, which is similar to the present study. Loo et al. (1999) found that only good responders to stimulants showed normalisation in the EEG. In the present study, subjects were tested after an assessment of the efficacy of the medication using a continuous performance task and a 6-month trial of the stimulant. If any problems arose from the medication during the trial, the child's parent was told to contact the doctor, and the medication was re-evaluated. This meant that no child in this study showed an obviously adverse response to medication, but there could have been some variability in the degree of positive response of these children.

In the review of individual subjects, there was considerable variability in the extent of normalisation of the EEG. Results indicated that most subjects with initially deviant power levels demonstrated some degree of normalisation (of at least 1 SD), with little evidence of the EEG abnormality becoming worse with medication. In previous studies from our laboratory, Clarke et al. (2001d, 2002) reported the existence of different EEG profiles in children with ADHD, including profiles suggestive of maturational lag, hypoarousal and hyperarousal. If stimulants primarily act by increasing cortical arousal, then children with a maturational-lag or hyperarousal EEG profile may not respond well to stimulant medication. This may account for the lack of change in the EEG found in some patients in this study, and needs further investigation.

While it has been proposed that stimulant medications act to increase catecholamines in the synaptic cleft (Spencer et al. 1996), the exact regions of the brain that these medications act on is not entirely clear. Swartwood et al. (1998) proposed that methylphenidate may act on subcortical regions of the brain, as they found no global changes in the EEG due to medication. This hypothesis is not supported by the present study, as significant EEG changes were found. While these results do not rule out the possibility of an effect of stimulants at a subcortical level, they do indicate affects on cortical functioning. This should not be surprising, as many of the deficits found in ADHD, such as deficits in inhibitory control (Rubia et al. 1998), are associated with cortical functioning.

This study investigated changes in the EEG of children with the combined type of ADHD. Results indicated that the unmedicated ADHD group had significantly greater absolute delta and theta, less posterior absolute beta, more relative theta, and less relative alpha than the control group, which is typical of EEG studies of children with

ADHD. The use of stimulant medications resulted in partial normalisation of the EEG, primarily evident in changes in the theta and beta bands. These results suggest that stimulant medications are effective in the treatment of some children with ADHD because they increase cortical arousal towards normal levels.

References

American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders, 4th edn. American Psychiatric Association, Washington D.C.

Benninger C, Matthis P, Scheffner D (1984) EEG development of healthy boys and girls. Results of a longitudinal study. Electroencephalogr Clin Neurophysiol 57:1–12

Callaway E, Halliday R, Naylor H (1983) Hyperactive children's event-related potentials fail to support underarousal and maturational-lag theories. Arch Gen Psychiatry 40:1243–1248

Capute A, Niedermeyer E, Richardson F (1968) The electroencephalogram in children with minimal cerebral dysfunction. Pediatrics 41:1104–1114

Castellanos F, Giedd J, Marsh W, Hamburger S, Vaituzis A, Dickstein D, Sarfatti S, Vauss Y, Snell J, Lange N, Kaysen D, Krain A, Ritchie G, Rajapakse J, Rapoport J (1996) Quantitative brain magnetic resonance imaging in attention-deficit hyperactivity disorder. Arch Gen Psychiatry 53:607–616

Chabot R, Serfontein G (1996) Quantitative electroencephalographic profiles of children with attention deficit disorder. Biol Psychiatry 40:951–963

Chabot R, Orgill A, Crawford G, Harris M, Serfontein G (1999) Behavioural and electrophysiologic predictors of treatment response to stimulants in children with attention disorders. J Child Neurol 14:343–351

Clarke A, Barry R, McCarthy R, Selikowitz M (1998) EEG analysis in attention-deficit/hyperactivity disorder: a comparative study of two subtypes. Psychiatry Res 81:19–29

Clarke A, Barry R, McCarthy R, Selikowitz M (2001a) Age and sex effects in the EEG: development of the normal child. Clin Neurophysiol 112:815–826

Clarke A, Barry R, McCarthy R, Selikowitz M (2001b) Age and sex effects in the EEG: differences in two subtypes of attention-deficit/hyperactivity disorder. Clin Neurophysiol 112:815–826

Clarke A, Barry R, McCarthy R, Selikowitz M (2001c) EEG differences in two subtypes of attention-deficit/ hyperactivity disorder. Psychophysiology 38:212–221

Clarke A, Barry R, McCarthy R, Selikowitz M (2001d) EEG-defined subtypes of children with attention-deficit/hyperactivity disorder. Clin Neurophysiol 112:2098–2105

Clarke A, Barry R, McCarthy R, Selikowitz M, Brown C (2002) EEG evidence for a new conceptualisation of attention deficit hyperactivity disorder. Clin Neurophysiol 113:1036–1044

Dykman R, Holcomb P, Oglesby D, Ackerman P (1982) Electrocortical frequencies in hyperactive, learning-disabled, mixed, and normal children. Biol Psychiatry 17:675–685

Filipek P, Semrud-Clikeman M, Steingard R, Renshaw P, Kennedy D, Biederman J (1997) Volumetric MRI analysis comparing subjects having attention-deficit hyperactivity disorder with normal controls. Neurology 48:589–601

Gordon M (1986) How is a computerized attention test used in the diagnosis of attention deficit disorder? J Child Contemp Soc 19:53–64

Howell D (1997) Statistical methods for psychology, 4th edn. Duxbury Press, California

Janzen T, Graap K, Stephanson S, Marshall W, Fitzsimmons G (1995) Differences in baseline EEG measures for ADD and normally achieving preadolescent males. Biofeed Self Reg 20:65–82

Lazzaro I, Gordon E, Whitmont S, Plahn M, Li W, Clarke S, Dosen A, Meares R (1998) Quantified EEG activity in adolescent attention deficit hyperactivity disorder. Clin Electroencephalogr 29:37–42

Lindgren S, Wolraich M, Stromquist A, Davis C, Milich R, Watson D (1990) Diagnostic heterogeneity in attention deficit hyperactivity disorder. Presented at the Fourth Annual NIMH International Research Conference on the Classification and Treatment of Mental Disorders in General Medical Settings, Bethesda, USA

Loo S, Teale P, Reite M (1999) EEG correlates of methylphenidate response among children with ADHD: a preliminary report. Biol Psychiatry 45:1657–1660

Lubar J (1991) Discourse on the development of EEG diagnostics and biofeedback for attention-deficit/hyperactivity disorders. Biofeed Self Reg 16:201–225

Lubar J, White J, Swartwood M, Swartwood J (1999) Methylphenidate effects on global and complex measures of EEG. Pediatr Neurol 21:633–637

Mann C, Lubar J, Zimmerman A, Miller C, Muenchen R (1992) Quantitative analysis of EEG in boys with attention deficit hyperactivity disorder: controlled study with clinical implications. Pediatr Neurol 8:30–36

Matousek M, Rasmussen P, Gilberg C (1984) EEG frequency analysis in children with so-called minimal brain dysfunction and related disorders. Adv Biol Psychiatry 15:102–108

Pelham W, Gnagy E, Greenslade K, Milich R (1992) Teacher ratings of DSM-III-R symptoms for the disruptive behaviour disorders. J Am Acad Child Adolesc Psychiatry 31:210–218

Rubia K, Oosterlaan J, Sergeant J, Brandeis D, Leeuwen T (1998) Inhibitory dysfunction in hyperactive boys. Behav Brain Res 94:25–32

Satterfield J, Cantwell D (1974) CNS function and response to methylphenidate in hyperactive children. Psychopharmacol Bull 10:36–37

Satterfield J, Cantwell D, Saul R, Lesser M, Podsin R (1972) Physiological studies of the hyperkinetic child: I. Am J Psychiatry 128:102–108

Satterfield J, Cantwell D, Saul R, Lesser M, Podsin R (1973a) Response to stimulant drug treatment in hyperactive children: predictions from EEG and neurological findings. J Autism Child Schizophr 3:36–48

Satterfield J, Lesser M, Saul R, Cantwell D (1973b) EEG aspects in the diagnosis and treatment of minimal brain dysfunction. Ann NY Acad Sci 205:274–282

Spencer T, Beiderman J, Wilens T, Harding M, O'Donnell, Griffin S (1996) Pharmacotherapy of attention-deficit hyperactivity disorder across the life cycle. J Am Acad Child Adolesc Psychiatry 35:409–432

Swanson J, McBurnett K, Wigal T, Pfiffner L (1993) Effect of stimulant medication on children with attention deficit disorder: a "Review of Reviews". Except Child 60:154–162

Swanson J, Sergeant J, Taylor E, Sonuga-Barke E, Jensen P, Cantwell D (1998) Attention-deficit hyperactivity disorder and hyperkinetic disorder. Lancet 351:429–433

Swartwood M, Swartwood J, Lubar J, Timmermann D, Zimmerman A, Muenchen R (1998) Methylphenidate effects on EEG, behavior, and performance in boys with ADHD. Pediatr Neurol 18:244–250

Tabachnick B, Fidell L (1989) Using multivariate statistics. Harper Collins, New York

Todd R, Botteron K (2001) Is attention-deficit/hyperactivity disorder an energy deficiency syndrome? Biol Psychiatry 50:151–158

Wikler A, Dixon J, Parker J (1970) Brain function in children and controls: psychometric, neurological and electroencephalographic comparisons. Am J Psychiatry 127:634–645

Wilens T, Biederman J (1992) The stimulants. Psychiatr Clin N Am 15:191–222