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EEG in children with subtypes of Attention-Deficit/Hyperactivity Disorder: effects of age, sex and comorbidity

Adam R. Clarke
University of Wollongong, aclarke@uow.edu.au

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EEG in Children with Subtypes of Attention-Deficit/Hyperactivity Disorder: Effects of Age, Sex and Comorbidity

A thesis submitted in partial fulfilment of the requirements for the award of the degree

DOCTOR OF PHILOSOPHY

from

UNIVERSITY OF WOLLONGONG

by

Adam R. Clarke
B.A., M.Sc.

Department of Psychology

2000
DECLARATION

I, Adam R. Clarke, declare that this thesis, submitted in partial fulfillment of the requirements for the award of Doctor of Philosophy, in the Department of Psychology, University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. The document has not been submitted for qualifications at any other academic institution.

Adam R. Clarke

15 March 2000
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This thesis examined EEG differences in children with a DSM-IV diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD) and age-matched control subjects. An eyes closed, resting EEG was used in all seven studies. Absolute and relative power estimates were calculated in the delta, theta, alpha and beta bands, as well as ratio coefficients between frequency bands, and the mean frequency of each band was calculated in some studies. This thesis extended previous research via investigation of (i) differences between ADHD and normal children (ii) differences between subtypes of ADHD (iii) age related changes in the EEG of ADHD and normal children (iv) sex differences in ADHD and normal children, and (v) effects of comorbidity in ADHD. The major results were that, (a) EEG measures were found that differentiated between normal children and children with ADHD, as well as between the inattentive and combined subtypes of the disorder; (b) Age analysis indicated that the EEG correlates of the hyperactive/impulsive components of ADHD mature with increasing age, but the inattentive components remain more stable; (c) Sex differences were found in the EEG of normal children and between the ADHD groups. Overall, the most important of these results indicated that there are two independent electrophysiological components in ADHD.
OVERVIEW

This thesis aimed to extend the existing electrophysiological knowledge of Attention-deficit/Hyperactivity Disorder (ADHD) by examining differences between the EEG profiles of children with ADHD and those of normal children. This aim was achieved through the comparison of two groups of children, with the combined and inattentive subtypes of ADHD, with normal children. As part of this investigation, age and sex effects, which have not been included in previous research into ADHD, were examined. In addition to these group differences, the effects of ADHD comorbid with diagnoses of Oppositional Defiant Disorder and Learning Disabilities were also separately examined. In the final study, atypical ADHD EEG profiles, noted in small numbers of patients in the previously mentioned studies, were further examined.

The first four chapters of this thesis provide comprehensive literature reviews on Attention-Deficit/Hyperactivity Disorder (Chapter 1), Comorbidity (Chapter 2), EEG in Normal Children (Chapter 3), and EEG in Attention-Deficit/Hyperactivity Disorder (Chapter 4).

Study 1 (Chapter 5) investigated differences in the EEG between children with ADHD of the Combined Type, ADHD of the predominantly Inattentive Type and normal controls. All subjects were between the ages of 8 and 12 years and groups were matched on age and gender. The EEG was recorded during an eyes-closed resting condition from 21 monopolar derivations and these were clustered into nine regions prior to analysis. The patient groups were found to have greater levels of theta and deficiencies of alpha and beta in comparison to
the control group. Children with ADHD of the Predominantly Inattentive Type were found to be significantly different from those of the Combined Type in the same measures, appearing to be closer to the normal profiles. The general results supported a maturational lag model of the central nervous system in ADHD. The differences between the subtypes suggested a difference in the severity of the disorder rather than a different neurological dysfunction.

Study 2 (Chapter 6) further investigated EEG differences between the same types of groups used in Study 1, with larger numbers and a wider range of measures. The EEGs were Fourier transformed to provide absolute and relative power estimates for the delta, theta, alpha and beta bands, and the mean frequency for each band was calculated. A series of ratio coefficients between frequency bands were also calculated. Differences between all three groups were found in the theta, alpha and beta bands. Similarly, differences were found between all three groups for the theta/alpha and theta/beta ratios and for the mean frequency of the total EEG. In each of these measures, the Inattentive group was positioned between the control group and the Combined group. However, three differences were found between the two clinical groups in absolute and relative theta, and the theta/alpha ratio in the frontal regions, where the groups were qualitatively different. These results support a model of ADHD resulting from a developmental deviation rather than a maturational lag in the CNS. The differences between the clinical groups in frontal activity suggests that different neuroanatomical systems are involved in the different subtypes of ADHD.

Age-related changes and sex differences in the EEGs of normal children were investigated in Study 3 (Chapter 7). Forty boys and forty girls between the
ages of 8 and 12 years participated in this study. Absolute delta activity decreased with age. In the relative power bands, a decrease was found for the delta and theta bands, and an increase in the alpha and beta bands, with increasing age. In both the theta/alpha and theta/beta ratios, decreases in slow wave activity were indicated with increasing age. Differences were also found in rates of development between the midline and the two hemispheres. In absolute delta and the theta/beta ratio, the midline had greater power than the two hemispheres and this difference became less with age. At the same time, beta band power was found to increase at the midline at a greater rate than in the two hemispheres. Sex differences were also found, with males having less theta and more alpha than females. These results suggest that compared to males, females have a developmental lag in the EEG.

Study 4 (Chapter 8) extended the investigation of the group differences found in Studies 1 and 2, by examining age-related changes and sex differences in the EEGs of the Combined type and Inattentive type subtypes of ADHD. Forty boys and forty girls were included in each group, with all subjects between the ages of 8 and 12 years. The ADHD groups had more absolute delta and theta, more relative theta, and less relative alpha and beta than normal control groups. Total power, absolute alpha and beta, and relative delta and alpha were also able to differentiate between the two ADHD groups, and the theta/alpha and theta/beta ratios differed between all three groups. Sex differences between groups, except for total power, indicated that the difference between ADHD subjects and the control group was greater in males than females and changed faster in males. With increasing age, the EEG profile of the ADHD Inattentive group was found
to change at a similar rate to the changes found in the normal group, with the between-group differences in power levels remaining constant. In the ADHD Combined group, power was found to change at a greater rate than in the ADHD Inattentive group, with the power levels of the two ADHD groups becoming similar with age. These results are supportive of a two component model of ADHD, with the EEG correlate of the hyperactive/impulsive component maturing with age and that of the inattentive component remaining more stable.

Study 5 (Chapter 9) investigated EEG differences between two groups of children with ADHD of the Combined type, with or without comorbid Oppositional Defiant Disorder (ODD), and normal control subjects. Each group consisted of twenty males. All subjects were between the ages of 8 and 12 years and groups were matched on age. The ADHD groups had more absolute and relative theta than the control group. Regionally, the ADHD groups had less relative alpha and more relative delta in posterior regions, and less relative beta in the frontal regions, than the control group. No significant group main effects were found between the ADHD group and the ADHD+ODD. These results suggest that ODD is not associated with abnormalities in central nervous system functioning.

In Study 6 (Chapter 10) EEG differences between two groups of children with ADHD of the Combined type, with or without Learning Disabilities (LD), and normal control subjects, were investigated. Twenty subjects were included in each group. All subjects were between the ages of 8 and 12 years and groups were matched on age and sex. The ADHD+LD had more relative theta, less relative alpha and a higher theta/alpha ratio than the ADHD group. A number of hemispheric differences were also found in the delta and alpha bands. These
results suggested that some of the EEG abnormalities found in the ADHD+LD group represent an electrophysiological component associated with the LD, which is independent of the EEG abnormalities found in ADHD.

Study 7 (Chapter 11) investigated the existence of a group of children with ADHD who have excess fast wave activity in their EEGs. In Studies 1 and 2, a small subset of children with excess beta activity in the EEG were noted, and were excluded as outliers in those studies. The aim of this study was to determine whether children with excess beta activity represent a distinct electrophysiological subtype of ADHD, to quantify the differences in their EEG profiles, and to determine if this group of children with ADHD have behavioural profiles different from other children with ADHD. The results indicated that children with excess beta represent a small independent subset of children diagnosed with ADHD, which primarily consist of children with a diagnosis of ADHD combined type. Behaviourally, this group was similar to other children with ADHD, although the excess beta group was reported as being more prone to temper tantrums and to be moody. The excess beta activity was primarily found in the frontal regions and may be associated with deficits in frontal lobe self-regulation and inhibition control.

An overall summary of the results obtained in the thesis, and suggestions for future research, are provided in Chapter 12.
The disorder that has now become known as Attention-Deficit/Hyperactivity Disorder (ADHD) has undergone considerable change in its conceptualisation, although the aetiology of the disorder remains largely unknown. In the last four editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (APA, 1968, 1980, 1987, 1994), ADHD has changed from a single disorder to a two dimensional disorder with three subtypes, and this has resulted in a number of subsequent changes in the name of the disorder.

In the DSM-IV (APA, 1994), ADHD has become a two-axes disorder. The first axis is identified as predominantly Hyperactive-Impulsive, which includes behaviours of restlessness, fidgety and excessive motor activity, as well as an inability to wait for their turn or often interrupting others. The second axis is an inattentive one, which is characterised by difficulty sustaining attention, careless work, an inability to follow instructions, being easily distracted and forgetful. A diagnosis of ADHD can be made if a child has a predominance of behavioural symptoms from one of the axis or a combination of the two. The three subtypes of ADHD are: Attention-Deficit/Hyperactivity Disorder, Predominantly Hyperactive-Impulsive Type; Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Type (ADHDin); and Attention-Deficit/Hyperactivity Disorder, Combined Type (ADHDcom).

Throughout this text, the DSM-IV (APA, 1994) title of Attention-Deficit/Hyperactivity Disorder will be used as the general descriptor for this disorder. Subtype names from earlier editions of the DSM will be used only if specific subtype differences are being discussed.
1.1 EPIDEMIOLOGY OF ADHD

ADHD is one of the disorders most commonly treated by child and adolescent psychiatrists in America, with this group of children comprising as much as 50% of child psychiatry clinic populations (Cantwell, 1996). This disorder 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 a 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. Studies using DSM-III-R criteria have found a rate of 6.1% for children in a school population (Lindgren, Wolraich, Stromquist, Davis, Milich, & Watson, 1990). Pelham, Gnagy, Greenslade and Milich (1992), in a national survey using teachers' ratings, found 4% of boys had ratings consistent with ADHD. In contrast to the rates of ADHD found in these studies, rates as high as 18.9% have been reported for a sample of inner-city parochial school students (Newcorn, Halperin, Healey, O'Brien, Pascualvaca, Wolf, Morganstein, Sharma, & Young, 1989).

The DSM-IV (APA, 1994) estimates the prevalence of ADHD in the general population at approximately 3% to 5% of school-age children. This figure does not take into account preschool, adolescent, and adult populations.

Baumgaertel, Wolraich and Dietrich (1995) and Wolraich, Hannah, Pinnock, Baumgaertel and Brown (1996) conducted two epidemiological studies using DSM-IV criteria (APA, 1994). Teacher information was the sole source of
data in both studies. Wolraich et al. (1996) had teachers complete a questionnaire, which included symptoms for disruptive behavioural disorders, for 8258 American children. Results indicated that 11.4% of children in this study met the criteria for a diagnosis of ADHD. Baumgaertel et al. (1995) studied 1077 children in ten public schools in Germany. They found that 17.8% of that population met the criteria for ADHD. The prevalence rates for the DSM-IV subtypes of ADHD have been more consistent than those for the overall disorder. In the American sample (Wolraich et al., 1996), rates of 5.4% were found for the diagnosis of ADHD of the primarily inattentive type, 2.4% for the hyperactive/impulsive type, and 3.6% for the combined type. Except for the primarily inattentive type, the German rates for the same subtypes were similar: 9.0%, 3.9% and 4.8%, respectively (Baumgaertel et al., 1995). Typically, higher rates of ADHD have been found in studies that have used DSM-IV criteria. This has been explained as resulting from the inclusion of the hyperactive/impulsive subtype, which has shown little correlation with previous DSM subtypes (Morgan, Hynd, Ricco & Hall, 1996).

1.2 HISTORY OF ADHD

ADHD was first documented in 1902 as a defect in moral control in children (Still, 1902). This disorder was characterised by spitefulness, lawlessness, jealousy, dishonesty, destructiveness, shamelessness, sexual immorality and viciousness. These behaviours were found in both boys and girls and were not restricted to children with low IQs, but were found in children with
normal mental abilities. Disruptive, hyperactive and impulsive behaviour, in conjunction with poor attention span, was considered to be a defect in moral development for the first part of the twentieth century.

After a severe influenza outbreak in 1918, a group of children were found to have developed a number of behavioural problems after the contraction of influenza-related encephalitis (Paterson & Spence, 1921; Kennedy, 1924). Many children who survived the acute phase of encephalitis developed an array of behaviours including disobedience, irritability, fits of temper, cruelty and kleptomania. These children appeared to have suffered little impairment of their intellectual abilities and were characterised as moral rather than mental imbeciles (Anderson, 1923).

A second group of children were also documented. These children had suffered from severely impaired intellect and did not present with the emotional or behavioural disturbances of the other group. The major difference between the two groups appeared to be the age at which they contracted encephalitis. Children who were older when they contracted encephalitis were more likely to develop the behavioural problems, whereas younger children mostly suffered from intellectual deficiencies. From these general findings, it was concluded that both the intellectual and behavioural problems were the result of minimal brain damage.

In 1920 a ward was established for post-encephalitis syndrome at the Bellevue Psychiatric Hospital in New York City (Bender, 1975). Bender (1942) described her experiences with 55 children with post-encephalitis syndrome. The behavioural disorders were characterized by the psychopathic personality type of
reaction with hyperkinesis, which was not modifiable by psychotherapy or environmental control. The behaviour was perceived as an organic “driveness” of brainstem origin. The hyperkinesis led the child to contact the environment continually by touching, taking and destroying. As the personality became integrated, there was a tendency for asocial behaviour such as sexual gratification, stealing and destroying property, resisting routine, and truanting and running away. Although the child had some awareness that he could not control his behaviour, he was not concerned with guilt or anxiety, but with fear of punishment.

The effect of other forms of brain injury were investigated as a possible link to behavioural disorders. Strecker and Ebaugh (1924) studied 30 children with histories of head injuries and concluded that their disorders were similar to those of post-encephalitic disorders. Blau (1936) described a group of children who showed mental changes following head trauma, and suggested that the disorder might be the result of a localized lesion of the prefrontal association areas. Later research however, tended to discount the effect of head injuries in childhood behavioural problems (Dencker, 1958; Harrington & Letemendia, 1958).

Birth injury was also studied as a possible cause of behavioural disorders in children. Birth was proposed as often causing trauma which resulted in hyperkinesis (Schilder, 1931). Shirley (1939) followed the progress of a number of premature babies for varying periods up to 5 years. On the basis of her observations she defined a syndrome with symptoms which included hyperactivity or sluggishness, short attention span, easily distracted and
stubbornness. From these findings, childhood behavioural disturbances were considered the result of some form of brain damage throughout most of the 1920s and 1930s (Kessler, 1980).

The model of ADHD as resulting from brain damage, began to lose favour in the 1950s and 1960s, as children without brain damage were diagnosed with hyperkinetic impulse disorder. In a study at the Bradley Home (Laufer, Denhoff & Solomons, 1957), a psychiatric hospital for children, 50 patients who showed symptoms of hyperkinetic impulse disorder were reviewed. In this group, only 11 patients had a clear history of factors commonly accepted as capable of causing brain damage.

The term “brain damage” was also seen as very nonspecific (Birch, 1964). Brain damage was seen to refer to any anatomical or psychological alteration in nervous tissue in the brain. This could then be used to categorise children with cerebral palsy, hemiplegia, and mental deficiency deriving from hydrocephalus or epilepsy. The concept of the “brain damaged child” does not necessarily apply to children from all of these groups. To better identify specific groups of children, the word “minimal” was added to the term “brain damage” to identify children who had deviations from normal neurological and behavioural patterns (Pasamanick & Knoblock, 1959). In a retrospective study of 500 children referred to the Baltimore Department of Education for behavioural problems (Pasamanick & Knoblock, 1960), pre- and peri-natal complications were significantly more common in the behavioural problem group, and hyperactivity was the most common problem.

One measure used to determine the existence of minimal brain damage
was the existence of neurological "soft signs" (Kennard, 1960). In the present context, "Soft signs" are associated with complex motor behaviour, where mistakes that are normal in younger children should disappear in the course of normal development (Kinsbourne, 1973a). If they persist for an unduly long time, they should be considered as an abnormality. At that time there were no uniform criteria for judging soft signs, which resulted in inconsistent reports in the literature (Kessler, 1980). This led some researchers to suggest that soft signs did not give a great enough magnitude of difference between groups to be of clinical usefulness (Adams, Kocsis & Estes, 1974).

Birch (1964, p.5), in a criticism of the minimal brain damage model of behavioural disorders, stated that "Regardless of any adjectives, we have the overriding obligation to demonstrate, in terms of replicable, valid and clearly defined criteria, that the multiplicity of aberrant behaviours we now attribute to 'minimal brain damage' are, in fact, the result of damage to the brain". Since this was an impossible undertaking, a subtle shift in terminology began to appear in the literature, with researchers changing the name of this disorder from "minimal brain damage" to "minimal brain dysfunction" (MBD) (Green & Chee, 1994). The first paper to propose this change was by Clements and Peters (1962). In that paper, the practice of trying to make a causative link between a number of childhood behavioural problems, such as sibling rivalry, rejecting parents and repressed hostility, and brain functioning, was criticised. It was considered possible that any brain dysfunction may have been secondary rather than primary to the problem, or even epiphenomenal.

These developments saw a change in the perception of the underlying
neurological problems associated with this population of children. In one study, Stevens, Boydstun, Dykman, Peterson and Sinton (1967) compared 26 normal control subjects with children assessed as having MBD, on a number of neuropsychological tests. They found that the MBD group was slower to respond, less able to follow verbal instructions, and poorer in tone discrimination and tapping. From these results, it was concluded that the deficits in performance suggested subtle deviant functioning of the central nervous system (CNS), whether of organic or genetic origin.

With this new conceptualisation of MBD came a broadening of the possible etiology. Possible causes included genetic variations, biochemical irregularities, perinatal brain insults, or resulting from illness and injuries sustained during the years critical for the normal development and maturation of the CNS (Clements, 1966). The inclusion of such factors as genetic variants made it impossible to place the focus solely on acquired damage to the brain, as genetic predisposition cannot be viewed as causing damage.

1.3 CHANGES IN DIAGNOSTIC CATEGORY

The DSM-II (APA, 1968) first listed diagnostic criteria for ADHD under the title "hyperkinetic reaction of childhood". This was a single disorder with no subtypes, and was characterised by overactivity, restlessness, distractibility and short attention span. The major emphasis in the diagnostic criteria for this disorder was placed on the overt behavioural aspects.

The DSM-II was generally criticised as having major limitations in
childhood psychiatric disorders (Cantwell, Russell, Mattison & Will, 1979). These included having categories which were too inclusive or vague, or too limited. Subsequent research (Douglas, 1972; Douglas & Peters, 1979) found that problems of poor sustained attention and impulse control were as important, if not more so, than the hyperactivity. Following from this research, the DSM-III (APA, 1980) renamed the disorder “Attention Deficit Disorder”, with the DSM-II emphasis on excessive motor activity changing to greater emphasis on the attentional aspects of the disorder (Edelbrock, Costello & Kessler, 1984). The DSM-III distinguished between two subtypes of the disorder, Attention Deficit Disorder with hyperactivity (ADD/H) and Attention Deficit Disorder without hyperactivity (ADD/WO). The main difference between these two subtypes of the disorder was that children with ADD/WO exhibited the inattention and impulsive features of the disorder, but not hyperactivity.

Lynn, Mirkin, Lanese, Schmidt and Arnold (1983) reviewed 1530 files of patients seen at the Ohio State University Child Psychiatry Outpatient Clinic. The results indicated that there was a large incongruity between DSM-II and DSM-III criteria. 52 patients met criteria for ADD/WO under DSM-III criteria, but these were originally given psychiatric diagnoses other than hyperkinetic reaction of childhood. The original diagnosis of hyperkinetic reaction of childhood, in 49 patients, was only based on the presence of hyperactive behaviour, in the absence of inattention and impulsivity. This was seen as a problem as hyperactive behaviour is sometimes found in other childhood disorders (Fish, 1971). These results were seen as supporting another diagnostic category of ADHD where the child had hyperactivity without distractibility.
In the DSM-III-R (APA, 1987), the disorder was renamed “Attention Deficit Hyperactivity Disorder” (ADHD) and was considered unidimensional in nature, with a single behavioural checklist being given for diagnosis. For a diagnosis of ADHD, a child had to exhibit eight out of fourteen behaviours. Under this diagnosis, criteria for a severity rating was provided, in which a child could be diagnosed as mild, moderate or severe. A second category, “Undifferentiated Attention Deficit Disorder” (UADD), was also included, with the predominant feature being marked inattention. Under the category of UADD, the DSM-III-R did not give specific diagnostic criteria and stated that “further research is necessary to determine if this is a valid diagnostic category and, if so, how it should be defined” (APA, 1987, p.95).

One reason the DSM-III-R reconceptualized ADHD and dropped the distinct subtypes was that at publication there was not enough empirical support for the DSM-III conceptualization of two distinct subtypes (Barkley, 1990b; Frick & Lahey, 1991; Lahey, Pelham, Schaugency, Atkins, Murphy, Hynd, Russo, Hartdagen & Lorys-Vernon, 1988; Lahey and Carlson, 1991; Schaugency & Rothlind, 1991). By making ADHD a unidimensional construct, DSM-III-R also avoided the problem of trying to categorize each symptom under a distinct domain (Newcorn et al., 1989). The polythetic approach was also consistent with the criteria for other DSM-III-R disorders, and with other empirical approaches to classification (Barkley, 1990b).

Several researchers have argued that DSM-III-R was published prematurely and that the APA should have waited for more empirical evidence about the validity of the DSM-III criteria (Cantwell & Baker, 1988; Werry,
Reeves & Elkind, 1987). Suggestions were also made that the revisions were more substantial than were warranted (Cantwell & Baker, 1988; Werry, 1988). The most significant effect of the changed nosology was that the group of children assigned the ADHD diagnosis was more heterogeneous than that assigned to the ADD/H diagnosis (Lahey, Loeber, Stouthamer-Loeber, Christ, Green, Russo, Frick & Dulcan, 1990; Newcorn et al., 1989).

A number of researchers (Goodman & Poillion, 1992; Shaywitz & Shaywitz, 1991b; Weinberg & Emslie, 1991) have identified some of the problems of the DSM-III and DSM-III-R diagnostic systems and the ambiguities associated with the ADD or ADHD diagnosis. However, research published shortly before and after the introduction of DSM-III-R helped to clarify the nature of the behavioural syndrome, offered insight as to whether DSM-III or DSM-III-R provided the better conceptualization, and guided the development of DSM-IV. Factor-analytic studies of symptom profiles further clarified how the disorder might be structured. This analysis suggested that, instead of viewing ADHD as consisting of symptoms clustered into inattention, impulsivity, and hyperactivity dimensions as in DSM-III, ADHD had two dimensions, the first dimension being inattention, and the second being a hyperactivity/impulsivity dimension (Bauermeister, 1992; Bauermeister, Alegria, Bird, Rubio-Stipec & Canino, 1992; Lahey et al., 1988; Lahey, Applegate, McBurnett, Biederman, Greenhill, Hynd, Barkley, Newcorn, Jensen, Richters, Garfinkel, Kerdyk, Frick, Ollendick, Perez, Hart, Waldman & Shaffer, 1994; Pelham et al., 1992; Morgan et al., 1996). Thus, in the DSM-IV (APA, 1994), the diagnostic criteria changed again, to a two axis disorder.
Morgan et al. (1996) found that the DSM-IV criteria for ADHD predominantly inattentive and combined types produce subtypes which can be reliably diagnosed and which have clinically meaningful differences. Gomez, Harvey, Quick, Scharer and Harris (1999) studied DSM-IV ADHD symptoms using parent and teacher ratings of primary school children on a scale comprising the 18 DSM-IV ADHD symptoms. This study used confirmatory factor analysis to compare three models, with all items in one factor, inattention in one and hyperactivity and impulsivity items in a separate factor, and inattention, hyperactivity, and impulsivity items in three separate factors. Results supported both the two- and three-factor models, with the three-factor model showing slightly better categorisation than the two-factor model.

A second, almost parallel criteria for hyperactivity is presented in the World Health Organisations International Statistical Classification of Diseases and Related Health Problems (ICD). The latest revision of the ICD, the ICD-10 (WHO, 1993) lists criteria for a single disorder entitled Hyperkinetic Disorder. For a child to meet criteria for this disorder, they must show symptoms of inattention, hyperactivity and restlessness. These symptoms must be present in a number of settings and onset of the disorder should not be after the age of 7 years old.

One of the main differences between the DSM-IV and ICD-10 criteria is that the ICD-10 requires symptoms in all three categorise of inattention, hyperactivity and restlessness to be present for a diagnosis (Swanson, Sergeant, Taylor, Sonuga-Barke, Jensen & Cantwell, 1998). The DSM-IV allows for a diagnosis of subtypes based on symptoms being found in only one domain. These
differences in criteria result in different prevalence rates with the DSM-IV criteria being applicable to approximately 5% of children and the ICD-10 criteria being applicable to only 0.5% of the child population (Taylor, 1998). This thesis contains research that was conducted using DSM-IV criteria for ADHD, and for this reason, the ICD classification system will not be considered further. However, it is important to note that some studies of hyperactivity cited in this thesis, may have used an ICD rather than a DSM criteria for their population.

1.4 RELATIONSHIP BETWEEN DSM-III, DSM-III-R AND DSM-IV SUBTYPES

Morgan et al. (1996) found that the DSM-III diagnoses of ADD/WO and ADD/H corresponded fairly closely with the DSM-IV diagnoses of ADHD predominantly inattentive type and combined type, respectively. No significant relationship was found between the DSM-III-R diagnosis of ADHD and the DSM-IV diagnosis of ADHD combined type. These findings for the DSM-III-R are consistent with studies that found children assigned the ADHD diagnosis under DSM-III-R constituted a heterogeneous group (Lahey et al., 1990; Newcorn et al., 1989).

The ADHD predominantly hyperactive/impulsive subtype is a new diagnostic subtype which has received little previous theoretical or investigative attention, and has no relation to previous subtypes from earlier versions of the DSM (Newcorn et al., 1989).
1.5 SEX DIFFERENCES IN ADHD

In both clinical and epidemiological samples, ADHD is more common in males than females (James & Taylor, 1990), with relative rates of up to 9 to 1 in clinical samples, and 4 to 1 in epidemiological studies (APA, 1994) being found, although community based studies have found ratios of males to females as low as 2.1 to 1 (Szatmari, 1992; Taylor, Heptinstall, Sonuga-Barke & Sandberg, 1998). For each of the DSM-IV subtypes of ADHD, sex differences in rates of diagnosis are approximately 4 to 1 for all three subtypes (De Quiros, Kinsbourne, Palmer & Rufo, 1994). However, the methodologies that have been used to investigate the prevalence of sex differences in ADHD have been criticised as possibly contributing to the magnitude of these differences.

The use of clinic-referred samples of children with various types of psychopathology has been criticised as these samples are not always representative of the greater population (Costello, 1990). The lower ratio within the general population indicates that proportionally more boys than girls with ADHD present to clinics. One explanation for these differences is that the lower referral rate may reflect a neglect of the problems experienced by girls with ADHD (Berry, Shaywitz & Shaywitz, 1985; Brown, Madam-Swain & Baldwin, 1991). Boys with ADHD show higher rates of conduct disorder and other externalizing problems than do girls. This results in boys displaying more disruptive behaviours in structured settings, which may lead to higher referral rates (Baumagaertel et al., 1995; Cantwell, 1994; Wolraich et al., 1996).
Conversely, the lower rate of externalizing behaviours displayed by girls with ADHD may reduce identification and numbers of referrals to clinics.

The population that the sample has been drawn from has also been found to affect the nature of observed sex effects, with only nonreferred samples of girls with ADHD showing less impairment than boys with ADHD in terms of inattention, internalizing behaviour, peer aggression, and peer disliking (Gaub & Carlson, 1997). Among clinic-referred populations, girls and boys with ADHD showed similar levels of impairment on these variables, though girls with behavioural problems are often referred to clinics at younger ages than boys (Arcia & Conners, 1998).

A number of epidemiological studies of ADHD used teacher ratings of children as their primary source of information (Baumgaertel et al., 1995; Wolraich et al., 1996). McGee and Feehan (1991) found that the apparent lower prevalence of ADHD among girls was largely due to the fact that teachers under-recognize inattentive behaviour in girls, perhaps because girls are less likely than boys to exhibit behaviour management problems. McGee and Feehan (1991) found that although both parents and teachers rated boys with ADHD as being more deviant on inattention and hyperactivity than girls with ADHD, the average effect size differences between sexes were significantly larger for teacher ratings than for parent ratings. This was seen as a possible reason for lower rates of identification of girls with ADHD.

While there has been some debate over the impact of different reporting systems for the identification of children with ADHD, and their impact on research of sex differences within the disorder, a number of sex differences have
been found. Gaub and Carlson (1997) conducted a meta-analysis of studies that investigated sex differences in ADHD. The results indicated behavioural differences in several areas. ADHD girls showed lower levels of hyperactivity, fewer conduct disorder diagnoses, lower rates of other externalizing behaviour, and greater intellectual impairment than boys. These intellectual impairments have been found on tasks such as picture vocabulary (Breen, 1989), spatial memory (Brown et al., 1991), and tests of attention and achievement (Seidman, Biederman, Faraone, Weber, Mennin & Jones, 1997). However, neuropsychological performance on tests of executive function was less impaired than previously documented in boys with ADHD. Collectively, these results suggest that although there are problems with the identification of ADHD in girls, sex differences do exist in the areas of behavioural symptomatology and intellectual impairments.

1.6 CENTRAL NERVOUS SYSTEM BASED MODELS OF ADHD

The view that ADHD represented some form of CNS dysfunction led to questions of the exact nature of this hypothesised brain disorder. The two main models of ADHD which have tried to explain the disorder in terms of brain functioning are the Maturational Lag Model and the Hypoarousal Model of ADHD.

1.6.1 The Maturational Lag Model of ADHD
Kinsbourne (1973a) noted that children with gross brain damage exhibit abnormalities on neurological examinations. However, the diagnosis of MBD is based on findings that are abnormal only in reference to children of the same age. If the child was younger, many of the findings would be considered normal. This was seen to hold for the overt behavioural aspects of the disorder, as well as the attentional component. The ability of a child to focus attention on a single fixation point develops with age. In children with MBD, the ability to attend to an activity was seen to take longer to develop than in normal children.

A number of studies that used neuropsychological tests to assess children with ADHD have found that the degree of deviation from normal control subjects became less with increasing age, among the ADHD groups. Grodzinsky and Diamond (1992) used the Trail Making Test (Reitan & Wolfson, 1985) to assess neuropsychological deficits in children with ADHD. This test requires the child to connect a series of numbered circles distributed randomly on a page. Results indicated that older children performed at a similar level to control subjects, whereas the performance of the younger subjects was more discrepant.

Studies of the auditory evoked potential have found that hyperactive children have significantly lower amplitudes and longer latencies of the N1 and P2 components than age matched controls (Satterfield, Cantwell, Saul, Lesser & Podsin, 1973). These findings were considered to be typical of younger children.

The major problem with the maturational lag model is the occurrence of ADHD in adults. The maturational lag model implies that as a child becomes older, the symptoms of ADHD should lessen. Studies of ADHD have estimated that between 10% and 70% of children with ADHD continue to show symptoms
of the disorder as adults (Bellak & Black, 1992; Gittelman, Mannuzza, Shenker & Bonagura, 1985; Hechtman, 1992; Mannuzza, Gittelman-Klein, Bonagura, Malloy, Giampino & Addalli, 1991; Mannuzza, Klein, Bessler, Malloy & LaPadula, 1993; Weiss, Hechtman, Milroy & Perlman, 1985). Little research has been undertaken into the adult forms of this disorder. However, its high prevalence in childhood, combined with the results of follow-up studies, suggests that approximately 0.5% to 2% of adults may suffer from ADHD (Spencer, 1996; Toone & Van Der Linden, 1997). The DSM-IV (1994) states that some of the behavioural problems, such as excessive gross motor activity, become less in adolescence and adulthood. It is thus possible that maturational lag underlies some components of ADHD but not the entire disorder. This suggests that there may be multiple independent components that combine together to form this disorder.

1.6.2 The Central Nervous System Hypoarousal Model of ADHD

A second model of ADHD which is not entirely incompatible with the maturational lag model, is the hypoarousal model. The hypoarousal model of ADHD proposes that ADHD is the result of a low level of CNS arousal (Satterfield & Cantwell, 1974). This low CNS arousal results in insufficient inhibitory control over motor functions and a lack of inhibitory control over sensory functions, resulting in distractibility. This causes low arousal children to respond to irrelevant stimuli as often as other stimuli. Zentall (1985) proposed that hyperactivity arises from low levels of arousal and serves to maintain an
optimal arousal level, by increasing stimulation. To investigate this theory, Satterfield and Dawson (1971) conducted a study of skin conductance levels (SCLs). This study found that 50% of the hyperactive children had abnormally low SCLs, supporting a model of low CNS arousal.

Studies of regional cerebral blood flow (RCBF) have found results supportive of the hypoarousal model (Lou, Henriksen, Bruhn, Borer & Nielsen, 1989). RCBF was studied in 20 children and adolescents with ADHD. Striatal regions were found to be hypoperfused in the ADHD group, which was hypothesized to result in low neural activity in the striatal regions.

Hyperactive children have been found to respond well to the use of stimulant medication and are often prescribed stimulants, as part of their clinical management (Spencer, Biederman, Wilens, Harding, O'Donnell & Griffin, 1996). Studies have found that reticular arousal and cortical inhibition vary together and that an increase in cortical arousal may result in an increase in cortical inhibition (Walley & Weiden, 1973). These drugs act as CNS stimulants and have the effect of increasing CNS arousal and also raise inhibitory levels in hyperactive children (Satterfield, Cantwell & Satterfield, 1974). Stimulants have been found to diminish the behaviours of ADHD, including overactivity, impulsivity, and inattentiveness. In addition to improving core symptoms of ADHD, stimulants also improve associated behaviours, including on-task behaviour, academic performance, and social function (Abikoff & Gittleman, 1985; Barkley, Karlsson, Strzelecki & Murphy, 1984; Klein, 1987; Rapport & DuPaul, 1986; Swanson, Granger & Kliewer, 1987; Tannock, Schachar, Carr & Logan, 1989; Whalen,
1989; Wilens & Biederman, 1992). The action of these drugs has been seen as further support for a hypoarousal model of ADHD.

The hypoarousal model has been criticized as there is some evidence that children with ADHD are over-aroused rather than under-aroused (Dawson, 1994). Rosenthal and Allen (1978) reviewed the results of electrophysiological studies of children with ADHD and concluded that these children did not exhibit lower levels of autonomic arousal than found in normal children. Other studies have found that children with ADHD may have problems modulating or controlling their arousal levels to meet situational demands, rather than a permanent state of hypoarousal (Douglas & Peters, 1979). These results have brought the hypoarousal model into question.

1.7 FRONTAL LOBE DYSFUNCTION IN ADHD

From these theories of CNS functioning, questions have arisen as to what particular structures are involved in ADHD, and how they effect behaviour. A number of researchers have investigated the possible involvement of impaired frontal lobe functioning in children with ADHD (Barkley, 1990a; Faraone & Biederman, 1998; Koziol & Stout, 1992). This line of research has largely resulted from the fact that the core symptoms of ADHD are similar to those found in studies of people with frontal lobe lesions (Blau, 1936; Levin, 1938; Mattes, 1980; Benson, 1991; Heilman, Voeller & Nadeau, 1991).

Although results within the neuropsychological literature are often conflicting, studies that have used the continuous performance task, Stroop test,
Hand Movements, and Go/No-Go tests have demonstrated a high degree of reliability (Barkley, Grodzinsky & DuPaul, 1992). The continuous performance task requires a person to respond to a given target stimulus (Rosvold, Mirsky & Sarason, 1956). A number of studies have reported that children with ADHD perform worse than normal controls on the continuous performance task (Overtoom, Verbaten, Kemner, Kenemans, Van Engeland, Buitelaar, Camfferman & Koelega, 1998; Barkley et al., 1992; Klee & Garfinkel, 1983). These children make more omission and commission (false positive responses) errors, show less ability to sustain attention, and frequently show slower reaction times.

The Stroop test requires the child to name the colour of the ink in which the name of a different colour is written (Stroop, 1935). ADHD subjects were found to be more impaired than normal children on the interference part of the test (Hopkins, Perlman, Hechtman & Weiss, 1979; Carlson, Lahey & Neeper, 1986; Gornstein, Mammato & Sandy, 1989; Boucagnani & Jones, 1989; Grodzinsky & Diamond, 1992). This was primarily a problem of the ADHD subjects taking a longer time to respond and making more errors.

Hand movement tests require a person to copy a progressively longer sequence of complex hand movements (Luria, 1966), and these have been used in various forms as a measure of frontal lobe functioning (Lezak, 1983). Children with ADHD have been found to show greater impairment on this task than normal children (Breen, 1989; Mariani, 1990).

The Go/No-Go test requires the person to perform a motor response to the Go stimulus and inhibit any response to the No-Go stimulus. This test has been found to be effective in discerning frontal lobe lesions in adults (Tromer,
Hoeppner, Lorber & Armstrong, 1988). Children with ADHD have been found to make more total errors and more multiple errors than normal children (Tromer et al., 1988; Shue & Douglas, 1989).

Most of these tests assess the ability of a person to inhibit motor responses on demand, especially while being required to perform competing responses. This type of response inhibition has been perceived as being mediated by the frontal lobes and the orbital-prefrontal and medial-prefrontal areas, and their connections to the striatum (Benson, 1991; Heilman et al., 1991; Struss & Benson, 1986). These results suggest that ADHD involves a disinhibition disorder arising from dysfunction of the brain in these areas (Barkley, 1990a; Quay, 1988).

Shue and Douglas (1992) investigated the usefulness of the frontal lobe model of ADHD, and questioned the validity of conceptualizing ADHD as purely a deficit in inhibitory or attentional systems. Inhibitory deficits are heightened when complex or speed tasks are presented, thus increasing the child’s tendency to respond to stimuli with greater saliency (Dykeman, Ackerman & Oglesby, 1979). From this, it was hypothesised that any model that based ADHD purely on inhibitory or attentional systems may address only partial aspects of greater mechanisms. Shue and Douglas (1992) note that the frontal lobes receive information from cortical and subcortical regions, with connections to sensory and motor areas. The frontal lobes integrate relevant prior learning and affective states with current conditions, and modulate responses appropriately. This process is an important function in problem solving, responsiveness to reinforcements, response consistency and other functions typically impaired in frontal lobe damaged people. From this, ADHD is conceptualised as an
impairment of higher order cognitive processing. Deficits found in children with ADHD, such as failure to inhibit responses and inattention, would be seen as resulting from difficulty integrating information in order to plan, set goals, monitor responses and anticipate outcomes.

A number of physiological assessment techniques have been used to assess frontal lobe abnormalities in ADHD. Magnetic Resonance Imaging (MRI) has been used to investigate structural differences between the brains of ADHD subjects and normal controls. Hynd, Semrud-Clikeman, Lorys Novey & Elioplus (1990) used MRI to investigate abnormalities in 10 children diagnosed with ADHD using DSM-III-R criteria. The ADHD group had smaller widths of the right anterior cortices. Castellanos, Giedd, Eckburg, Marsh, Vaituzis, Kaysen, Hamburger, Rapoport & Rapoport (1994) found children with ADHD had smaller right caudate volume than normal children and that this structure did not develop in normal ways during childhood and adolescence. Giedd, Castenatos, Korzuch, King, Hamburger & Rapoport (1994) demonstrated reduced volume in the rostrum and rostral body of the corpus callosum. These results have been interpreted as being consistent with an alteration of functioning of the frontal and anterior cingulate cortices of the brain, in addition to altered premotor function (Steere & Arnsten, 1995).

The pathophysiology of ADHD has also been investigated using other imaging techniques, including RCBF and positron emission tomography (PET) (Lou, Henriksen & Bruhn 1984; Lou, Henriksen & Bruhn 1990; Lou et al., 1989; Zametkin, Nordahl, Gross, King, Semple, Rumsey, Hamburger & Cohen, 1990). RCBF studies found that the periventricular region was hyperperfused, which
indicated low metabolic and functional activity in frontal and central brain structures (Lou et al., 1984). In an attempt to clarify these results, a further study was conducted with a better defined population and larger numbers (Lou et al., 1989). This study found focal cerebral hypoperfusion of striatum and hyperperfusion in sensory and sensorimotor areas. Zametkin et al. (1990) used PET to investigate adults with ADHD who also had a child with ADHD. Compared with normal adults, these ADHD adults had lower cerebral glucose metabolism in the premotor cortex and in the superior prefrontal cortex. These brain areas are involved in the control of motor activity and attention. In a second study (Zametkin, 1993), PET was used to investigate adolescents with ADHD. In this study, the results were not as conclusive. Adolescent females with ADHD had global reductions in glucose metabolism compared with normal control females and males, and compared with males with ADHD.

Collectively, the results of neuropsychological assessments and studies of the pathophysiology of ADHD suggest that these children have dysfunctions of some frontal and prefrontal systems which are associated with inhibition and self regulation. All of these studies investigated ADHD children with a hyperactive component to their diagnosis, without investigating children who were predominantly inattentive.

1.8 GENETIC FACTORS IN ADHD

The influence of genetic factors has been implicated in the etiology of ADHD for approximately the last 30 years (Cantwell, 1996). Family prevalence
studies have shown that ADHD and other related problems occur in the families of ADHD children (Faraone, & Biederman, 1997). Biederman, Munir & Knee (1987) found a higher rate of psychopathology in relatives of children with ADHD than normal control children, according to parental interviews which were based on the DSM-III (APA, 1980) criteria. These authors recognized that they could not differentiate between genetic and environmental etiology because of the small sample size and their use of intact nuclear families. Faraone, Biederman & Chen (1992) applied segregation analysis to data from 257 ADHD probands and their 808 first-degree relatives, using structured interviews based on DSM-III-R (APA, 1987) criteria. The familial distribution of ADHD was consistent with the effects of a single major gene. These authors identified considerable nonshared environmental effects, with the disorder being found in only 46% of the boys and in 31% of the girls with the putative gene. Goodman and Stevenson (1989) conducted a twin study where one or both of the siblings had extreme hyperactivity scores as rated by mothers, fathers, or teachers. The results showed a probandwise concordance rate of 51% for monozygotic twins and 30% for dizygotic twins. This study was limited by the small number of twins who met diagnostic criteria and by the small number of ADHD items (three) used to define "clinical relevance".

One criticism of many genetic studies is that environmental effects may influence the outcome that is being observed, and that the greater levels of concordance found in monozygotic twins may result from these twins having more similar environments than would be found in other siblings. Levy, Hay, McStephen, Wood & Waldman (1997) investigated genetic and environmental
factors in 5067 children, including 3876 twins. Results indicated that ADHD was more common in monozygotic twins than dizygotic twins with the effect of environmental influences being small. These results are also supported by adoption studies that have found results which support a genetic model of ADHD rather than an environmental model (Barkley, 1990; Cantwell, 1975).

High rates of heritability, as well as the high rate of concordance in monozygotic twins, is likely to increase the chance of finding a gene of major effect for ADHD, if one exists (LaHoste, Swanson, Wigal, Glabe, Wigal, King & Kennedy, 1996; Warren, Odell, Warren, Burger, Maciulis, Daniels & Torres, 1995). To date at least three genes have been implicated in ADHD. These include HLA on chromosome 6 (Cardon, Smith, Fulker, Kimberling, Pennington & De Fries, 1994), dopamine transporter gene on chromosome 5 (Cook, Stein, Krasowski, Cox, Olkon, Kieffer & Leventhal, 1995), and D4 receptor gene D4 DR on chromosome 11 (LaHoste et al., 1996). These results suggest that ADHD is likely to be oligogenic if not polygenic, although further research is needed to validate these results and to determine how these genes may interact, if at all.

1.9 DIFFERENCES IN SUBTYPES OF ADHD

Since the inclusion of a second subtype of ADHD in the DSM-III (APA, 1980), there has been a considerable debate as to whether the hyperactive and inattentive subtypes are actually two separate disorders. The DSM-III stated that “it is not known if they are two forms of a single disorder or represent two distinct disorders“ (APA, 1980, p.41). Although there are commonalities of
symptoms among ADHD children, they do not represent an homogeneous group, having a diversity of related psychiatric symptoms, family backgrounds, developmental courses and responses to treatments (Barkley, 1990a).

Studies conducted into the two subtypes of ADHD have found differences other than hyperactivity. Children with ADD/H have been found to be more impulsive (Lahey, Schaughency, Hynd, Carlson & Nieves, 1987; Cantwell & Baker, 1992; Lahey, Schaughency, Frame & Strauss, 1985; Lahey et al., 1987), have more conduct disorder problems (Barkley, DuPaul & McMurray, 1990; Cantwell & Baker, 1992; Edelbrock et al., 1984; Hynd, Lorys, Semrud-Clikeman, Nieves, Huettner & Lahey, 1991; King & Young, 1982; Lahey et al., 1987; Lahey, Schaughency, Strauss & Frame, 1984) but are less anxious (Lahey et al., 1984, 1987), than children with ADD/NO. Differences in social behaviour between the two groups have been found, with ADD/NO children being more socially withdrawn and shy (Edelbrock et al., 1984; Lahey et al., 1984), while children with ADD/H are more unpopular (Edelbrock et al., 1984; Lahey et al., 1984; Lahey & Carlson, 1991) and less socially competent (Barkley et al., 1990; Cantwell & Baker, 1992; Hynd et al., 1991). These findings suggest that the two subtypes are substantially dissimilar in ways other than hyperactivity, and perhaps should not be considered as subtypes of the same disorder (Lahey et al., 1985).

Results for tests of academic achievement are mixed, with a number of studies finding ADHD children had higher rates of learning disabilities than control subjects, but no subtypes were more impaired than another (Barkley et al., 1990; Carlson et al., 1986). In contrast to these results, a few studies have found indications that learning disabilities are more common in the inattentive subtypes
of the disorder (Edelbrock et al., 1984). Hynd et al. (1991) found significantly higher rates of math learning disabilities in predominantly inattentive children. A similar result was found by Morgan et al. (1996).

Cognitive differences between the groups have also been reported in neuropsychological studies (Goodyear & Hynd, 1992). Different types of executive system deficits were found between the hyperactive/impulsive and inattentive subtypes of the disorder. This has led some researchers to postulate that the attentional differences between the subtypes may reflect dysfunctions in different neuroanatomical loci and different neurotransmitter systems (Barkley, 1990a).

Within the literature, questions have been raised as to whether the inattention found in the inattentive and combined subtypes of ADHD are the same (Barkley et al., 1990; Goodyear & Hynd, 1992; Lahey & Carlson, 1992; Barkley, 1997). The predominantly hyperactive-impulsive subtype of ADHD has shown signs of being a developmental precursor to the combined subtype. In the DSM-IV field trials, the hyperactive-impulsive subtype was primarily found among preschool aged children (Applegate, Lahey, Hart, Biederman, Hynd, Barkley, Ollendick, Frick, Greenhill, McBurnett, Newcorn, Kerdyk, Garfinkel, Waldman & Shaffer, 1997). In contrast to the hyperactive-impulsive subtype, the combined subtype was more often found in school aged children, as was nearly the entire sample of the inattentive type. In the inattentive subtype, the onset of inattention symptoms appeared to be later than the inattention symptoms found in the combined subtype.

Research on the inattentive subtype suggests that these children show
symptoms of daydreaming, are easily confused, stare frequently, are lethargic, hypoactive and passive (Barkley et al., 1990; Lahey & Carlson, 1992). This subtype has deficits in speed of information processing and in focused or selective attention (Goodyear & Hynd, 1992; Lahey & Carlson, 1992). The attention deficits in the combined subtype of ADHD are more a problem of sustained attention (persistence) and distractibility (Barkley, 1997). This could have the implication that children with the combined subtype, who develop the inattentive subtype with age (because of a reduction in the hyperactive behaviour) are not actually changing subtypes of ADHD at all, as the type of inattention that they continue to exhibit (lack of persistence and distractibility) remains qualitatively different to that of children with a diagnosis of inattentive subtype (Barkley, 1997).

1.10 ADHD IN ADULTS

In recent years, a growing body of literature has reported that ADHD is not limited to children and adolescents, but is also found in adults (Klein & Mannuzza, 1991). Estimates place the number of children with ADHD, who continue to have a diagnosable disorder as adults as high as 70% (Bellak & Black, 1992). These adults have substantial differences in the types of symptoms found, compared with children. The gross motor activity of childhood diminishes with age, which is recognized in the DSM-IV (APA, 1994). Within the literature, a variety of different symptoms have been described in adults which are not present in the descriptions of childhood ADHD. These include the presence of
disorganization which has an impact in the workplace, often requiring written lists of activities to be used as reminders. Poor concentration may continue to persist into adult life, leading to shifting activities, not finishing projects, and moving from one activity to another (Hallowell & Ratey, 1994). Procrastination is present, as are intermittent explosive outbursts (Wender, 1994). Also compared with matched normal controls, adults with ADHD have been shown to suffer significantly higher levels of impulsiveness and restlessness, nonmedical drug use, court referrals, incarceration, and personality disorders (Hechtman, Weiss, Perlman & Amsel, 1984; Hechtman, Weiss, Perlman, Hopkins & Wener, 1979; Loney, Whaley-Klahn, Kosier & Conboy, 1983).

At the diagnostic level, follow-up studies of hyperactive children into young adulthood have shown that approximately 50% continue to have emotional disorders, including ADHD, antisocial disorder, and drug use disorder (Mannuzza et al., 1991). Consistent with these findings, it has also been shown that adult probands who had been seen for hyperactivity at a child guidance clinic 25 years earlier, were between three and four times more likely than their brothers to report psychological problems of nervousness, restlessness, depression, lack of friends, and low frustration tolerance in adulthood (Borland and Heckman, 1976).

From these results it would appear that ADHD is a disorder that persists into adulthood. However, many of the main features found in children, especially the gross motor activity, appear to diminish with age, and other problems that are more psychiatric in nature become prominent. This has important implications for any developmental models of ADHD.
CHAPTER 2. COMORBIDITY
ADHD commonly occurs with other conditions. As many as two thirds of elementary school-age children, who have been referred for clinical evaluation for ADHD, have at least one other diagnosable psychiatric disorder (Arnold & Jensen, 1995; Nottelmann & Jensen, 1995). Bird, Canino, Rubio-Stipec, Gould, Ribera, Sesman, Woodbury, Huertas-Goldman, Pagan and Sanchez-Lacay (1988; Bird, Gould & Staghezza, 1993) conducted a two-stage epidemiological survey of children, aged 4 to 16 years, in Puerto Rico. Among 222 children with a DSM-III diagnosis of attention deficit disorder, 93.0% had comorbid conduct/oppositional disorders. Comorbidity with internalizing disorders was also relatively high, ranging between 50.8% for anxiety disorders and 26.8% for depressive disorders.

Cohen, Velez, Brook and Smith (1989; Velez, Johnson & Cohen, 1989) conducted a longitudinal community-based study of 776 children and adolescents, aged 9 to 18 years. Pooled data from the two stages of the study (Cohen, Velez, Brook & Smith, 1993) indicated that among the children with ADHD, 56% had comorbid conduct disorder (CD), 54% had oppositional defiant disorder (ODD), 23% had anxiety disorder, 24% had separation anxiety, and 13% had a major depressive disorder.

High rates of comorbidity with ADHD were also found in the Ontario Child Health Study (Offord, Boyle & Racine, 1989; Offord, Boyle, Szatmari, Rae-Grant, Links, Cadman, Byles, Crawford, Blum & Byrne, 1987). The Survey Diagnostic Instrument was used to operationalize DSM-III criteria for four disorders (CD, hyperactivity [ADD/H], emotional disorder, and somatization). This was administered to parents and teachers, for children younger than age 12,
and to parents and adolescents aged 12 to 16 years old. Among the hyperactive children, 42.7% had comorbid CD, whereas rates of comorbid internalizing disorders (somatization and emotional disorder) among children with ADHD were lower (17.3% and 19.3%, respectively). Comorbidity rates have also been reported in the Dunedin longitudinal birth cohort study in New Zealand (Anderson, Williams, McGee & Silva, 1987). This study investigated the prevalence of DSM-III disorders based on child, parent, and teacher reports, in 792 children aged 11 years. These children were drawn from the general population. Fifty-three children (6.7%) met criteria for ADHD. Of these children, 26.4% also had a comorbid anxiety disorder, 15.1% had a comorbid depressive disorder, and 47.2% had comorbid CD/ODD.

Several population-based studies have used scales to estimate prevalence and comorbidity rates of ADHD and other DSM defined disorders (Fergusson, Horwood & Lynskey, 1993a,b). McConaughy and Achenbach (1994) compared comorbidity rates, based on reports from parents, teachers, and subjects, using groups matched from community and clinical samples. Comorbidity rates in the clinical sample were significantly higher than those found in the general population sample, regardless of informant or instrument. On all instruments, odds ratios were high for comorbidity of aggressive behaviour, with attention problems, and attention problems with social problems. The odds ratio was also high for anxious/depressed with attention problems, as measured on the Child Behaviour Checklist and the Youth Self-Report.

Cantwell (1994) lists the major comorbid conditions as: language and communication disorders, learning disorders, conduct and oppositional defiant
disorder, anxiety disorders, mood disorders, and Tourette's syndrome or chronic
tics. He also identifies a type of comorbidity described as "lack of social savoir-
faire" which is not a diagnosable condition in the DSM. However, it does
describe a common problem that many ADHD children, adolescents, and adults
have. This is an inability to identify and act on social cues, which leads to
difficulties in interpersonal relationships.

The major clinical problem that comorbidity poses is that it complicates
the diagnostic process and can have an impact on the prognosis and the
management of children, adolescents, and adults with ADHD. Assessment and
treatment of the comorbid disorder is often as equally important as assessing and
treating the ADHD symptomatology. It may be that some of the comorbid
conditions, such as ADHD and Tourette's syndrome, or ADHD and conduct
disorder, may be subgroups of ADHD, with different natural histories and
possibly different underlying etiological factors, and subsequently, different
responses to treatment. This means that the clinician must consider the possibility
of other types of disorders when assessing a child who has ADHD. In particular,
the internalizing problems such as anxiety and mood disorders may be
underreported by parents and teachers, who are better able to recognise the
externalizing behaviours.

2.1 DISORDERS OF CONDUCT IN CHILDREN AND ADOLESCENTS

Within the literature, there is considerable agreement that young people
who engage in antisocial behaviour are not homogeneous in terms of the nature of
their antisocial behaviour (Hinshaw, Lahey & Hart, 1993; Kazdin, 1995; Lahey, Loeber, Quay, Frick & Grimm, 1992; Loeber, 1988; Moffit, 1993; Quay, 1987). A number of researchers have advocated subtyping in order to reduce heterogeneity in studies of youths who engage in antisocial behaviour, and several categorical systems have been proposed to distinguish homogeneous subtypes. The DSM-III (APA, 1980) was the first edition to list separate diagnostic criteria for CD and ODD. In DSM-III, four types of CD are described. These are firstly categorised by the young person’s social interactions with peers, and the young person is considered to be either socialized or undersocialized according to the nature of these interactions. The second category identifies the young person as either aggressive or nonaggressive, depending on the level of violence they partake in. The age of onset is usually prepubertal for the undersocialised type and pubertal or post pubertal in the socialized subtype (APA, 1980). The DSM-III also lists the disorder as being more common in families of adults with antisocial personality disorder and alcohol dependence, and it is also associated with ADHD. For each of the subtypes of CD, the person had to meet three of the diagnostic criteria under each category.

The DSM-III (APA, 1980) also listed diagnostic criteria for a second disorder, ODD. This was associated with patterns of disobedience, negativistic and provocative opposition to authority. Within these criteria, a diagnosis cannot be made if the person violates the basic rights of others, or age appropriate social norms. This oppositional behaviour is normally directed towards family members, in particular parents. Age of onset for this disorder was from three years. The DSM-III did not list any information on prevalence, sex ratio or family
patterns.

The DSM-III-R (APA, 1987) changed the criteria for both CD and ODD. The diagnostic criteria for CD changed, with two subtypes being identified, group type and solitary aggressive (Frick, Lahey, Loeber & Tannenbaum, 1993; Quay, 1964, 1987). In the group type, there is a predominance of conduct problems that occur as a group activity, and in the solitary type, there is a predominance of aggressive physical activity which is directed towards peers and adults. To meet these criteria for CD, a person had to exhibit at least 3 behaviours from a list of 13. The DSM-III-R made allowance for the diagnosis of the disorder as either mild, moderate or severe. The DSM-III-R also made changes to the criteria of ODD, with a person having to exhibit at least 5 behaviours out of a list of 9. As with CD, a diagnosis of mild, moderate or severe could be made.

The changes in the DSM-III-R criteria for both ODD and CD saw a decrease in the prevalence of both disorders (Lahey et al., 1990). The rise in the threshold of the diagnostic criteria for CD was criticized because research indicated that only one or two symptoms in childhood predicted adverse outcomes in adults (Robins & Price, 1991). Research has also suggested that ODD is merely a milder form of CD, and should not be considered as a separate disorder (Werry et al., 1987). Studies have shown that the majority of young people who meet the criteria for CD before the age of puberty, met the criteria for ODD at an earlier age (Lahey et al., 1992; Loeber, Lahey & Thomas, 1991; Lahey, Loeber, Quay, Frick & Grimm, 1994). In addition to this, ODD and CD have been found to be related to the same correlates of lower socioeconomic status, inadequate parenting and parental antisocial behaviour (Lahey, Applegate,
Barkley, Garfinkel, McBurnett, Kerdyk, Greenhill, Hynd, Frick, Newcorn, Biederman, Ollendick, Hart, Perez, Waldman & Schaffer, 1994). However, CD is more strongly related to these factors than ODD (Lahey et al., 1992).

In contrast, studies into the two disorders have identified three main reasons why the disorders should not be considered a continuum of a single disorder. Firstly, many children and adolescents with ODD do not go on to meet the criteria for CD (Loeber, Keenan, Lahey, Green & Thomas, 1993; Russo, Loeber, Lahey & Keenan, 1994). Second, while many children who develop CD during childhood have also developed ODD, a substantial number of adolescents who develop CD for the first time during adolescence, have not previously exhibited ODD (Lahey et al., 1992; Loeber et al., 1991; Lahey, Loeber et al., 1994). Finally, the symptoms of ODD and CD constitute reasonably distinct clusters of intercorrelated behaviours, as judged by factor analyses of previous data sets (Frick, Lahey, Loeber & Strouthamer-Loeber, 1991), and diagnostic utility analyses of the data from the DSM-IV field trials for the disruptive behaviour disorders (Frick, Lahey, Applegate, Kerdyck, Ollendick, Hynd, Garfinkel, Greenhill, Biederman & Barkley, 1994).

Other researchers have suggested that sub-typing of antisocial behaviour in youth could be better done by focusing on the age of onset of the antisocial behaviour instead of the patterns of antisocial behaviour. Blumstein, Farrington & Moitra (1985), Loeber (1988), Moffit (1993), and Tolan (1987) have all suggested that youths who engage in the most persistent, serious, and aggressive antisocial behaviour initiate this during childhood rather than adolescence. In contrast, youths who do not engage in antisocial behaviour until adolescence tend...
to exhibit antisocial behaviours that are less aggressive, less serious, and less likely to persist into adulthood. Robins, Tipp and Pryzbeck (1991) found that the probability of a young person with CD meeting diagnostic criteria for antisocial personality disorder in adulthood is twice as high if the antisocial behaviour began in childhood than if it began in adolescence.

In the DSM-IV (APA, 1994), for a diagnosis of CD, a young person must show persistent patterns of behaviour in which three behaviours from a list of fifteen behaviours are exhibited. The DSM-IV further divided CD into two subtypes based on the age of onset. The child-onset type is defined by the onset of at least one criterion characteristic prior to the age of 10 years. In contrast, the adolescent-onset type is defined by no criterion behaviours being present prior to the age of 10 years. The DSM-IV also returned to allowing for a diagnosis of mild, moderate or severe. For a diagnosis of ODD, the DSM-IV changed the criteria so that four behaviours out of eight possible had to be present for at least six months prior to the diagnosis being made. Unlike CD, the DSM-IV does not provide criteria for a diagnosis of severity in ODD.

The shift in the DSM-IV, to subtyping CD on the basis of age of onset was done for two reasons. First, because level of aggression fluctuates over the course of development (Lahey, Loeber, Hart, Frick, Applegate, Zhang, Green & Russo, 1995), and subtyping on the basis of age of onset is simpler in clinical assessments. Second, it was hoped that a focus on age of onset would encourage both clinicians and researchers to think in terms of the developmental course of CD. Because children and adolescents are in a period of rapid developmental change, a developmental perspective is essential (Lahey, Loeber, Quay,
CD and ODD are the most common of all the comorbid disorders found in children with ADHD (Jensen, Martin & Cantwell, 1997). Studies have found that as many as 93% of children with DSM-III attention deficit disorder had CD or ODD (Bird et al., 1993). Other studies have obtained rates of comorbidity of 47% (Anderson et al., 1987) and 42% (Offord et al., 1989). In the DSM-IV (APA, 1994), a diagnosis of CD or ODD with ADHD can be made if the diagnostic criteria for both disorders are met.

ADHD is a significant predictor of the future development of ODD (Biederman et al., 1987; Loeber & Dishion, 1983). For this reason it is necessary to distinguish the role played by ADHD from that of ODD, as there is some evidence that ADHD is also a precursor of CD (Gittelman-Klein, Mannuzza, Shenker & Bonagura, 1985). This has raised the question of whether ADHD, ODD and CD are different parts of a single disorder, or are independent disorders that commonly occur together (Biederman et al., 1987). ADHD has also been linked to an early rather than late onset of conduct problems (Farrington, Loeber & van Kammen, 1990). This issue is important because there is a consensus among studies that early age of onset of CD symptoms is predictive of the persistence of the symptoms over time and is one of the best predictors of chronic offending (Loeber, 1982). Because the early onset of CD symptoms is associated with chronicity, there is a need to know more about those factors that predict early- compared with late-onset CD (Loeber, Green, Keenan & Lahey, 1995) and how these three disorders interact.
2.2 EEG IN OPPOSITIONAL DEFIANT DISORDER AND OTHER RELATED BEHAVIOURAL DISORDERS

As has been noted in studies of ADHD, studies of behavioural disorders in children and adolescents have used a number of different criteria and definitions. The results are also often confounded as most studies have not accounted for possible comorbid factors, such as ADHD, affecting their results.

A lot of the early EEG research into violent or antisocial behaviour resulted from a belief that violence and epilepsy are often associated (Gunn & Bonn, 1971; Ounsted, 1969; Pincus, 1981; Stevens & Hermann, 1981). This has led researchers to investigate links between EEG abnormalities and antisocial behaviour. Forssman and Frey (1953) investigated EEG abnormalities in chart recordings of 100 antisocial boys who were residents of a reformatory. Most differences between the clinical population and control subjects failed to reach significance. The low alpha band was the only measure where group differences were found, with more low frequency alpha being found in the clinical group. Lewis, Pincus, Shanok and Glaser (1982) examined EEG chart recordings in 97 incarcerated delinquent boys. The results indicated that 25% had abnormal rhythms in their EEG. Hsu, Wisner, Richey and Goldstein (1985) failed to find any EEG abnormalities in chart recordings of a 120 juvenile delinquents. This study was limited in that it used psychiatric inpatients as a control group instead of normal control subjects. Matsuura, Okubo, Toru, Kojima, He, Hou, Shen and Lee (1993) studied EEG differences in 153 children with ADHD and other
deviant behaviours. The EEG was analysed by using calculations of the number of waves in each frequency, average amplitude and percentage time. Deviant behaviour was identified using the Rutter Child Questionnaire (Rutter, Tizard & Whitemore, 1970), with a cutoff of 13 or more being used on the parents questionnaire and 9 or more on the teachers questionnaire. EEG results indicated that the deviant behaviour group had EEG profiles that were similar to normal children.

Phillips, Drake, Hietter, Andrews and Bogner (1993) conducted the only study that has investigated EEG abnormalities in children with a DSM diagnosis of CD. Chart recordings from 86 children and adolescents who met criteria for a DSM-III-R diagnosis of conduct disorder were reviewed. Results found that 91% of the clinical group had normal EEGs.

These studies used both clinical assessments of chart recordings, as well as quantitative EEG techniques. From these results, abnormal EEG activity, both in the form of spike or other epileptiform activity, or quantitative differences in the EEG, does not appear to be associated with most forms of antisocial behaviour. This has led some researchers to suggest that deviance might arise from psychosocial causes rather than from a biological factor such as abnormal CNS functioning (Matsuura et al., 1993).

2.3 EEG IN COMORBID ADHD AND OPPOSITIONAL DEFIANT DISORDER
Only one study has investigated EEG differences in children or adolescents with comorbid ADHD and an antisocial behavioural disorder. Satterfield and Schell (1984) investigated the EEGs of hyperactive adolescents, both with and without signs of delinquent behaviour. A diagnosis of hyperactivity was made before the advent of formal DSM criteria for ADHD, though for inclusion, an adolescent had to exhibit hyperactivity, inattention and impulsivity. This group was then divided into delinquent and non-delinquent, with “delinquent” defined by a history of two or more arrests for a felony. The non-delinquent hyperactivity group had higher total power and absolute alpha and beta, higher relative alpha and beta, and less relative theta compared to normal control subjects. The EEGs of the delinquent hyperactive group were similar to the control group. From these results it was concluded that hyperactive children with abnormal EEGs had a childhood disorder which was secondary to an underlying brain dysfunction. In comparison to this, the delinquent group, with normal EEGs, had a childhood disorder which was secondary to an underlying environmental-social factor.

This study used an eyes open condition, where the adolescent was observing a cartoon on a monitor, and the EEG was taken from 500 ms of trace following the final component of an auditory evoked potential. This methodology had the potential to significantly impact on the results obtained and makes comparison with other EEG studies difficult.

As ADHD is so commonly found in children with ODD and CD, and there are suggestions that ADHD could be a precursor to further behavioural disorders in later adolescence and adulthood, there is a need for further
electrophysiological studies to determine the nature of the association between these disorders.

2.4 LEARNING DISABILITIES

Estimates of the prevalence rate of learning disabilities (LD) depends on the particular definition used, the criteria used to measure LD, and the reason that it is measured. Studies in the Isle of Wight (Rutter et al., 1970) found specific reading disabilities in approximately 5% of the sample. The DSM-IV estimates prevalence rates between 2% and 10%, but estimates the prevalence of LD in United States children at about 5% (APA, 1994).

Within the literature, what should be used as an appropriate definition of LD is a contentious issue, as a chosen definition has different implications for identification, service provision, and research. Several definitions of LD exist. These definitions vary across several dimensions including the emphasis placed on underlying etiology, the importance of specific academic skill deficits, and the definition of underachievement as an aptitude-achievement discrepancy or a more broadly defined age or grade level expectation (Beitchman & Young, 1997). The most cited and utilized definition (Hammill, 1990) is that of the National Joint Committee on Learning Disabilities, which states: "Learning disabilities is a general term that refers to a heterogeneous group of disorders manifested by significant difficulties in the acquisition and use of listening, speaking, reading, writing, reasoning, or mathematical abilities. These disorders are intrinsic to the
individual, presumed to be due to central nervous system dysfunction, and may occur across the life span” (NJCLD, 1987, p. 1).

The DSM-IV (APA, 1994) divides learning disorders into disorders of specific academic skills and a "not otherwise specified" category. Those involving specific academic skills include reading disorder, mathematics disorder, and disorder of written expression. The "not otherwise specified" category includes disorders in learning that do not meet criteria for any specific learning disorder. Within each of the specific academic skill disorders, the diagnostic criteria require that an individual's actual achievement in a specific academic skill is substantially below his or her expected achievement as determined by standardized ability measures, and that the learning problems interfere with academic achievement or related daily activities.

While this definition appears relatively simple, a number of conceptual and pragmatic issues remain. The specific method used to define a discrepancy, and the size of a discrepancy needed to qualify as "serious" are not specified. The specific methods used to compute discrepancies differ, and each approach will identify a somewhat different group of children as LD (Reynolds, 1984). Thus, despite the consensus that LD impairs a child's ability to achieve at an age-appropriate level, recurrent conceptual and methodological issues arise with nearly all definitions. Despite these difficulties, useful guidelines are available for practical decision-making and assessment of learning disabilities (Sattler, 1989). Beitchman and Young (1997) recommend that a child's actual level of functioning be considered as a first step in diagnosis. If a child is not functioning below expected level for age or grade, he or she is unlikely to require special help
to remediate a disability and should not be referred to as learning-disabled, even if his or her IQ and ability scores are discrepant.

As with studies of ADHD, a number of imaging techniques have been used to ascertain the existence of brain structure and functioning abnormalities in children with LD. A number of studies have found evidence that supports a model of left hemisphere deficit in people with LD. Deficiencies in the planum temporale have been found, with L > R asymmetries being found in children with language and learning disorders (Galaburda, Sherman, Rosen, Aboitiz & Geschwind, 1985; Hynd & Semrud-Clikeman, 1989), although difficulties in reliably identifying the boundaries of the planum continue to impede attempts to replicate earlier findings (Jernigan, Hesselink, Sowell & Tallal, 1991). PET studies involving language tasks have found differences in the left hemisphere of learning-disabled subjects compared with non-LD subjects (Flowers, 1993). CBF studies (Flowers, 1993) have shown that there is a left temporal component associated with both phonological and orthographic skills requiring fine auditory discrimination, and an inferior left parietal component associated with word meaning. Galaburda et al. (1985) and Kaufman and Galaburda (1989) also found that the brains of reading-disabled individuals had significantly more focal dysplasias, particularly in the language regions that border the sylvian fissure, than those of normal controls.

While none of these findings can yet be considered conclusive, they support the view that, at a neurofunctional and neuroanatomical level, some LD children differ from non-LD children. There are, nevertheless, important reasons to view these findings cautiously. First, there are many examples in neurology in
which structure and function are not well correlated. The current view is that many brain functions have a distributed or network representation in the brain rather than being localized (Logan, 1996). As a result, any one of the many interconnecting neural networks could be implicated as a causative factor among LD children. Second, the problem of diagnostic heterogeneity remain unresolved and limits the generalizability of the neuroanatomical findings (Beitchman & Young, 1997). Third, although the positive neuroanatomical results may represent the findings at the more extreme end of the LD continuum, these findings must be reconciled with the research that suggests that learning disabilities fall along a continuum and do not constitute a discrete entity (Shaywitz, Fletcher & Shaywitz, 1996).

To summarise, LD constitutes the second most common disorder to be found in conjunction with ADHD. The presence of a LD in children with ADHD has been estimated at between 20% and 25% (Pliszka, 1998), although estimates in the literature have ranged from 10% to 92% (Biederman, Newcorn & Sprich, 1991). While a high levels of comorbidity has been found for ADHD and LD, the two disorders are generally considered to be independent (Shaywitz & Shaywitz, 1991a; Pliszka, 1998).

2.5 EEG IN LEARNING DISABILITIES

Studies of children with LD have typically found that these children have an increase in slow wave activity in comparison to normal children (Sklar, Hanley & Simmons, 1973; Hanley & Skyler, 1976; Njokikjien, Visser & de Rijke, 1977;
Robert, Wexler & Sproul, 1978; Lubar, Bianchini, Calhoun, Lambert, Brody & Shabsin, 1985). Roberts (1966) found children with LD were more likely to have more excess slow wave activity below 8 Hz, and particularly in the 3 to 4 Hz range, than normal children. Duffy, Denckla, Bartels and Sandini (1979) found differences between dyslexic and normal control subjects. These were primarily in the left hemisphere, especially in the left posterior regions, but differences were also found in the frontal lobes. Lubar et al. (1985) found LD children had more frontal theta and less posterior beta than control subjects, for absolute power measures. Discriminant analysis was found to be able to correctly identify 98% of children as either LD or normal. In contrast to these results, Fein, Galin, Yingling, Johnstone, Davernport and Herron (1986) found dyslexic boys had lower power in the high beta band, but did not find increased delta or theta activity. Ahn, Princep, John, Baird, Trepetin and Kaye (1980) investigated relative power differences between LD and normal children using an eyes closed resting condition. 88% of the LD children were found to have more delta and theta, primarily in posterior regions, and a deficiency of relative alpha.

Harmony, Hinojosa, Marosi, Becker, Rodriguez, Reyes and Rocha (1990) studied absolute and relative power differences in four groups of children who were rated from academically good to very poor. In absolute power, increased delta and theta were found in the LD groups, primarily in the left hemisphere. In relative power, increased left hemisphere delta was again found, and an increase in central-posterior theta. These results were interpreted as being indicative of a maturational lag in children with LD.
John, Princhep, Ahn, Easton, Fridman and Kaye (1983) identified two distinct groups of LD children based on EEG profiles. The first group had EEG profiles that resembled younger normal children. The second group had EEG profiles that could not be considered as normal for a person at any age.

Studies of EEG coherence have found an increase in coherence in temporal and posterior regions, and a decrease in coherence in frontal regions with increasing age among normal children (Marosi, Harmony, Sanchez, Becker, Bernal, Reyes, Diaz de Leon, Rodriguez & Fernandez, 1992). In LD children, maturation was found to be qualitatively different to normal children, with little change in coherence being found in most regions. From these results, it was determined that the EEG findings for LD subjects are unlikely to represent a maturational lag in CNS functioning.

2.6 EEG DIFFERENCES BETWEEN ADHD AND LD CHILDREN

A number of studies have investigated EEG differences between children with ADHD and those with LD. Ackerman, Dykman, Oglesby and Newton (1994) studied the EEG of children with dyslexia, and a group of slow learners, and compared their results to normally-reading group of children with ADHD. The EEG was recorded while subjects viewed strings of words and letters. The major difference between groups was in the low beta band, where the ADHD group had greater power at the parietal and midline sites. The slow learner group also had marginally greater low beta in the left temporal sites compared to the right temporal sites, with the opposite trend found for the dyslexic and ADHD
groups. The slow learner group also had increased levels of delta and alpha in the right parietal sites.

Chabot, Merkin, Wood, Davenport and Serfontein (1996) performed a discriminant analysis study of children with ADHD and a second group with LD. Subjects known to have both disorders were excluded from the study. However, the LD group was not screened for ADHD. The discriminant function analysis used 9 EEG variables and was able to classify the ADHD group with 93.1% accuracy and the LD group with 89.7% accuracy. From these results, it was concluded that EEG differences existed between the two clinical groups. It was also observed that discriminant function analysis was more accurate in the ADHD group than the LD group. This was explained as the LD group being a more heterogeneous group than the ADHD group. The use of multiple EEG measures instead of a single measure from one frequency band was also found to be a more accurate measure of group differences. The 9 EEG variables used in this study were mostly drawn from one lead in a monopolar recording or from two leads where a bipolar reading was used. This makes the comparison of these results with other studies difficult.

No studies have investigated EEG differences between children with ADHD, and children with ADHD and comorbid LD.
CHAPTER 3. EEG IN NORMAL CHILDREN
3.1 NORMAL MATURATION OF THE EEG IN CHILDREN AND ADOLESCENTS

Maturational changes in the EEG were reported as early as the 1930s, with activity in the low frequencies decreasing and higher frequencies increasing with age (Smith, 1938; Lindsley, 1939). These initial studies used visual assessment techniques to evaluate changes in the EEG with age, and have subsequent limitations. With the development of computer aided spectral analysis, maturational changes could be quantified with greater accuracy. However, only a small number of studies have been conducted that used this form of EEG analysis.

Matousek and Petersen (1973) studied the mean EEG amplitudes of 401 normal children and 160 normal adolescents between the ages of 1 and 21 years. An eyes-closed resting condition was used in this study, with six 10 second, artifact-free epochs being selected for analysis. The EEG was analysed in six frequency bands, delta (1.5-3.5 Hz), theta (3.5-7.5 Hz), alpha 1 (7.5-9.5 Hz), alpha 2 (9.5-12.5 Hz), beta 1 (12.5-17.5 Hz) and beta 2 (17.5-25 Hz).

For inclusion in this study, all subjects had to have an uneventful prenatal, perinatal and neonatal period, no disorders of consciousness, no head injury with cerebral symptoms, no history of central nervous system diseases, no obvious somatic diseases, no convulsions, no history of convulsive disorders, no paroxysmal headache or abdominal pain, no enuresis or encopresis after the fourth birthday, no tics, stuttering, pavor nocturnes or excessive nailbiting, no
obvious mental diseases, no conduct disorders and no deviation with regard to mental and physical development.

Results indicated that delta activity decreased almost linearly with age. Theta activity increased until a child was approximately 4 years old, when it reached maximum amplitude, and then decreased. Alpha 1 activity increased until approximately 8 years of age, and then proceeded to decrease. Alpha 2 activity increased throughout childhood, with amplitude levels remaining mostly stable during adolescence. For beta activity, the amplitudes decreased slightly with age. The total amplitude for all six frequency bands was found to decrease significantly with age during childhood, but not significantly during adolescence.

In a study of 600 normal children, John, Ahn, Princherp, Trepetin, Brown and Kaye (1980) developed 32 linear regression equations, predicting the frequency composition of the EEG, for four bilateral regions of the brain, as a function of age. Subjects included both boys and girls between the ages of 6 and 16 years old. The criteria of normality used by Matousek and Petersen (1973) was used in this study. The EEGs were 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). The EEGs were recorded under both an eyes open and eyes closed resting condition. Results indicated poor test-retest replicability for absolute power in both the eyes open and eyes closed conditions. Data were then converted to relative power by dividing the power for each frequency band by the total power. The eyes open condition still showed substantial variation after transformation, however, in the eyes closed condition, a high degree of reliability was found.
Relative power data for the eyes closed condition were transformed using a log transformation, and 32 fourth order orthogonal polynomials were calculated. These equations were calculated for fronto-temporal, temporal, central and parieto-occipital regions, in each frequency band. The equations were able to predict relative power as a function of age with 93 percent reliability, and were interpreted to indicate that development of the normal EEG in children and adolescents was linear in nature.

In the second stage of this study, 32 regression equations were calculated for Matousek and Petersen's (1973) group of Swedish children, which showed strong similarities to those of the American children in the John et al. (1980) study. This methodology was also used in studies of normal children in Barbados (Ahn et al., 1980) and Cuba (Alverez, Valdes & Pascual, 1987), with similar results being obtained in both studies. From these results, it was concluded that the normal development of the EEG is independent of ethnicity, culture, socio-economic or sex factors (John et al., 1983).

Epstein (1980) studied changes in the EEG from childhood into early adulthood. Results indicated that the percentage of EEG power that was found in the alpha frequency band, changed from about zero at birth to about 70% of EEG power in adults. This rise in power was found to occur mainly in five stages, with the age of each correlating with a different stage of brain development which was marked by an increase in brain weight.

Katada, Ozarki, Suzuki and Suchara (1981) investigated changes in the dominant and subordinate EEG frequency of children between the ages of 7 and 15 years old. Results indicated that the dominant frequency of the EEG increased
with age until it reached approximately 10 Hz. These changes were found to occur earliest in occipital regions, followed by later changes in the central and then the frontal regions.

Benninger, Matthis and Scheffner (1984) conducted a longitudinal study of 96 boys and girls for a mean period of 4.6 years. This study used an eyes-closed, resting condition. The EEG was recorded from electrodes placed in the central and posterior regions, and relative power estimates were calculated in the theta, slow alpha and fast alpha bands. In all regions, theta activity decreased with age, and this decrease was estimated at approximately 2.5% per year in the central regions. In the alpha bands, power was found to increase with age. The results of this study demonstrated that differences between subjects were greater within an age group than between age groups.

Ogawa, Sugiyama, Ishiwa, Suzuki, Ishihara and Sato (1984) investigated the EEGs of 150 normal children between the ages of 20 days and 15 years, during an eyes closed resting condition. The EEG was analysed in nine frequency bands. Results indicated that relative delta activity decreased with age, especially from 1 to 3 years old, and alpha and beta activity increased with increasing age. Theta activity increased from 2 to 4 years old, and then decreased gradually with increasing age.

Gasser, Verleger, Bacher and Sroka (1988) found that except for alpha 2 activity, all frequency bands and total power showed a continuous decrease with age. For relative power, a strong complementary replacement of theta by alpha 2 activity was found up to the age of 14. Delta, theta and alpha 1 frequencies decreased with age, and higher frequencies increased.
These studies found a decrease in slow wave activity and an increase in faster frequency bands with age, with this change being largely linear in nature.

Wada, Ogawa, Sonoda and Sato (1996) studied the relationship between changes in the relative power between different areas of the scalp in 244 children between the ages of 3 and 15 years. The EEG was recorded during an eyes-closed, resting condition. The results indicated that delta and theta activity showed small developmental changes with increasing age. Theta activity was dominant in early childhood, and was found to be a precursor to the alpha rhythm. Both the alpha and beta bands were found to undergo the most significant changes with increasing age.

Martinovic, Jovanovic and Ristanovic (1998) investigated developmental changes in quantitative EEG in a sample of 72 pairs of healthy twins between the ages of 7 and 15 years. The EEG was analysed in absolute and relative power for the delta, theta, alpha 1, alpha 2 and beta bands. Absolute power was found to decrease with increasing age in all bands. With increasing age, relative alpha 2 increased, and this was inversely related to a decrease in relative alpha 1 and theta activity. The mean frequency in all frequency bands increased with age.

Somsen, van't Klooster, van der Molen, van Leeuwen and Licht (1997) studied developmental changes in the EEG of children between the ages of 5 and 12 years. Results indicated that absolute delta and theta activity decreased gradually with age, while power in the alpha and beta bands changed very little. Changes in power were relatively larger between the ages of 6 and 7 years and between 9, 10 and 11 years. The dominant frequency was found to increase between the ages of 5 and 12 years, with the spectrum shifting from fast theta to
slow alpha, and then to fast alpha. Relative power was found to be a better indicator of maturational changes than absolute power. Changes in absolute alpha were only found in the oldest children, but because of the substantial decrease in relative delta and theta with increasing age, the proportion of relative alpha was increased, making identification of changes easier. Relative alpha was found to be a good indicator of the general maturational trends.

The results of these studies indicate that the delta frequency band is dominant in children at birth, and proceeds to decrease with increasing age. Theta activity increases until about the age of 4 years and then decreases. Slow alpha activity increases until about the age of 8 years and then decreases. Fast alpha and beta activity increase throughout childhood and adolescence. There also appears to be an association between the decrease in theta activity and the increase in alpha.

3.2 TOPOGRAPHY

Lazzaro, Gordon, Whitmont, Plahn, Li, Clarke, Dosen and Meares (1998) reported topographic differences in 26 normal children between the ages of 11 and 17, who were part of a study of ADHD. The EEG was recorded during an eyes-open resting condition, and Fourier transformed to provide absolute and relative power estimates in delta, theta, alpha 1, alpha 2 and beta bands. The posterior regions had greater absolute power than the frontal regions in delta, theta, alpha 1, alpha 2, and total power. Significantly more alpha 1 and beta power was found in the right hemisphere than the left hemisphere. In relative power, the frontal regions had greater activity than the posterior regions in delta,
theta and beta. The posterior regions had greater power than the frontal regions in the alpha 1 and alpha 2 bands. The right hemisphere had more beta activity than the left hemisphere. Age effects were not investigated in this study.

Topographic studies of EEG maturation have found that the EEG changes in different areas at different rates. Benninger et al. (1984) found that the rate of change in the EEG in occipital areas was twice that of the central areas, and this was greater in younger children than in children over the age of 10 years. Theta activity was found to remain higher in the central regions than the frontal regions, and slow alpha activity was always prominent in the occipital regions. Fast alpha was found to be greater in the central regions than the occipital regions up to about the age of 9 years. After this age, fast alpha was found in both the central and occipital regions. No trends were found which suggested earlier maturation in either of the hemispheres. In 5% of subjects, hemispheric power asymmetries were found, with one hemisphere having up to 1.5 times the power of the other hemisphere.

Gasser, Verleger, et al. (1988) found that certain regions of the brain matured before other regions. Absolute delta, theta and alpha 1 frequency bands were found to decrease, and amplitudes became similar with age. The decline was found to be greatest in posterior regions. Frontally, delta and theta were found to develop in parallel, whereas theta dominated delta in all other areas. Alpha activity showed a strong posterior increase, whereas at frontal and central regions, the increase started later and remained small.

Topographic studies of maturation have found that changes take place primarily from posterior to anterior regions. Gasser, Jennen-Steinmetz, Sroka,
Verleger and Mocks (1988) found that delta, theta and alpha waves developed earliest occipitally followed by parietal, central and frontal regions. Beta waves developed earliest in central regions, followed by parietal, occipital and then frontal regions. In the central area, the midline was found to have more low frequency power than the two hemispheres, whereas high frequency power was found more evenly distributed between the three regions.

Buchsbaum, Mansour, Teng, Zia, Siegel and Rice (1992) investigated relative amplitude changes in 30 normal males between the ages of 16 and 22 years. Delta activity decreased throughout this age range, with the decrease being greatest in the left frontal and temporal regions. However, this was not found in the occipital regions. Relative amplitude decreased with age in alpha, delta, and theta bands, while beta remained constant or increasing. These changes were greatest in the left temporal and left frontal regions. In both the delta and theta bands, significantly greater decreases with age were found in the left parietal region compared to the right parietal region. These results were interpreted as suggesting that certain cortical areas continue to mature in the second decade of life. Martinovic et al. (1998) found the topographic distribution of these spectral bands matured earlier in the mid parietal or occipital regions compared to frontal and central regions.

3.3 SEX DIFFERENCES IN THE EEG OF NORMAL CHILDREN AND ADOLESCENTS
Reports of sex differences in the normal maturation of the EEG have been mixed. Petersen and Eeg-Olofsson (1971) found girls had higher alpha frequencies until the age of 11 years. Matousek and Petersen (1973) found adolescent females had more beta activity than males. These findings are suggestive of earlier maturation in girls. However, Cohn, Kircher, Emmerson and Dustman (1985) and Gasser, Jennen-Steinmetz et al. (1988) failed to find EEG differences between males and females, or the existence of a pubertal spurt. In contrast to this, Matthis and Scheffner (1980) found that at age six, girls had more relative theta and less relative alpha. By age eleven, girls had surpassed boys for relative slow alpha in occipital areas, but still had deficiencies of alpha in frontal regions. Benninger et al. (1984) confirmed the results of Matthis and Scheffner (1980), with girls up to six years old having greater levels of theta than boys, and boys having greater alpha levels until ten years old. However, the rate of change in girls was greater, and a pubertal spurt was found from about 11 to 13 years, which resulted in girls catching up with boys by adolescence. Similar results were also found in another study by Diaz De Leon, Harmony, Marosi and Becker (1988). Girls had less absolute and relative alpha than boys, but the rate of change in the alpha band was greater in girls compared to males which resulted in their EEGs becoming similar with increasing age. Harmony, Marosi, Diaz de Leon, Becker and Fernandez (1990) studied sex differences in the maturation of normal children between the ages of 6 and 12 years old, using an eyes closed resting condition. EEG measures were calculated for total power, and absolute and relative delta, theta, alpha and beta. Results failed to indicate any sex differences in absolute power with increasing age. In relative power, boys had more alpha,
and less delta, theta and beta than girls. These sex differences were greater at age 6 than at age 12, with girls showing a developmental spurt. This spurt was found to be greater in the posterior regions. Martinovic et al. (1998) examined sex differences in the EEGs of twins. The results indicated that the mean frequency of the alpha 2 band was higher in the older females (13 to 15 year olds) than males. This suggested that after puberty, adolescent boys exhibited signs of a maturational lag behind girls.

Eeg-Olofsson (1980) found that before and during the course of puberty, there were large maturational changes in the EEG. These were in the form of rhythmic and paroxysmal patterns which related to both age and sex. After puberty, the EEG in girls matures faster than boys, and by early adulthood, the EEGs of both sexes become similar once the maturational process ended in later adolescence.

Overall, these results suggest that girls have a developmental lag in their EEG during childhood in comparison with boys. The EEG in girls develops at a greater rate than in boys, and by about the onset of puberty, girls reach a similar developmental level to boys. This change in girls may be assisted by a developmental spurt at puberty. During adolescence, the EEG in girls matures at a greater rate than in boys, and the EEG in both sexes becomes similar towards adulthood.

3.4 THE ASSOCIATION BETWEEN IQ AND EEG
Studies of the relationship between IQ and EEG have generally been inconclusive (Bosaeus, Matousek & Petersen, 1977). Satterfield, Cantwell, Saul and Yusin (1974) found that hyperactive children who had an increase in slow wave activity, also had higher measures of intelligence. In contrast to these findings, Corning, Steffy and Chaprin (1982) performed a discriminant function analysis on two groups of children. Subjects were placed into two groups based on the presence or absence of increased slow wave activity or a high theta/alpha ratio coefficient. The study found that the two groups differed on their levels of IQ, with the slow wave activity group having lower IQs. These results were determined to represent the presence of a maturational lag in the low IQ group. In further support of these findings, Gasser, Von Lucadou-Muller, Verleger and Bacher (1983) studied the effect of IQ differences on the EEG. Results indicated a small correlation between increased IQ and EEG measures indicative of increased maturation. Bosaeus et al. (1977) investigated the EEG in 138 normal children. Their results failed to find any EEG component that was related to IQ. This study was limited in that it only investigated normal children rather than including children with low IQs. Chabot and Serfontein (1996) compared the EEGs of normal and lower intelligence children with ADHD. They concluded from their results that the greatest group variance was related to the diagnosis and not intelligence.

From these results, it is probable that intelligence is associated with differences in the EEG, with low IQ children having EEG profiles that are indicative of a slight maturational lag in comparison to children with higher IQs. However, the correlation between IQ and EEG results appears to be small.
CHAPTER 4. EEG IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER
4.1 EEG DIFFERENCES BETWEEN CHILDREN WITH AND WITHOUT ADHD

One of the earliest studies to identify EEG abnormalities in children with MBD was conducted by Jasper, Solomon and Bradley in 1938. Seventy one children who were admitted to a home for behavioural problems were investigated. All children were between the ages of 2 and 16 years and all except 5 children had an IQ above 70. Both males and females were examined. These children were divided into two groups. The first group consisted of thirty five children who had histories suggestive of a CNS disorder. This included a history of encephalitis, birth and head injuries, severe paroxysmal attacks or asphyxia in childhood. The second group had no history or physical signs of CNS disease. Within these groups, three classes of children were identified. The first were predominantly hyperactive and impulsive, the second class were withdrawn and emotionally immature, and the third class were delinquent in nature. Results revealed that over half the subjects had abnormalities in the EEG. The predominant feature of the abnormalities was an increase in slow wave activity in one or more regions of the head. This was in the form of a regular rhythm of smooth waves between 2 and 6 Hz and was often located in frontal regions. These EEG abnormalities were found in all groups of children irrespective of whether there was an historical indicator of a CNS disorder.

Lindsley and Cutts (1940) compared EEG records from 50 children who were identified by their parents as having behavioural problems, and 36 normal control subjects. They found that 2 to 5 Hz activity was two to three times more
common in children with behavioural problems. Kennard (1949) studied the EEGs of 131 children with various behavioural disorders. Results indicated that 60% of the disordered group had EEG abnormalities. Green (1961) reported 4 case studies of normal intelligence children with varied behavioural problems. Focal spike wave activity was found in the occipital regions of all of these children. However, these children had not experienced any seizures and responded poorly to anticonvulsant medication. Anderson (1963) investigated the EEGs of 30 children with a hyperkinetic behaviour disorder, between the ages of 8 and 12 years. EEG abnormalities were found in the chart recordings of 26 of the clinical group, but only in 4 of the normal children. These abnormalities consisted of focal abnormalities of an unspecified kind in six children, and nonfocal abnormalities in the other 20. Capute, Niedermeyer and Richardson (1968) studied EEG abnormalities in 106 children between the ages of 2 and 16 years old. All children had a diagnosis of MBD, and were randomly selected from patients referred to the Johns Hopkins Diagnostic and Evaluation Centre for Handicapped Children. Fifty percent of the children showed EEG abnormalities in their traces. Of these children with EEG abnormalities, 45 were rated as having slight to moderate abnormalities and 8 had very abnormal recordings. Focal abnormalities were only found in 14 patients, with the rest having non-focal abnormalities. The most common non-focal abnormality was increased bilateral slow wave activity in the posterior regions.

Wikler, Dixon and Parker (1971) investigated the chart recordings of EEGs from 25 hyperactive or aggressive children. The EEG was recorded during
an eyes-closed resting condition. The hyperactive group had more slow wave activity, and more abnormal transient discharges, than non-hyperactive subjects.

All of these studies used visual evaluation of paper recordings of the EEG. This resulted in many of the studies reporting percentage differences in abnormalities between clinical and control groups rather than identifying the exact nature of the underlying abnormality. This methodology had limitations in comparison to later studies which used computer aided analysis. However, the results from those studies that identified the nature of the EEG abnormality are largely consistent with later studies which generally found hyperactive children had increased slow wave activity in comparison to normal control subjects.

Satterfield, Cantwell, Lesser and Podosin (1972) conducted a three week controlled double-blind study of the response to methylphenidate of 31 hyperkinetic boys. The EEG was recorded during an eyes-open resting condition. The results from the good responders to methylphenidate were compared to those from the poor responders. The hyperkinetic children who were good responders to stimulant medication, had higher mean resting amplitude ranges and higher mean resting power in the 0-8 Hz frequency range.

Dykman, Holcomb, Oglesby and Ackerman (1982) used principal component analysis to investigate EEG differences in four groups hyperactive: learning-disabled, hyperactive/learning-disabled or mixed, and normal children. A visual search task was used during the recording of the EEG. The hyperactive group was found to have lower loadings than the control group on a factor that loaded on the 16 to 20 Hz (beta band) range.
Callaway, Halliday and Naylor (1983) investigated event-related potentials and EEG spectral differences between 18 hyperactive children and 18 age-matched normal subjects. The EEG was recorded from three posterior electrode sites during both an eyes-open and eyes-closed resting condition. In all bands except the delta band, the eyes-closed condition showed a greater level of power than the eyes-open condition. Hyperactive children had lower power in the alpha and beta band compared to normal control subjects.

Matousek, Rasmussen and Gilberg (1984) investigated the EEGs of 38 children with a diagnosis of MBD or ADD. The EEG was recorded during an eyes-closed resting condition, using hyperventilation, photic stimulation and sleep activation. One minute of trace was also recorded for spectral analysis. From the visual analysis, 70% of the MBD subjects and 30% of control subjects had some form of EEG abnormality. The highest correlating measures with MBD were relative delta in posterior regions, and the theta/alpha ratio.

Mann, Lubar, Zimmerman, Miller and Muenchen (1992), studied EEG differences between normal children and children with a diagnosis of ADHD without hyperactivity. Subjects were seated in a reclining chair and the EEG was recorded during three conditions, a baseline eyes-open condition, a reading condition and a drawing condition. Results indicated that the ADHD group had an increase in absolute power in the theta band which was predominantly in the frontal regions. ADHD children showed a greater increase in theta activity in frontal and central regions during cognitive tasks, and a greater decrease in beta activity in posterior and temporal regions with tasks requiring sustained attention. The ADHD children were found to have EEG frequency distributions that
resembled profiles typical of younger children. Mann et al. (1992) concluded that this finding supported the view that ADHD reflects maturational delays in the systems that subserve attention.

Matsuura et al. (1993) conducted a cross cultural EEG study in children with deviant behaviour, and children with a DSM-III-R diagnosis of ADHD. Results indicated that the ADHD group had a higher average amplitude of delta, higher percentage time of delta and slow theta, and lower percentage time of alpha than normal control subjects. In the ADHD group, mean maximum amplitude was found in the 8 Hz band, whereas in control subjects, this was in the 9 Hz band.

Janzen, Graap, Stephanson, Marshall and Fitzsimmons (1995) studied EEG differences in 8 children with a DSM-III-R diagnosis of ADHD and 8 normal control subjects. The EEG was recorded using an eyes-open, eyes-closed, and a number of different cognitive task conditions. Results indicated that ADHD children had a significantly higher theta amplitude than control subjects. The results of this study are limited due to the small sample size that was used.

Chabot and Serfontein (1996) investigated EEG differences in 407 children who were diagnosed using DSM-III criteria for ADHD. This study found children with ADHD had an increase in absolute and relative theta, primarily in the frontal regions and at the frontal midline. A slight elevation in relative alpha, and a diffuse decrease in mean frequencies in the alpha and beta bands were also found in some children with ADHD. Interhemispheric asymmetries were found in the parietal and posterior temporal areas. Intrahemispheric abnormalities were found with asymmetries between frontal/temporal and frontal/occipital regions.
These patterns of EEG abnormalities were seen to represent a deviation from normal development, not a maturational lag.

Lazzaro et al. (1998) investigated EEG differences between 26 male adolescents with a DSM-IV (APA, 1994) diagnosis of ADHD, and 26 age and sex matched normal control subjects. The EEG was recorded during an eyes-open resting condition, and was Fourier transformed to obtain absolute and relative power estimates of delta, theta, alpha and beta power. Results indicated that the ADHD group had increased absolute theta and alpha 1 activity in frontal regions and reduced relative beta in posterior regions. This study is one of only a few studies to use an adolescent population rather than children.

Although these studies have used a number of different diagnostic categories for their clinical groups, and several different methods to quantify the EEG differences between clinical groups and normal children, a number of commonalities were found. Most studies found that the ADHD groups had an increase in slow wave activity in comparison to normal children. This was primarily in the theta band, with the maximal amount of theta being found in the frontal regions. In posterior regions, an increased level of delta was found, with decreases in both the alpha and beta bands.

4.2 ELECTROPHYSIOLOGICAL MODELS OF ADHD

While mostly consistent EEG results have been found by a number of studies, the interpretation of what these results represent remains contentious
within the literature. Two main models of ADHD have been proposed, based on EEG studies. These are the Maturation Lag model, and the Developmental Deviation model.

4.2.1 The Maturational Lag Model of ADHD

The Maturational Lag model proposes that ADHD results from a developmental lag in CNS functioning. Children with ADHD are developmentally inappropriate for their age, but act in a way that would be normal in younger children. From an electrophysiological perspective, for this model to be accurate, their EEG measures would need to be considered as normal in younger children.

Satterfield, Lesser, Saul and Cantwell (1973) found that ADHD children who responded well to stimulant medication were those who had increased slow wave activity in their EEG, and longer latencies and lower amplitudes in evoked cortical responses. These results were considered to support a model of delayed maturation in such children, rather than being indicative of some form of brain damage. Matsuura et al. (1993) conducted a cross cultural EEG study in children with deviant behaviour, and children with a DSM-III-R diagnosis of ADHD. Results indicated that the ADHD group had a higher average amplitude of delta, higher percentage time of delta and slow theta, and lower percentage time of alpha than normal control subjects. In the ADHD group, mean maximum amplitude was found in the 8 Hz band, whereas in control subjects, this was in the 9 Hz band. Hypothetical EEG age was calculated for the clinical groups, using
the procedures outlined by John, Princep and Easton (1987). This indicated that the children with ADHD showed signs of a maturational lag in brain functioning. From these results it was concluded that ADHD has a biological background.

Lazzaro et al. (1998) found that ADHD subjects had increased absolute theta and alpha 1 activity in frontal regions and reduced relative beta in posterior regions. These results were interpreted as representing a maturational lag in adolescents with ADHD.

All of these studies found results that were supportive of the maturational lag model. There was more slow wave activity in the EEG, and less posterior fast wave activity, which would be expected in the EEGs of younger children.

4.2.2 Developmental Deviation Model of ADHD

In the Developmental Deviation model, ADHD is conceptualised as resulting from an abnormality in the functioning of the CNS. Electrophysiological measures from these children are not considered to be normal in children of any age, and the EEG is not considered likely to mature in a normal fashion.

Klinkerfuss, Lange, Weinberg and O’Leary (1965) found 90% of children with hyperactivity had abnormalities in their EEGs and 30% had markedly disordered traces. When the EEGs were examined within age groups, the percentage of slowing of the EEG did not increase or decrease with increasing age. This indicated that the EEG of these children was not maturing, and was supportive of a developmental deviation model of ADHD. Wikler, Dixon and Parker (1970) investigated EEG abnormalities in 25 children between the ages of
5 and 15 years old, during an eye-closed, resting condition. The EEGs were visually appraised and rated on the amount of each frequency band, using calculations of percent time. Hyperactive children were found to have increased slow wave activity in comparison to normal controls. It was also noted that the abnormally slow EEG activity of the hyperactive children did not increase or decrease with age.

Chabot and Serfontein (1996) found that children with ADHD had an increase in absolute and relative theta which was primarily in the frontal regions and at the frontal midline. A slight elevation in relative alpha, and a diffuse decrease in mean frequencies in the alpha and beta bands was also found in some children with ADHD. This study used a paradigm described by John, Prichep, Fridman and Easton (1988) whereby EEG measures were converted to Z scores and compared to a normative data base (John et al., 1980). If the measures obtained from a subject fell within a statistically determined band derived from a group of younger normal children, the EEG was deemed to represent a maturational lag. If the results fell outside these parameters, the EEG was viewed as a developmental deviation (John et al., 1983). From this analysis, Chabot and Serfontein (1996) concluded that their results represented a deviation from normal development, as the EEG could not be considered normal in a child of any age.

These studies found that the EEG profile of children with ADHD did not change with increasing age, and was not normal for a child at any age. From these results it was concluded that ADHD resulted from a developmental deviation in CNS functioning.
4.2.3 Limitations of Both the Maturational Lag and Developmental Deviation Models of ADHD

Both of these models fail to adequately explain results from behavioural studies of ADHD. The hyperactive/impulsive behaviours found in children have been found to decrease with age (Kinsbourne, 1973a), and this can be explained by a maturational lag model. As a child with ADHD becomes older, the CNS matures to an age-appropriate level and a subsequent reduction in the hyperactivity occurs. A major problem with the maturational lag model is that ADHD is often found in adults (Bellak & Black, 1992). Conceptually, it is not possible to have a maturational lag that persists into adulthood, and consequently this would have to be considered part of a more pervasive developmental deviation. Studies of adults with ADHD have found that the gross motor activity of childhood diminishes with age, but the inattentive symptoms remain (APA, 1994). This change in behaviour can not be adequately explained by either model.

4.3 SUBTYPE STUDIES OF ADHD

The DSM-IV (APA, 1994) lists three subtypes of ADHD which have not been extensively studied using electrophysiological techniques.

Only three studies have investigated EEG differences in the subtypes of ADHD. Matousek et al. (1984) studied EEG differences between children with MBD and normal control subjects. EEG was recorded from eight bipolar
derivations, using an eyes-closed resting condition. EEGs were analysed using both visual and computer analysis. Results indicated that there was a general slowing of the EEG in children with MBD. Subjects were also divided into three groups based on degree of severity of the disorder (none, mild-moderate, severe). Significant correlations were obtained between the severity of the disorder and posterior delta, and the theta/alpha ratio. The severe group had more posterior delta, and a higher theta/alpha ratio than the mild-moderate group, and the mild-moderate group had more delta, and a higher theta/alpha ratio than the normal group.

Chabot and Serfontein (1996) found children with ADHD had an increase in absolute and relative theta compared to normal control subjects. The ADHD groups also had a diffuse decrease in mean frequencies in the alpha and beta bands compared to normal children. EEG differences between the hyperactive and inattentive subtypes of ADHD were also examined. The differences between the two ADHD groups were mainly in the degree of abnormality, not the type, with the EEG measures from the inattentive subtype falling between those obtained from the hyperactive subtype and the normal children.

Both of these studies found that the degree of EEG abnormality increased with an increase in the severity of the ADHD diagnosis. The Chabot and Serfontein (1996) study used hyperactive and inattentive subtypes of ADHD. The main difference between these two subtypes is that the hyperactive subtype has all the inattentive symptoms of the inattentive subtype, plus additional gross motor activity. From this, the inattentive subtype can be considered as a less severe type of ADHD, and the EEG results obtained were not as deviant from the control
subjects as the hyperactive subtype.

Kuperman, Johnson, Arndt, Lindgren and Wolraich (1996) used DSM-III-R criteria to study the quantitative EEG differences between children with ADHD, UADD and normal children. For relative power, main effects of band were found, with the control group having more delta than the UADD subjects and less beta than both groups of children with ADHD. The UADD group had hemispheric differences, with decreased delta and increased beta in the left hemisphere. In relative alpha and beta, the UADD group had more extreme EEG results, in comparison to the control group, than the ADHD group. These results are not consistent with those of Chabot and Serfontein (1996) or Matousek et al. (1984). This study used an eyes-open condition which makes comparisons with the results of those studies difficult.

No studies have investigated EEG differences between DSM-IV (APA, 1994) subtypes of ADHD.

4.4 AGE RELATED CHANGES IN THE EEG OF CHILDREN WITH ADHD

One problem with most studies that have proposed a model of ADHD based on EEG measures, is that they have used measures from children at one point in time and then interpreted these based on what has been found in the developmental literature from normal children. Only two studies have investigated EEG changes with age in an ADHD population.

Satterfield, Schell, Backs and Hidaka (1984) conducted a cross sectional and longitudinal study of age effects in hyperactive children between the ages of 6
and 12 years, using an eyes-closed resting condition. In the first stage of the study, a diagnosis by age analysis was conducted, with the EEGs of the hyperactive group being compared to control subjects. Results indicated a significant age effect in all frequency bands except slow beta. The EEG amplitudes of the control subjects were found to decline faster with age. In the second stage of this study, a four year follow-up of a subset of the original group was performed. Results indicated that the rate of change in the EEG was greater in the younger subjects and that this change slowed in older subjects. Change in the EEG was also slower in the hyperactive group than in the control group. This resulted in an age by group interaction, with younger hyperactive subjects having EEG profiles typical of older normal children, and the older hyperactive subjects had EEG profiles that were more like those of younger normal children. From these results it was concluded that hyperactivity was an aberrant disorder rather than a maturational lag.

Bresnahan, Anderson and Barry (1999) investigated differences in the EEG of ADHD subjects who were divided into three age groups, children, adolescents and adults. The results indicated that theta activity remained elevated in adults, but there was a decrease in beta activity with age. From these results, it was concluded that beta activity may be linked to hyperactivity and increased theta activity to impulsivity, though this needed further investigation.

No studies have investigated age changes in subtypes of the disorder.

4.5 ATYPICAL EEG RESULTS IN CHILDREN WITH ADHD
Studies of EEG differences between children with ADHD and normal children have mostly found children with ADHD have excess theta activity, and this primarily occurs in the frontal areas (e.g. Mann et al., 1992). Chabot and Serfontein (1996) reported two EEG differences between their ADHD groups and normal control subjects, that have not been reported in other studies. The first of these was a pronounced increase in theta activity, in the frontal midline sites, and the second was a generalised increase in beta activity across the scalp.

4.5.1 Frontal Midline Theta

Frontal midline theta rhythm has primarily been reported in studies of EEG abnormalities in chart recordings, and consists of rhythmic runs of activity in the 5 to 7 Hz range (Westmoreland & Klass, 1990). The rhythm is usually maximal in the central leads and can spread to the frontal midline or adjacent parasagittal electrodes. This rhythm is found during both wakeful and drowsy states, but disappears during sleep. Frontal midline theta was first described by Ciganek (1961), under the title of “theta discharges in the midline”. This type of activity was found mainly in patients with temporal lobe epilepsy. This rhythm was first thought to represent an after-discharge from an epileptogenic focus in the mesial basal parts of the temporal lobe, that was transmitted via the limbic structures to the cingulate gyrus. From here, the activity was then reflected over the midline region of the scalp.

In a later study of a less specific group of patients, midline theta was found in patients who had other conditions (Mokran, Ciganek & Kabatnik, 1971). Patients with head trauma, brain abscess, vascular disease and multiple sclerosis,
were all found to exhibit this type of activity. In a review of patients who would normally receive an EEG (Westmoreland & Klass, 1986), midline theta rhythm was found in about 0.01% of people. Groups who exhibited this activity included those with degenerative diseases, headaches, labyrinthine disease, syncopal episodes and seizures. In patients with seizures, the midline rhythm was not unique to one particular type of seizure and was seen in patients with seizures arising from the temporal, frontal, parietal lodes, and the midline regions.

Yamaguchi (1994) found frontal midline theta spread to the frontal half of the scalp and rarely to posterior regions, and was considered to be an EEG entity associated with concentration. Frontal midline theta was not found in all subjects, although those exhibiting it were found to have a more extroverted personality type.

4.5.2 Excess Beta Activity in ADHD

Chabot and Serfontein (1996) found excess beta activity in approximately 13% of their sample of children with ADHD, which has not been reported in any other studies of children with ADHD.

Beta activity rarely occurs in children and adolescents, and should not exceed 25 μV (Fisch, 1994). Kellaway (1990) found beta activity was 20 μV or less in 98% of normal awake children, and less than 10 μV in 70%. Increased levels of beta activity have typically been associated with drug usage (Kozelka & Pedley, 1990), and beta activity can be increased by the use of benzodiazepines (Pichlmayr & Lips, 1980; Giaze, 1990).
Studies of beta activity have found excessive levels in patients with psychiatric illnesses (Gibbs & Gibbs, 1950). This has been reported in schizophrenic patients (Morihisa, Duffy & Wyatt, 1983), major depressive disorders (Pollock & Scheider, 1990), and in association with anxiety (Kilohm McComas, Osselton & Upton, 1981).

4.6 EFFECTS OF CHANGED RECORDING CONDITIONS ON THE EEG

Within the EEG studies of ADHD, a major methodological difference is whether an eyes-open or eyes-closed resting condition was used. These two conditions have been found to differ in their effect on EEG results. Low voltage beta wave activity is typical in frontal and central regions when a person is aware and alert, and has their eyes open (Thibodeau & Patton, 1996). During eyes-closed conditions, alpha wave activity dominates EEG activity in parietal, occipital, and the posterior temporal lobe regions. Callaway et al. (1983) investigated EEG spectral differences between hyperactive and normal children. The EEG was recorded using both an eyes-open and eyes-closed resting condition. In all bands except the delta band, the eyes-closed condition showed a greater level of power than the eyes-open condition.

These two conditions have also been shown to change the reliability of results obtained. John et al. (1980) conducted a study of the normal development of the EEG in children and adolescents. EEGs were recorded under both an eyes-open and eyes-closed resting condition. Results indicated poor test-retest reliability, in both absolute and relative power, for EEGs recorded using an eyes-
open condition. During an eyes-closed condition, absolute power still showed poor test-retest replicability. However, data converted to relative power showed a high degree of replicability.

4.7 DIFFERENCES IN TYPES OF EEG ANALYSIS.

A number of approaches have been used to assess changes in the EEG of children with normal development. This has included the analysis of waveform amplitude (Matousek and Petersen, 1973), absolute and relative power (John et al., 1980; Gasser, Verleger et al., 1988; Gasser, Jennen-Steinmetz et al. 1988), dominant and subordinate frequency analysis (Katada et al., 1981; Katada and Koike, 1990), mean frequency (Chabot & Serfontein, 1996), the wave percentage time (Matsuura, Matsuura. Yamamoto, Fukuzawa, Okubo, Uesugi, Moriwa, Kojima & Shimazono, 1985), and ratio coefficient analysis between waveforms (Matousek et al., 1973; Mattis & Schaffner, 1980).

With the advance of computer aided spectral analysis, the most commonly used form of EEG analysis in studies of ADHD has been the calculation of absolute and relative power estimates. These provide an easily-interpreted and reliable method of quantifying changes in the EEG under different conditions, as well as differences between various clinical and normal groups (Matthis, Schaffner & Benninger, 1981). In addition to these measures, calculations of ratio coefficients between frequency bands, and the calculation of the mean frequency of different bands, have been used to further quantify differences between experimental groups.
4.7.1 Ratio Analyses Between Frequency Bands

Benninger et al. (1984) conducted a longitudinal study of normal children over an average of 4.6 years. The results of this study indicated that, on measures of relative power, the difference between subjects from within a one year age group was greater than the difference between subjects from consecutive one year age bands. The calculation of ratio coefficients has been proposed as a better measure of group differences than the use of a single frequency band alone (Lubar, 1991). While different subjects might have large differences in the amount of power in their EEGs, the ratio of the power in two frequency bands is more stable, and will be the same irrespective of the total power differences between subjects.

Matousek and Petersen (1973) calculated ratio coefficients between each of the six frequency bands that were used in their study of normal children. The theta/alpha ratio was found to be the best ratio for quantifying age-related changes.

Ratio coefficients have also been used to quantify group differences in the study of children with ADHD. Matousek et al. (1984) found that the theta/alpha ratio was one of only two measures that discriminated between children with different levels of severity of a diagnosis of MBD. Measures of theta or alpha alone did not discriminate between the groups. Corning, Steffy, Anderson and Bowers (1986) used the theta/alpha ratio to evaluate changes, over an 18 month period, in the EEG of children with diffuse slow wave activity. This group was
drawn from a population of children who presented to a university clinic for behavioural or learning disabilities. The theta/alpha ratio was found to be useful for evaluating the nature of the maturational changes that occurred. Results indicated that there was little change in the EEG of the diffuse slow wave group. The EEG of these children was not found to be approaching that of children without slow wave activity, but was considered to be developing in parallel, but at a deviant level. Results also indicated that there might be more than one group of children within the sample, based on the patterns of EEG development found. Ucles and Lorente (1996) used the theta/alpha ratio to investigate differences between children with a DSM-III diagnosis of ADHD and normal control subjects, during an eyes-closed resting condition. Significant group differences were found in the occipital leads, with the ADHD having a higher ratio coefficient than control subjects. This was explained as a reduction in alpha activity rather than an increase in theta activity, and was believed to result from a localised deficit in the cortical chain of neurons interacting by means of cortico-cortical fiber systems, or the thalamo-cortical fiber system. This study was not able to identify which of these systems was likely to be involved. However, delayed maturation somewhere in the alpha rhythm circuits was seen as the most plausible explanation for the results found.

The theta/beta ratio has also been used to evaluate the EEG of children with ADHD. The theta/beta ratio was proposed by Lubar (1991) as a possible measure that would be better than using relative theta or beta separately. This ratio was believed to take into account the fact that different individuals have large variability in their amplitude or power levels. The theta/beta ratio should also
decrease with increasing age, allowing an assessment of maturational changes, as well as differences between ADHD and control subjects. Lubar (1991) calculated theta/beta ratios for 25 ADHD and 27 control subjects during a drawing task. The ADHD subjects had a greater ratio at all sites compared to the control subjects, with the greatest difference being found in the frontal electrode sites.

Janzen et al. (1995) found children with ADHD without hyperactivity (DSM-III-R) had higher amplitude theta than control subjects, during an eye-closed resting condition. No differences in amplitude in the beta band were found between subjects. When the theta/beta ratio was calculated, children with ADHD had a higher ratio than normal control subjects. From these results, theta/beta ratios were viewed as a good discriminator of differences between ADHD and normal children.

4.7.2 Frequency Analyses of the EEG

Measures of the mean frequency of the EEG have also been shown to discriminate between children with ADHD and normal children. Children with ADHD have been found to have a lower dominant mean frequency than control subjects (Matsuura et al., 1993). This was explained as a delay in functional maturity of the brain since the profiles obtained resembled those of healthy younger children. Chabot and Serfontein (1996) found that subjects with ADHD had a diffuse decrease in the mean frequency of the alpha and beta bands compared to normal control subjects. From these results, the mean frequency can
be used to differentiate children with ADHD and normal children, as well as provide an estimate of maturational changes in the EEG.

4.8 OVERVIEW AND LIMITATIONS OF EEG STUDIES INTO ADHD

From all of these studies, children with ADHD have been found to have excess theta activity which primarily occurs in the frontal regions. Excess delta and decreased alpha and beta in the posterior regions has also been associated with ADHD. The major limitation with most of these studies is that they have only investigated one subtype of ADHD, and this has primarily been children with hyperactivity. Studies that have investigated either different levels of severity within their population, or different subtypes of the disorder, have primarily found results that suggest that children with ADHD fall along a continuum from less severe to more severe, and the subtypes differ on the bases of how impaired they are.

Two main perspectives have been proposed to explain the general EEG findings for children with ADHD. These conceptualise ADHD as either a maturational lag or a developmental deviation in CNS functioning. These models have been based on similar results or ADHD children, and extrapolated from the normal developmental literature, and to date there is no conclusive evidence of one model over the other. Few studies have investigated developmental changes in children with ADHD. From those studies that have conducted age analysis of their data, results suggest that some components of the EEG remain stable while others change with increasing age.
The DSM-IV (APA, 1994) lists criteria for three subtypes of ADHD. Only one study has investigated EEG differences between children with ADHD and normal children under these criteria. No studies have investigated EEG differences in DSM-IV subtypes of ADHD, or how the EEG of these children may change with increasing age. This type of analysis has the potential to provide a greater understanding of the relationship between the subtypes of the disorder, as well as the underlying CNS dysfunction that is present in children with this disorder.
CHAPTER 5. STUDY 1. EEG ANALYSIS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A COMPARATIVE STUDY OF TWO SUBTYPES

\footnote{This Study has been published as: Clarke, A., Barry, R., McCarthy, R. & Selikowitz, M. (1998). EEG analysis in attention-deficit/ hyperactivity disorder: A comparative study of two subtypes. Psychiatry Research, 81, 19-29.}
5.1 INTRODUCTION

Over the course of this century the disorder that has become known as ADHD has undergone clarification in its etiology. Initially ADHD was believed to result from brain damage, but this explanation lost favour as children without brain damage were diagnosed with ADHD. Subsequently, researchers in the 1950s and 1960s changed the name of this disorder from "minimal brain damage" to "minimal brain dysfunction" (Green & Chee, 1994). In 1968 the DSM-II first listed diagnostic criteria for ADHD under the title "hyperkinetic reaction of childhood", characterised by overactivity, restlessness, distractibility and short attention span. Much of the literature from the 1960s and 1970s used both “MBD” and “hyperactive” to describe the same disorder. In the DSM-III (1980), the title was changed to "Attention Deficit Disorder" and two groups were identified, children with and without hyperactivity. In the DSM-IV (1994), the diagnostic criteria have changed again, with three main groups being identified: Attention-Deficit/Hyperactivity Disorder of the Predominantly Hyperactive-Impulsive Type, Attention-Deficit/ Hyperactivity Disorder of the Predominantly Inattentive Type (ADHDin) and Attention-Deficit/Hyperactivity Disorder of the Combined Type (ADHDcom).

EEG research into ADHD has not progressed at the same speed as the changes in the conceptualisation and diagnostic criteria of this disorder. Satterfield, Cantwell, Saul, Lesser et al. (1973), with a group of ADHD children who were good responders to stimulant medication, found an increase in slow wave activity and greater power in the lower frequency bands between 0 and 8
Hz, prior to medication being prescribed. Matousek et al. (1984) found the highest correlates of MBD in the relative delta band for parieto-occipital derivations. Mann et al. (1992), in a study of children with ADHD, found an increase in absolute amplitude in the theta band during a resting condition, predominantly in the frontal regions. During cognitive tasks, ADHD children showed a greater increase in theta activity in frontal and central regions, and a decrease in beta activity in posterior and temporal regions, with tasks requiring sustained attention.

Most studies of ADHD have used populations of children exhibiting hyperactive behaviours with few studies investigating subtypes of ADHD, even though the last three editions of the DSM (APA, 1980, 1987, 1994) have listed criteria for multiple subtypes. Chabot and Serfontein (1996) studied EEG differences in children with ADHD with or without hyperactivity, using DSM-III criteria. The children with ADHD were found to have an increase in absolute and relative theta, with the greatest increase being found in frontal regions and at the midline. A slight elevation in relative alpha was also noted and in a small group of subjects (13%), an increase in beta was found. The differences between the two ADHD groups was mainly a difference in degree of abnormality, not type.

Kuperman et al. (1996), using DSM-III-R criteria, studied quantitative EEG differences between children with ADHD, UADD and normal children. For relative power, main effects of band were found, with the control group having more delta than the UADD subjects and less beta than both groups of children with ADHD. Only the UADD group had hemispheric differences, with decreased delta and increased beta in the left hemisphere. This study investigated
topographic effects only where a significant main effect was found for the band and this may have resulted in significant regional differences being overlooked. An eyes open condition was also used, making comparison with most other EEG studies of ADHD difficult.

The studies outlined above have led researchers to propose two models of ADHD with a neurophysiological basis. The first model proposes that ADHD is the result of a low level of CNS arousal (Satterfield & Cantwell, 1974). To investigate this, Satterfield and Dawson (1971) conducted a study of skin conductance levels (SCLs). This study found that 50% of the hyperactive children had abnormally low SCLs, supporting a model of low CNS arousal. Hyperactive children have been found to respond well to the use of stimulant medication and are often prescribed stimulants as part of their clinical management (Spencer et al., 1996). Two of the drugs most commonly used in the treatment of ADHD in Australia are dexamphetamine and Ritalin (Serfontein, 1991). Both of these act as CNS stimulants and have the effect of increasing concentration and reducing excessive motor activity. Chabot and Serfontein (1996) concluded that the EEG patterns found in their study of ADHD children would not ordinarily be found in normal children of any age, and represented a deviation from normal development. These findings support a model of low CNS arousal.

A second model of ADHD is the maturational lag model. Studies of the auditory evoked potential have found that hyperactive children have significantly lower amplitudes and longer latencies than age matched controls (Satterfield, Lesser, Saul & Cantwell, 1973). These findings are typical of younger children. Mann et al. (1992) found that the EEG profiles of their ADHD children were
similar to those found in normal younger children. From these results it was concluded that this finding supported the view that ADHD reflects maturational delays in the systems that subserve attention.

These models of ADHD have been proposed, based on what has been found in studies of maturational processes in the EEG of normal children. With normal maturation, EEG frequencies increase as a function of age, with slow wave activity apparently being replaced by faster waveforms (Matousek & Petersen, 1973; Matthis & Schaffner, 1980). John et al. (1980) developed 32 linear regression equations predicting the frequency composition of the EEG as a function of age. The results indicated that development of the normal EEG was linear in nature. Benninger et al. (1984), in a longitudinal study of 96 boys and girls, found that theta activity decreased as alpha increased and that the speed of change in occipital areas was almost twice that of central areas. Gasser, Verleger et al. (1988) found that certain regions of the brain matured before other regions. Absolute power in delta, theta and alpha 1 frequency bands was found to decrease and amplitudes became similar with age. The decline was found to be greatest in posterior regions. Frontally, delta and theta were found to develop in parallel, whereas theta dominated delta in all other areas. Alpha activity showed a strong posterior increase. At frontal and central regions, the increase started later and remained small. All beta activity showed a decline with age. Except for alpha 2 activity, all frequency bands and total power showed a continuous decrease in power with age. For relative power, a strong complementary replacement of theta by alpha 2 activity was found up to the age of 14. Delta, theta and alpha 1 frequencies decreased with age and higher frequencies increased. All of these
studies found a decrease in slow wave activity and an increase in faster frequency bands with age, with this change being linear in nature.

At the time of conducting this study, no EEG research had been published that used DSM-IV criteria for ADHD. The DSM-IV (1994) outlined diagnostic criteria for three sub-groups of children with ADHD. This study aimed to extend the previous EEG research into ADHD by investigating EEG differences between children with a DSM-IV diagnosis of ADHD and normal children. This was further extended by an investigation of two of the sub-groups of children with ADHD: children with ADHDcom and ADHDin, to determine whether the two sub-groups differ from each other in their EEG. This was conducted to determine if the sub-groups were neurologically independent.

5.2 METHOD

5.2.1 Subjects

Three groups of 20 children, with 16 boys and 4 girls in each group, participated in this study, with the gender ratio of 4:1 to represent the ratio of boys to girls often found for this disorder. All children were between the ages of 8 and 12 years and right handed and footed. For inclusion, all subjects were assessed using the WISC-III and were required to have a full scale score of 85 or higher. The groups used were children diagnosed with ADHDcom or ADHDin and a control group. Both groups of children with ADHD were drawn from new patients referred by their family doctor to a Sydney-based paediatric practice for
an initial assessment for ADHD. The ADHD subjects had not been diagnosed as having ADHD previously, had no history of medication use for the disorder, and were tested before being prescribed any medication. The control group came from local schools and community groups. Subjects were obtained from these sources for every study in this thesis.

5.2.2 Subject Inclusion Criteria

Inclusion in the ADHD groups was based on a clinical assessment by a paediatrician and a psychologist. Diagnostic criteria used were from the DSM-IV for both ADHDcom and ADHDin. Assessment was based on a clinical history from a parent, school reports for a minimum period of the previous 12 months, reports from any other health professionals and behavioural observations made during the assessment. Inclusion as a control subject was based on a structured interview with a parent. Subjects who scored outside the normal age range on the Neale Analysis of Reading or below the average range on the Wide Range Achievement Test (WRAT) spelling were excluded from the control group. The CPRS-48 Conners rating scale was used, with subjects who scored above a T-score of 65 on any of the six measures being excluded.

Inclusion in all groups was also based on the following criteria: an uneventful prenatal, perinatal and neonatal period, no disorders of consciousness, head injury with cerebral symptoms, history of central nervous system diseases, obvious somatic diseases, convulsions, history of convulsive disorders, paroxysmal headache, enuresis or encopresis after the fourth birthday, tics, stuttering, obvious mental diseases and no deviation with regard to mental and
physical development. Any children who showed signs of depression, anxiety, oppositional behaviour or syndromal disorders were excluded from this study. Children in all groups were excluded if atypical spike wave activity was present in the EEG. These criteria was used for the control group and the ADHD groups in every study in this thesis.

Across all groups, subjects were matched in one year age bands and by sex.

5.2.3 Procedure

All subjects were tested in a single session lasting approximately 2.5 hours. Subjects were first assessed by a paediatrician, using a structured interview, when a clinical history and physical examination were undertaken. Subjects then had a psychometric assessment by a psychologist. This involved the administration of a WISC-III, Neale analysis of reading and WRAT spelling. At the conclusion of this assessment, subjects had a neurological assessment consisting of evoked potentials and an EEG. The EEG was recorded using an eyes closed resting condition, with subjects seated on a reclining chair. Recording of the EEG was stopped for a break if subjects became restless or drowsy. Electrode placement was in accordance with the international 10-20 system, using an electrocap produced by Electrocap International. The activity in 21 derivations was divided into 9 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. Linked ear references were used with all EEG, and reference and ground leads were 9 mm tin disk electrodes. 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 microvolts per centimetre, 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 second epochs.

Thirty 2.5 second epochs were selected from the real-time 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 microvolts. The technician also visually appraised every epoch and decided to accept or reject it. These were further reduced to 24 epochs (1 minute) for Fourier analysis by a second technician. This procedure was used for every subject in this thesis.

The EEG was analyzed in four frequency bands: Delta (0.5-2.5 Hz), Theta (2.5-7.5 Hz), Alpha (7.5-13.5 Hz) and Beta (13.5-20.5 Hz), for both absolute and relative power, as well as the total power of the EEG (0.5-20.5 Hz). Relative power was calculated by dividing absolute power in the frequency band by the total power and multiplying this by 100.
5.2.4 Statistical analysis

Analysis of variance was performed examining the effects of region and group for each band in absolute and relative power and for the total power. 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 regions with the posterior regions, and their mean with the central regions. 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 planned contrasts allow optimal clarification of site effects within the regions studied. Within the Group factor, planned contrasts compared the patient groups with the control group (to establish ADHD differences from normals) and the ADHDcom group with the ADHDin group. 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 $\alpha$ is required (Tabachnick & Fidell, 1989). A variant of these planned contrasts were used for group comparisons in every study in this thesis.

5.3 RESULTS

No significant age differences were found between groups (see Table 5.1). The control group had a significantly higher mean IQ than the ADHD groups ($F(1,53) = 29.68$, $p<.001$), which did not differ on IQ.
Four subjects in the ADHDcom group were found to be statistical outliers with beta levels greater than 3 standard deviations above the mean. These subjects were excluded from further analysis.

Table 5.1
Mean Ages and IQ Scores for the ADHDcom, ADHDin and Control groups.

<table>
<thead>
<tr>
<th>MEAN</th>
<th>CONTROL GROUP</th>
<th>ADHDcom GROUP</th>
<th>ADHDin GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (MONTHS)</td>
<td>122.1</td>
<td>122.7</td>
<td>123.6</td>
</tr>
<tr>
<td>FULL SCALE IQ (WISC-III)</td>
<td>116.5</td>
<td>98.8</td>
<td>100.9</td>
</tr>
</tbody>
</table>

5.3.1 Topography Across Groups

Across all groups, total power was greater in the posterior regions compared to the frontal regions ($F(1,53) = 36.81, p<.001$), and the central regions had less power than the mean of the frontal and posterior regions ($F(1,53) = 35.08, p<.001$). The right hemisphere had significantly greater power than the left hemisphere ($F(1,53) = 10.4, p<.01$), and the midline had greater power than the two hemispheres ($F(1,53) = 126.23, p<.001$). This midline difference was maximal at the central regions ($F(1,53) = 93.15, p<.001$).

In absolute delta, the posterior regions had greater power than the frontal regions ($F(1,53) = 15.71, p<.001$), and the central regions had less power than the mean of the frontal and posterior regions ($F(1,53) = 8.82, p<.01$). An effect of laterality was found, with the right hemisphere having greater power than the left hemisphere ($F(1,53) = 9.33, p<.01$), and the midline having greater power than
the two hemispheres ($F(1,53) = 308.91$, $p<.001$). The difference between the midline and the two hemispheres was greatest at the central regions ($F(1,53) = 214.36$, $p<.001$).

For relative delta, more power was found in frontal regions than posterior regions ($F(1,53) = 133.42$, $p<.001$). A significant effect of laterality was found with the midline having less power than the two hemispheres ($F(1,53) = 30.41$, $p<.001$). This difference was greater at the frontal regions than the posterior regions ($F(1,53) = 23.58$, $p<.001$), and was smallest at the central regions ($F(1,53) = 20.23$, $p<.001$).

In absolute theta, greater power occurred in the posterior regions than the frontal regions ($F(1,53) = 5.11$, $p<.05$). Laterally, the midline had greater power than the two hemispheres ($F(1,53) = 112.61$, $p<.001$), and the right hemisphere had greater theta power than the left hemisphere ($F(1,53) = 13.58$, $p<.001$). This difference was significantly greater at the frontal regions compared to the posterior regions ($F(1,53) = 6.05$, $p<.05$). A significant interaction of sagittal effect by laterality was found with maximum power occurring at the central midline region ($F(1,53) = 101.64$, $p=.001$).

In the relative theta band, more theta was found in the frontal regions compared to the posterior regions ($F(1,53) = 63.66$, $p<.001$), and the central regions had more theta than the mean of the frontal and posterior regions ($F(1,53) = 56.66$, $p<.001$). Laterally, the midline had more theta than the two hemispheres ($F(1,53) = 134.60$, $p<.001$), and this difference was greater at the frontal regions than the posterior regions ($F(1,53) = 86.96$, $p<.001$). The difference between the midline and the two hemispheres was greater at the central regions than the mean of the frontal and posterior regions ($F(1,53) = 16.80$, $p<.001$). The difference between the central regions and the mean of the frontal and posterior regions was greater in the left hemisphere than the right hemisphere ($F(1,53) = 5.75$, $p<.05$).
In absolute alpha, greater power was found in the posterior regions than the frontal regions (F(1,53) = 55.1, p<.001), and the central regions had less power than the mean of the frontal and posterior regions (F(1,53) = 51.18, p<.001). An effect of laterality was found with greater power occurring at the midline than the two hemispheres (F(1,53) = 28.52, p<.001). This difference was greater at the posterior regions than the frontal regions (F(1,53) = 6.99 p<.05), and greater at the central regions than the mean of the frontal and posterior regions (F(1,53) = 4.03, p<.05).

For relative alpha, more power was found in the posterior regions compared to the frontal regions (F(1,53) = 339.5, p<.001), and less at the central regions than the mean of the frontal and posterior regions (F(1,53) = 74.45, p<.001).

For absolute beta, greater power was found in the posterior region than the frontal regions (F(1,53) = 22.83, p<.001), and the central regions had less power than the mean of the frontal and posterior regions (F(1,53) = 13.74, p<.001). Laterally, greater power was found in the right hemisphere compared to the left hemisphere (F(1,53) = 16.31, p<.001), and the greatest power occurred at the midline (F(1,53) = 14.18, p<.001).

For relative beta, more power was found in the frontal regions than posterior regions (F(1,53) = 118.69, p<.001), and the central regions had more power than the mean of the frontal and posterior regions (F(1,53) = 9.65, p<.01). Laterally more power was found in the right hemisphere than the left hemisphere (F(1,53) = 5.28, p<.05) and the midline had less power than the two hemispheres (F(1,53) = 143.92, p<.001). The difference between the midline and the two hemispheres was greater at the posterior regions compared to the frontal regions (F(1,53) = 25.54, p<.001), and the central regions had greater power than the mean of the frontal and posterior regions (F(1,53) = 44.22, p<.001). In the left hemisphere, the central region had more beta than the mean of the frontal and
posterior regions, whereas in the right hemisphere the central region had less beta than the mean of the frontal and posterior regions (F(1,53) = 4.45, p<.05).

5.3.2 Group Differences

Figure 5.1 (top left) shows the results for total power. The ADHD groups had a greater difference than the controls in their midline versus left/right activity (Figure 5.2, top left) at the frontal compared with posterior regions (F(1, 53) = 4.13, p<.05), and at the central region compared with the frontal and posterior regions (F(1, 53) = 5.02, p<.05), suggesting a largely frontal midline enhancement in total activity in ADHD.

In the absolute delta band (Figures 5.1 & 5.2, top right), the difference between the midline and the left and right hemispheres was greater in the ADHD groups than in the control group (F(1, 53) = 4.44, p<.05). For relative delta, the ADHD groups had more posterior (compared with frontal) activity than the control group (F(1, 53) = 5.90, p<.05) and this effect was greater in the ADHDcom group than the ADHDin group (F(1, 53) = 4.66, p<.05).

The distribution of absolute theta is shown in Figure 5.1 (centre). The ADHD groups had greater theta power than the control subjects (F(1, 53) = 5.63, p<.05). The ADHDcom group had greater theta power than the ADHDin group, a difference approaching significance (F(1, 53) = 3.85, p = .055). The difference between the midline and the two hemispheres (Figure 5.2, centre) was significantly greater in the ADHD groups than the control group (F(1, 53) = 5.00, p<.05). This interaction was greater at the frontal regions than the posterior regions (F(1, 53) = 6.05, p<.05), and greater at central regions than either frontal
Figure 5.1 Absolute power from frontal to posterior regions: Total Power (top left), Absolute Delta (top right), Absolute Theta (centre), Absolute Alpha (bottom left), Absolute Beta (bottom right).

or posterior regions ($F(1, 53) = 7.71, p<.01$), indicating a fronto-central maximum for this interaction. The difference between the midline and the two hemispheres was greater at frontal regions than posterior regions in the ADHDcom group compared to the ADHDin group, an interaction approaching significance ($F(1, 53) = 3.87, p = .054$). Similar results were found in the relative theta band, with significant differences in level between the ADHD groups and control group
Figure 5.2 Frequency distribution as a function of scalp region, sagittal section, for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre), Absolute Alpha (bottom left), Absolute Beta (bottom right).

(F(1, 53) = 46.7, p<.001), and between the ADHDcom and ADHDin groups (F(1, 53) = 14.79, p<.001). An effect of laterality approached significance, with the ADHDcom group having a greater difference between the midline and the two hemispheres at frontal compared with posterior regions, than the ADHDin group (F(1, 53) = 3.90, p = .053). In the absolute alpha band (Figures 5.1 & 5.2,
bottom left), a main effect approaching significance was found, with the ADHD groups having less absolute alpha than the control group (F(1, 53) = 3.93, p = .053). The control group had relatively greater alpha power in posterior regions than the frontal regions, compared to the ADHD groups (F(1, 53) = 5.12, p<.05). The difference between central regions and the mean of the frontal and posterior regions was also greater in control subjects (F(1, 53) = 6.23, p<.05). For relative alpha, the control group had more activity than the ADHD groups (F(1, 53) = 23.72, p<.001) and the ADHDin group had more alpha than the ADHDcom group (F(1, 53) = 5.49, p<.05). The control group had a greater enhancement of relative alpha at posterior regions, compared with the ADHD groups (F(1, 53) = 4.42, p<.05), and this difference between groups was least at the central regions compared with frontal/posterior regions (F(1, 53) = 5.65, p <.05). A significant difference occurred between the control group and the ADHD groups in relative alpha at the midline compared with the two hemispheres, with the control group showing the largest effect (F(1, 53) = 4.82, p<.05).

Patterns across regions for absolute beta are presented in Figures 5.1 and 5.2 (bottom right). The control group had somewhat more beta than the ADHD groups (F(1, 53) = 4.00, p = .051). This difference was greater in the posterior than the frontal regions (F(1, 53) = 5.29, p<.05). For relative beta, the control group had more power than the ADHD groups (F(1, 53) = 15.26, p<.001) and the ADHDin group had more power than the ADHDcom group (F(1, 53) = 7.57, p<.01). The control group and the ADHD groups differed for the sagittal effect, with the greatest difference between groups occurring at frontal regions (F(1, 53) = 19.49, p<.001). With laterality, the difference between the midline and the two
hemispheres was greater in the controls than the ADHD groups (F(1, 53) = 6.19, p<.05). The midline enhancement at the central regions was greater than at the frontal and posterior regions in the control group compared to the ADHD groups (F(1, 53) = 5.33, p<.05).

5.4 DISCUSSION

A significant difference was found between the IQ of the control group and the two ADHD groups. Previous studies of ADHD have reported similar differences but this has not been considered likely to have affected the EEG results (e.g., Satterfield et al., 1972). Chabot and Serfontein (1996) compared two groups of children with ADHD, one group with normal IQs and the other with a low IQ. They concluded that the greatest variance in EEGs was related to the diagnosis and not IQ. The IQ difference between the control group and the clinical groups was possibly exacerbated here by the inclusion criteria for control groups of average performance in reading and spelling. Studies of EEG and IQ have generally been inconclusive (Bosaeus et al., 1977), but Gasser, Mocks et al. (1983) found small correlations between increasing IQ scores and measures on the EEG. It is thus possible that some of the between group differences reflect differences in IQ. The importance of this possibility is reduced by the observation of substantial differences between the two ADHD groups, which did not differ on IQ.

Previous studies of Hyperactive children have found an increase in slow wave activity and an increase in amplitude in the 0 to 8 Hz frequency range in the
EEG compared with normal controls (Capute et al., 1968; Satterfield, Cantwell, Saul, Lesser et al., 1973; Satterfield & Cantwell, 1974). Similar findings were obtained in this study, with the ADHD subjects having greater levels of both absolute and relative theta over all regions. Most previous studies have found an increase in theta primarily located in the frontal derivations (Mann et al., 1992; Chabot & Serfontein, 1996). However, this study found significantly more frontal midline theta. The ADHD groups here had a significant increase in relative delta in the posterior regions, confirming Matousek et al.'s (1984) finding that the greatest correlation of MBD and EEG abnormalities occurred in the relative delta band at posterior sites. Mann et al. (1992) reported that subjects with ADHD had a decrease in absolute amplitude of the beta band in posterior regions. This study confirms the Mann et al. (1992) results for absolute beta, with the ADHD groups having less posterior beta than the control group. Chabot and Serfontein (1996) found an increase in alpha activity in children with ADHD. This was not found in the present study, where the ADHD groups had decreased relative alpha across all sites, with the greatest difference occurring in the posterior regions.

Gasser, Verleger et al. (1988) found a systematic decrease in slow wave activity and a complimentary increase in faster frequencies with increasing age. This was greatest in the theta and alpha bands, with a high correlation between the decrease in theta and the increase in alpha activity. In the delta band, the strongest decrease with maturation was found in posterior regions. The present findings support a maturational lag model of the CNS in ADHD. The increased posterior delta, increases in theta and a reduction in the alpha bands are all indicative of a maturational lag.
Significant differences across all regions were found between patient
groups in the relative theta and alpha bands. ADHDcom subjects had a greater
percentage of theta than ADHDin subjects for all regions. In the alpha band, the
reverse was found, with the ADHDin subjects having greater alpha than the
ADHDcom subjects. A similar finding for relative delta in posterior regions was
noted: ADHDcom subjects had a greater percentage of delta than the ADHDin
subjects.

This study demonstrated the existence of measurable differences between
children with ADHDcom and ADHDin. These differences appear to be in the
degrees of severity of the differences from the control group, rather than in the
nature of the EEG abnormalities, suggesting that these two sub-groups of ADHD
are not neurologically independent. This is compatible with the results of Chabot
and Serfontein (1996).

The principal difference in the diagnosis of the two subtypes of ADHD
involves behavioural aspects. Children with ADHDcom are often restless and
fidgety, impulsive, have a short concentration span and are easily distracted.
Children with ADHDin have the concentration problems but do not have the
gross behavioural aspects of ADHDcom. This study found that ADHDin subjects
exhibited EEG abnormalities indicative of a maturational lag, but that the lag was
not as great as in those subjects with ADHDcom. These data suggest that the
more behavioural problems that are exhibited by a child with ADHD, the greater
is the level of the associated EEG abnormalities. This finding is consistent with
other studies (e.g., Matousek et al., 1984) that report an increase in EEG
abnormalities correlating highly with an increase in the level of abnormality exhibited by the child.

If ADHD is the result of a maturational lag, then it would be expected that a decrease in the percentage of slow wave EEG activity should be found with increasing age in ADHD. Wikler et al. (1970) noted that the abnormally slow EEG activity of hyperactive children did not increase or decrease with age. Chabot and Serfontein (1996) felt that the EEG abnormalities found were indicative of a deviation from normal maturation, not the result of a maturational lag. Katada et al. (1981), in a study of mentally retarded children, found that the EEG did mature in the same direction as in normal children, although the process was delayed. The study of age factors in the development of children with ADHD could provide valuable information relative to the nature of the maturational lag.

The major problem with the maturational lag model is the occurrence of ADHD in adults. The maturational lag model implies that as a child with ADHD gets older, the symptoms of ADHD should lessen. Studies of ADHD have estimated that between 30% and 70% of children with ADHD continue to show symptoms of the disorder as adults (Bellak & Black, 1992). The DSM-IV (1994) states that some of the behavioural problems such as excessive gross motor activity become less in adolescence and adulthood. It is thus possible that maturational lag underlies some components of ADHD but not the entire disorder. Further research is needed to investigate this problem.

An increase in midline theta, compared to the two hemispheres, was found in the frontal regions, with the ADHDcom group having more theta than the ADHDin group. Yamaguchi (1994) found frontal midline theta spread to the
frontal half of the scalp and rarely to posterior regions and was considered an EEG entity associated with concentration. Frontal midline theta was not found in all subjects, although those exhibiting it were found to have a more extroverted personality type. As such an increase in theta was found only in the ADHDcom group, it is possible that it corresponds to a specific behavioural component of ADHD unique to ADHDcom. The frontal and central midline regions were the only regions where the ADHD groups had greater total power than the control group. The overt behavioural problems exhibited by children with ADHDcom may be primarily related to the functioning of the frontal regions of the brain.

Four individuals in the ADHDcom group were excluded from analysis because they had much higher levels of beta than was typical of the entire group. This EEG profile has only been noted once before in children with ADHD (Chabot & Serfontein, 1996), comprising approximately 13% of their sample. This subset of subjects in two studies, although small in number, suggests the existence of a subtype of ADHDcom, characterised by an increase in beta activity, and this needs further investigation.

This study obtained general results similar to other studies (e.g. Mann et al., 1992, Chabot & Serfontein, 1996), with ADHD subjects having increased levels of theta wave activity, especially in frontal regions, and a decrease in posterior beta. Additionally, a decrease in relative alpha was noted in the present study. Differences in the EEG were also found between the ADHDcom group and the ADH Din group in the theta, alpha and beta bands. This study has demonstrated that EEG can be used to differentiate normal children and children with ADHD, as well as subtypes of the disorder. These data suggest that the
subtypes differ in severity rather than in the nature of the underlying neurological impairment. The findings confirm that EEG may be useful in the clinical assessment of ADHD. Further research is needed in relation to the subtypes of ADHD and aspects of comorbidity within the population, as well as to investigate the reliability of these results for clinical use.
CHAPTER 6. STUDY 2. EEG DIFFERENCES IN TWO SUBTYPES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

This Study has been accepted for publication as: Clarke, A., Barry, R., McCarthy, R. & Selikowitz, M. EEG Differences in two Subtypes of Attention-Deficit/Hyperactivity Disorder. Psychophysiology.
6.1 INTRODUCTION

Study 1 of this thesis investigated EEG differences between children with a DSM-IV diagnosis of ADHD and normal children, as well as differences between the ADHDcom and ADHDin subtypes of the disorder. The results of Study 1 found EEG differences between children with ADHDcom, ADHDin and control subjects during an eyes closed resting condition. These differences occurred across all sites in absolute and relative theta and in relative alpha and beta. In posterior regions, relative delta estimates were able to differentiate between all three experimental groups. From these results it was concluded that children diagnosed with ADHDcom and ADHDin can be differentiated from normal children and from each other using EEG measures. The differences between the two subtypes of the disorder appeared to be a quantitative difference only, rather than the two subtypes being independent in nature.

Both Chabot and Serfontein (1996), and the results of Study 1 suggested that the differences between the subtypes of ADHD were in the degree of severity rather than the subtypes being qualitatively different. Although two different diagnostic criteria were used in the two studies, the results for the clinical groups are largely comparable. The inattentive groups had EEG measures that were different from those of normal control subjects and the combined groups were different again from the inattentive groups. The differences between the combined groups and the control groups were of the same nature as between the inattentive and control groups except that the difference was greater. From these
results, it appeared that the two subtypes were part of a disorder with multiple
degree of severity.

In contrast to these results, studies conducted into the hyperactive and
inattentive subtypes of ADHD have found differences other than hyperactivity.
Children with ADD/H have been found to be more impulsive (Lahey et al., 1987),
have more conduct disorder problems (Barkley et al., 1990; Mattison, Cantwell &
Baker, 1992), but are less anxious (Lahey et al., 1984) than children with
ADD/WO. Differences in social behaviour between the two groups have also
been found, with ADD/WO children being more socially withdrawn and shy
(Edelbrock et al., 1984), while children with ADD/H are more unpopular (Lahey
et al., 1984; Lahey & Carlson, 1991). These findings suggested that the two
subtypes are substantially dissimilar in ways other than hyperactivity, and some
researchers have proposed that the subtypes should not be considered as part of
the same disorder (Lahey et al., 1985). The conclusions drawn from these studies
are contradictory to those from Study 1, and from other EEG studies of ADHD
(e.g. Chabot & Serfontein, 1996).

Studies of normal maturation of the EEG have found that EEG
frequencies increase as a function of age, with slow wave activity apparently
being replaced by faster waveforms (Matousek & Petersen, 1973; Matthis &
Schaffner, 1980). Theta activity decreases as alpha increases, and changes occur
faster in the occipital areas (Benninger et al., 1984). Gasser Verleger et al. (1988)
found that certain regions of the brain matured before other regions. Absolute
power in delta, theta and alpha 1 frequency bands was found to decrease and
amplitudes became similar with age. The decline was found to be greatest in
posterior regions. Alpha activity showed a strong posterior increase, and except for alpha 2 activity, all frequency bands, and total power showed a continuous decrease in power with age. In relative power, a strong complementary replacement of theta by alpha 2 activity was found up to the age of 14. Delta, theta and alpha 1 frequencies decreased with age and higher frequencies increased.

In Study 1, the ADHD groups had greater levels of both absolute and relative theta, decreased relative alpha, increased relative delta, and decreased relative alpha and beta in the posterior regions compared to the control group. All of these results are consistent with a maturational lag model of ADHD. From the studies of normal children, the results would appear to be normal if they were found in younger children. However, research has been published where similar results have been found, and the results have been interpreted as representing a developmental deviation (Wikler et al., 1970; Chabot & Serfontein, 1996).

Within the literature, a number of EEG measures other than absolute and relative power have been calculated to quantify both maturational changes, as well as differences between ADHD children and normal children. To quantify the rate of change of the EEG with increasing age, Matousek and Petersen (1973) calculated ratio coefficients between each of the six frequency bands that were studied. The theta/alpha ratio was found to be the best ratio for quantifying age related changes. In studies of ADHD, the theta/beta ratio was found to differentiate between children with ADHD and normal control subjects (Jansen, 1995). Lubar (1991) proposed that the theta/beta ratio is a better measure of the
differences between children with ADHD and normal children than theta levels alone.

Measures of the mean frequency of the EEG have also been shown to discriminate between children with ADHD and normal children. Chabot and Serfontein (1996) found that subjects with ADHD had a diffuse decrease in the mean frequency of the alpha and beta bands. Children with ADHD have also been found to have a lower dominant mean frequency than control subjects, which was explained as a delay in functional maturity of the brain since the profiles obtained resembled those of healthy younger children (Matsuura et al., 1993).

While studies of EEG differences between children with ADHD and normal children have found mostly consistent results, the reliability of these results has been questioned (Rey, 1997). This has resulted in strong opposition to the use of QEEG techniques in the diagnosis and treatment of children with ADHD. This study aimed to replicate Study 1, to determine the stability of the results within larger independent samples of children diagnosed with ADHDcom or ADHDin, and a control group. This study also aimed to extend the investigation of electrophysiological differences between the two subtypes of ADHD by examining a wider range of EEG measures, to determine the nature of the underlying neurological differences in this disorder.

6.2 METHOD
6.2.1 Subjects

All subjects in this study were independent of those used in Study 1. Three groups of 40 children, with 32 boys and 8 girls in each group, representing the approximate gender ratio found for the disorder, participated in this study. All children were between the ages of 8 and 12 years and right handed and footed. Subjects had a full-scale WISC-III IQ score of 85 or higher. The groups used were children diagnosed with ADHDcom or ADHDin and a control group. The criteria for subject inclusion in this study were the same as in Study 1.

Across all groups, subjects were matched in one year age bands and by sex.

6.2.2 Procedure

The testing procedure used in this study was the same as Study 1 (section 5.2.3). The EEG was analyzed in four frequency bands: Delta (0.5-2.5 Hz), Theta (2.5-7.5 Hz), Alpha (7.5-13.5 Hz) and Beta (13.5-20.5 Hz), for both absolute and relative power, as well as the total power of the EEG (0.5-20.5 Hz). The mean frequency was calculated for each band and for the total EEG. The mean frequency is the frequency at which half the power lies above and below that frequency for the given band. A series of ratio coefficients were also calculated between the frequency bands by dividing the power of the slower frequency band by the power of the faster frequency band. These were calculated for delta/theta,
theta/alpha, theta/beta, alpha/beta and slow/fast (delta+theta/alpha+beta) frequencies.

6.2.3 Statistical analysis

Analysis of variance was performed examining the effects of region and group for each band in absolute and relative power and the total power, mean frequencies and ratio coefficients. The effects of region were examined using the same planned contrasts as were used in Study 1. Within the Group factor, planned contrasts compared the patient groups with the control group (to establish ADHD differences from normals) and the ADHDcom group with the ADHDin group.

6.3 RESULTS

Eight subjects in the ADHDcom group and one subject in the ADHDin group were found to be statistically significant outliers with beta levels greater than three standard deviations higher than the mean for their group. These subjects were excluded from further analysis and replaced by other subjects to make up the designated numbers for this study.

No significant differences were found between groups for age or between the ADHDin and ADHDcom groups for IQ (see Table 6.1). A significant difference was found between the control group and the combined ADHD groups.
for IQ, with the ADHD groups having a lower mean IQ than the control group
\((F(1,118) = 50.36, p<.001)\).

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<th>ADHDin</th>
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<td>125.0</td>
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<tr>
<td>(WISC-III)</td>
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</table>

### 6.3.1 Topography

Across all groups, total power was greater in the posterior regions
compared to the frontal regions \((F(1,117) = 117.70, p<.001)\), and the central
regions had less power than the mean of the frontal and posterior regions
\((F(1,117) = 83.37, p<.001)\). The right hemisphere had significantly greater power
than the left hemisphere \((F(1,117) = 43.91, p<.01)\), and this was greater in the
posterior regions compared to the frontal regions \((F(1,117) = 12.41, p<.001)\). The
midline had greater power than the two hemispheres \((F(1,117) = 241.95, p<.001)\),
and this was greater in the frontal regions than the posterior regions \((F(1,117) =
7.04, p<.01)\). This midline difference was maximal at the central regions
\((F(1,117) = 242.63, p<.001)\). The difference between the mean of the frontal and
posterior regions and the central regions was greater in the right hemisphere
compared to the left hemisphere \((F(1,117) = 10.34, p<.01)\).
In absolute delta, the posterior regions had greater power than the frontal regions \( (F(1,117) = 41.62, p<.001) \), and the central regions had less power than the mean of the frontal and posterior regions \( (F(1,117) = 27.7, p<.001) \). An effect of laterality was found, with the right hemisphere having greater power than the left hemisphere \( (F(1,117) = 25.38, p<.01) \), and the midline having greater power than the two hemispheres \( (F(1,117) = 424.25, p<.001) \). The difference between the midline and the two hemispheres was greatest at the central regions \( (F(1,117) = 411.79, p<.001) \).

For relative delta, more power was found in the frontal regions compared to the posterior regions \( (F(1,117) = 417.84, p<.001) \), and the central regions had more power than the mean of the frontal and posterior regions \( (F(1,117) = 7.57, p<.01) \). A significant effect of laterality was found with the left hemisphere having more power than the right hemisphere \( (F(1,117) = 5.91, p<.05) \). The midline had less power than the two hemispheres \( (F(1,117) = 49.40, p<.001) \). This midline difference was greater at the frontal regions compared to the posterior regions \( (F(1,117) = 64.16, p<.001) \), and was smallest at the central regions \( (F(1,117) = 65.39, p<.001) \).

In absolute theta, greater power occurred in posterior regions than frontal regions \( (F(1,117) = 28.58, p<.001) \), and the central regions had less power than the mean of the frontal and posterior regions \( (F(1,117) = 6.80, p<.01) \). The right hemisphere had greater theta power than the left hemisphere \( (F(1,117) = 21.68, p<.001) \), and the midline had greater power than the two hemispheres \( (F(1,117) = 192.29, p<.001) \). A significant interaction of sagittal by laterality effect was found with the maximum power occurring at the central midline region \( (F(1,117) = 203.41, p=.001) \).

In the relative theta band, more theta was found in the frontal regions compared to the posterior regions \( (F(1,117) = 106.91, p<.001) \), and the central regions had more theta than the mean of the frontal and posterior regions.
Laterally, the midline had more theta than the two hemispheres ($F(1,117) = 332.10, p<.001$), and this difference was greater at the frontal regions than the posterior regions ($F(1,117) = 181.93, p<.001$). The difference between the midline and the two hemispheres was greater at the central regions than the mean of the frontal and posterior regions ($F(1,117) = 47.93, p<.001$), and the difference between the left and right hemispheres was greater in the posterior regions compared to the frontal regions ($F(1,117) = 8.27, p<.01$).

In absolute alpha, greater power was found in the posterior regions than the frontal regions ($F(1,117) = 161.12, p<.001$), and the central regions had less power than the mean of the frontal and posterior regions ($F(1,117) = 144.90, p<.001$). An effect of laterality was found with greater power occurring at the midline than the two hemispheres ($F(1,117) = 80.99, p<.001$). This difference was greater at the posterior regions than the frontal regions ($F(1,117) = 17.90, p<.001$), and greater at the central regions than the mean of the frontal and posterior regions ($F(1,117) = 8.26, p<.001$). Greater power was found in the right hemisphere compared to the left hemisphere ($F(1,117) = 17.72, p<.01$), and this was greater in the posterior regions compared to the frontal regions ($F(1,117) = 13.81, p<.001$). The difference between the mean of the frontal and posterior regions, and the central regions was greater in the right hemisphere compared to the left hemisphere ($F(1,117) = 11.25, p<.001$).

For relative alpha, more power was found in the posterior regions compared to the frontal regions ($F(1,117) = 657.45, p<.001$), and less at the central regions than the mean of the frontal and posterior regions ($F(1,117) = 239.15, p<.001$). The right hemisphere had more power compared to the left hemisphere ($F(1,117) = 6.07, p<.05$), and this was greater in the posterior regions compared to the frontal regions ($F(1,117) = 12.92, p<.001$). The difference between the two hemispheres and the midline was less at the central regions.
compared to the mean of the frontal and posterior regions \(F(1, 117) = 14.45, p<.001\).

For absolute beta, greater power was found in the posterior region compared to the frontal regions \(F(1, 117) = 69.78, p<.001\), and the central regions had less power than the mean of the frontal and posterior regions \(F(1, 117) = 66.79, p<.001\). Laterally, greater power was found in the right hemisphere compared to the left hemisphere \(F(1, 117) = 37.62, p<.001\), and the greatest power occurred at the midline \(F(1, 117) = 38.28, p<.001\). The difference between the midline and the two hemispheres was greater at the central regions than the mean of the frontal and posterior regions \(F(1, 117) = 6.89, p<.01\).

For relative beta, more power was found in the frontal regions than posterior regions \(F(1, 117) = 219.93, p<.001\), and the central regions had more power than the mean of the frontal and posterior regions \(F(1, 117) = 16.52, p<.01\). Laterally more power was found in the right hemisphere than the left hemisphere \(F(1, 117) = 4.23, p<.05\), and this was greater in the posterior regions compared to the frontal regions \(F(1, 117) = 19.40, p<.001\). The midline had less power than the two hemispheres \(F(1, 117) = 419.60, p<.001\). The difference between the midline and the two hemispheres was greater at the posterior regions compared to the frontal regions \(F(1, 117) = 29.82, p<.001\), and the central regions had greater power than the mean of the frontal and posterior regions \(F(1, 117) = 125.48, p<.001\). In the left hemisphere, the central region had more beta than the mean of the frontal and posterior regions, whereas in the right hemisphere the central region had less beta than the mean of the frontal and posterior regions \(F(1, 117) = 4.72, p<.05\).

In the delta/theta ratio, a greater ratio occurred in the frontal regions compared to the posterior regions \(F(1, 117) = 34.24, p<.001\), and the central regions had a lower ratio than the mean of the frontal and posterior regions \(F(1, 117) = 79.30, p<.001\). The midline had a lower ratio than the two
hemispheres ($F(1,117) = 274.59, p<.001$), and this was greater in the frontal regions compared to the posterior regions ($F(1,117) = 179.75, p<.001$). The difference between the two hemispheres and the midline was less at the central regions than the mean of the frontal and posterior regions ($F(1,117) = 7.33, p<.01$).

In the theta/alpha ratio, a greater ratio occurred in the frontal regions compared to the posterior regions ($F(1,117) = 99.86, p<.001$), and the central regions had a higher ratio than the mean of the frontal and posterior regions ($F(1,117) = 18.78, p<.001$). The midline had a higher ratio than the two hemispheres ($F(1,117) = 43.94, p<.001$). The difference between the two hemispheres and the midline was greater at the frontal regions compared to the posterior regions ($F(1,117) = 17.17, p<.001$), and maximal at the central regions ($F(1,117) = 7.33, p<.01$).

In the theta/beta ratio, a greater ratio occurred in the posterior regions compared to the frontal regions ($F(1,117) = 8.55, p<.01$), and the central regions had a higher ratio than the mean of the frontal and posterior regions ($F(1,117) = 163.22, p<.001$). The midline had a higher ratio than the two hemispheres ($F(1,117) = 274.59, p<.001$). The difference between the two hemispheres and the midline was greater at the central regions than the mean of the frontal and posterior regions ($F(1,117) = 7.33, p<.01$). The difference between the two hemispheres was greater in the posterior regions compared to the frontal regions ($F(1,117) = 209.62, p<.001$).

In the alpha/beta ratio, a greater ratio occurred in the posterior regions compared to the frontal regions ($F(1,117) = 259.81, p<.001$), and the central regions had a lower ratio than the mean of the frontal and posterior regions ($F(1,117) = 141.51, p<.001$). The midline had a higher ratio than the two hemispheres ($F(1,117) = 185.61, p<.001$). The difference between the two hemispheres and the midline was greater at the posterior regions compared to the
frontal regions ($F(1,117) = 18.36, p<.001$), and maximal at the central regions ($F(1,117) = 14.91, p<.001$). The difference between the two hemispheres was greater in the posterior regions compared to the frontal regions ($F(1,117) = 11.29, p<.001$). The difference between the mean of the frontal and posterior regions compared to the central regions was greater in the right hemisphere than the left hemisphere ($F(1,117) = 6.18, p<.05$).

In the slow/fast ratio, a greater ratio occurred in the frontal regions compared to the posterior regions ($F(1,117) = 217.73, p<.001$), and the central regions had a higher ratio than the mean of the frontal and posterior regions ($F(1,117) = 23.86, p<.001$). The midline had a higher ratio than the two hemispheres ($F(1,117) = 62.83, p<.001$). The difference between the two hemispheres and the midline was greater at the frontal regions compared to the posterior regions ($F(1,117) = 27.66, p<.001$), and maximal at the central regions ($F(1,117) = 101.19, p<.01$).

In the total EEG, the mean frequency was greater in the posterior regions compared to the frontal regions ($F(1,117) = 199.08, p<.001$), and the central regions had less power than the mean of the frontal and posterior regions ($F(1,117) = 12.31, p<.001$). The right hemisphere had a significantly higher mean frequency than the left hemisphere ($F(1,117) = 9.21, p<.01$). The midline had a lower mean frequency than the two hemispheres ($F(1,117) = 276.01, p<.001$). This was greater in the frontal regions than the posterior regions ($F(1,117) = 55.99, p<.001$), and maximal at the central regions ($F(1,117) = 71.56, p<.001$).

For the delta band, the central regions had a higher mean frequency than the mean of the frontal and posterior regions ($F(1,117) = 23.92, p<.001$). An effect of laterality was found, with the midline having a higher mean frequency than the two hemispheres ($F(1,117) = 13.20, p<.001$), and this difference was greater at the frontal regions compared to the posterior regions ($F(1,117) = 5.09, p<.05$).
In the theta band, a greater mean frequency was found in the posterior regions compared to the frontal regions \( (F(1,117) = 23.43, p<.001) \), and the central regions had less a lower mean frequency than the mean of the frontal and posterior regions \( (F(1,117) = 110.64, p<.01) \). The right hemisphere had a higher mean frequency than the left hemisphere \( (F(1,117) = 8.42, p<.01) \), and the midline had a higher mean frequency than the two hemispheres \( (F(1,117) = 24.69, p<.001) \).

In the alpha band, the mean frequency was less in the posterior regions than the frontal regions \( (F(1,117) = 8.40, p<.01) \), and the central regions had a higher mean frequency than the mean of the frontal and posterior regions \( (F(1,117) = 12.54, p<.001) \). An effect of laterality was found with a lower mean frequency occurring at the midline than the two hemispheres \( (F(1,117) = 154.58, p<.001) \). This difference was maximal at the central regions \( (F(1,117) = 124.41, p<.001) \).

For the beta band, a larger mean frequency was found in the frontal regions than posterior regions \( (F(1,117) = 327.94, p<.001) \), and greater in the central regions than the mean of the frontal and posterior regions \( (F(1,117) = 7.05, p<.01) \). The midline had a lower mean frequency than the two hemispheres \( (F(1,117) = 227.64, p<.001) \), and this difference was greater at the frontal regions compared to the posterior regions \( (F(1,117) = 382.56, p<.001) \). The difference between the mean of the frontal and posterior regions and the central regions was greater the left hemisphere compared to the right hemisphere \( (F(1,117) = 382.56, p<.001) \).

6.3.2 Replication Study
A summary of the results of the replication of Study 1 are shown in Table 6.2. In the comparison of the combined ADHD groups with the control group, the results for relative power mostly remained stable. No changes in significance were found for the main effects of group or for the contrasts of frontal regions with posterior regions. Control subjects had more relative alpha (F(1,117) = 40.38, p<.001), relative beta (F(1,117) = 19.04, p<.001) and less relative theta (F(1,117) = 81.5,
Figure 6.2 Frequency distribution as a function of scalp region, sagittal section, for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre), Absolute Alpha (bottom left), Absolute Beta (bottom right).

p<.001) than the combined ADHD groups. In the relative delta (F(1,117) = 9.01, p<.01) and alpha bands (F(1,117) = 9.53, p<.01), the difference between groups was again found to be greater at the posterior regions compared to the frontal regions. In the relative beta band, the difference between groups was greater at frontal regions than at posterior regions (F(1,117) = 22.91, p<.01). In the relative beta band, two significant comparisons were found which were not present
in the previous study. The difference between the central regions and the mean of the frontal and posterior regions was greater in the control group than the combined ADHD groups ($F(1,117) = 7.52, p<.01$), with the greatest power occurring at central regions. An effect of laterality was also found, with the left hemisphere having greater power than the right hemisphere, and this difference was greater in the combined ADHD groups than the control group ($F(1,117) = 7.52, p<.01$). Two effects of laterality were replicated for relative alpha ($F(1,117) = 6.78, p<.01$) and relative beta ($F(1,117) = 4.7, p<.05$), with the difference between the two hemispheres and the midline being greater in the control group than the combined ADHD groups. In the relative theta band it was found that the combined ADHD groups had greater power at the frontal midline, compared to the two hemispheres, than did the control group ($F(1,117) = 6.62, p<.05$). This effect was previously found in the absolute theta band, but this failed to reach significance in the present analysis.

In absolute power, the main effect of group for the theta band (Figure 6.1, centre) was replicated, with the combined ADHD groups having greater absolute theta than the control group ($F(1,117) = 10.41, p<.01$). In the present study, two main effects of group strengthened to become significant in the alpha (Figure 6.1, bottom left; $F(1,117) = 7.46, p<.01$) and beta bands (Figure 6.1, bottom right; $F(1,117) = 4.9, p<.05$), with the control group having more power than the combined ADHD groups in both bands. In the absolute alpha band, the anterior-posterior comparisons remained significant, with the difference between the control group and the combined ADHD groups being greater at the posterior regions compared to the frontal regions ($F(1,117) = 8.82, p<.01$), and the
**Table 6.2**

Summary of Significant Comparisons Between Groups and Changes Between the two Studies.

<table>
<thead>
<tr>
<th>Comparison</th>
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<th>Relative Power</th>
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<td>F vs P X L/R vs M</td>
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Note: *p<.05, **p<.01, ***p<.001, _ = previously significant, a = previously approaching significance, vs = versus, F = frontal, P = posterior, C = central, L = left hemisphere, R = right hemisphere, M = midline
difference between the central regions and the mean of the frontal and posterior regions being greater in the control group \((F(1,117) = 9.98, p<.01)\). In the previous study an anterior-posterior difference between the control group and the ADHD groups was found for absolute beta. This was not replicated in the present study. The group differences for laterality were replicated in the absolute delta (Figure 6.2, top right; \(F(1,117) = 4.53, p<.05\)) and theta bands (Figure 6.2 centre; \(F(1,117) = 10.18, p<.01\)) with the ADHD groups having a greater difference between the midline and the two hemispheres, than the control group, for both frequency bands. A difference for total power was found at the frontal midline in the previous study, but failed to reach significance in this study (Figure 6.2; top left).

In the comparison of the ADHDcom group with the ADHDin group, no changes were found in the significance of effects in the relative theta \((F(1,117) = 18.46, p<.001)\), alpha \((F(1,117) = 9.8, p<.01)\) or beta bands \((F(1,117) = 4.16, p<.05)\). The ADHDcom group had more theta and less alpha and beta than the ADHDin group. The anterior-posterior differences for relative delta and beta remained stable in this second analysis. The difference between the ADHDcom group and the ADHDin group for relative delta was greater at posterior regions than frontal regions \((F(1,117) = 5.55, p<.05)\) and for relative beta, the difference was greater at the frontal regions than the posterior regions \((F(1,117) = 5.11, p<.05)\). In the relative alpha band, a sagittal effect was found in the present study, with the difference between the ADHDcom and the ADHDin groups being greater at the posterior regions compared to the frontal regions \((F(1,117) = 5.98, p<.05)\). In the relative theta band, three significant comparisons were found which
were not significant in the previous study. The difference between the mean of the frontal and posterior, compared to the central regions, was greater in the ADHDin group than the ADHDcom group \((F(1,117) = 4.49, p<.05)\). An effect of laterality was also found with the ADHDcom group having more relative theta in the left hemisphere than the right hemisphere whereas the ADHDin had the reverse \((F(1,117) = 4.44, p<.05)\). An interaction which approached significance in the previous study, became significant, with the difference between the left and right hemispheres and the midline being greater at frontal regions than posterior regions in the ADHDcom group compared to the ADHDin group \((F(1,117) = 10.89, p<.001)\). An effect of laterality was also found in this study for relative delta, with the difference between the left and right hemispheres being greater at frontal regions in the ADHDin group and greater in posterior regions in the ADHDcom \((F(1,117) = 4.78, p<.05)\).

For absolute power, three group differences which were not significant previously were found for the theta band. A significant main effect of group was found, with the ADHDcom group having greater theta (Figure 6.1, centre) than the ADHDin group \((F(1,117) = 4.72, p<.05)\). This group difference approached significance in the previous study \((p = .055)\). A sagittal effect was found, with the difference between the mean of the frontal and posterior regions compared to the central regions being greater in the ADHDcom group than the ADHDin group \((F(1,117) = 4.47, p<.05)\). This group difference, which occurs at the frontal regions, represents the only qualitative difference between the two groups of children with ADHD. An effect of laterality was found in absolute theta (Figure 6.2, centre), with the difference between the ADHDcom group and the ADHDin
group being greater in the right hemisphere than the left hemisphere ($F(1,117) = 3.91, p<.05$).

6.3.3 Ratio Analysis

In the delta/theta ratio (Figure 6.3, top left), a significant main effect of group was found, with the control group having a higher ratio than the combined ADHD groups ($F(1,117) = 39.2, p<.001$). For laterality (Figure 6.4, top left), the ratio difference between the midline and the two hemispheres was greater in the control group than the combined ADHD groups ($F(1,117) = 26.07, p<.001$).

The results for the theta/alpha ratio are shown in Figure 6.3 (centre). The combined ADHD groups had a greater ratio than the control group ($F(1,117) = 23.63, p<.001$) and the ADHDin group had a greater ratio than the ADHDcom group ($F(1,117) = 15.98, p<.001$). Anterior-posterior differences were found, with the difference between the control group and the combined ADHD groups ($F(1,117) = 8.6, p<.01$), and between the ADHDin group and the ADHDcom group ($F(1,117) = 6.68, p<.05$), being greater at frontal regions than posterior regions. The difference between the midline and the two hemispheres (Figure 6.4, centre) was greater in the combined ADHD group than the control group ($F(1,117) = 9.76, p<.01$). This lateral difference was larger at frontal regions than posterior regions for the combined ADHD groups compared with the control group ($F(1,117) = 10.93, p<.001$), and for the ADHDcom group compared with the ADHDin group ($F(1,117) = 12.23, p<.001$).
Figure 6.3 Ratio coefficient distributions as a function of scalp distribution, Delta/Theta (top left), Theta/Alpha (centre), Theta/Beta (top right), Alpha/Beta (bottom left), Slow/Fast (bottom right).

The combined ADHD groups had a greater theta/beta ratio (Figure 6.3, top right) than the control group (F(1,117) = 19.8, p<.001) and the ADHDcom group had a greater ratio than the ADHDin group (F(1,117) = 11.97, p<.001). Group differences were found for laterality (Figure 6.4, top right), with the difference between the midline and the two hemispheres being greater in the combined ADHD groups than in the control group (F(1,117) = 14.33, p<.001).
Figure 6.4 Ratio coefficient distributions as a function of scalp distribution, sagittal section, Delta/Theta (top left), Theta/Alpha (centre), Theta/Beta (top right), Alpha/Beta (bottom left), Slow/Fast (bottom right).

This difference between groups was greater at frontal regions than posterior regions ($F(1,117) = 5.56$, $p<.05$) and greatest at the central regions ($F(1,117) = 7.51$, $p<.01$). A similar difference between the midline and the two hemispheres was larger in the ADHDcom group than the ADHDin group ($F(1,117) = 7.54$, $p<.01$). This was also greater at frontal regions than posterior
regions ($F(1,117) = 8.12, p<.01$) and greatest at the central regions ($F(1,117) = 3.94, p<.05$).

Results for the alpha/beta ratio are shown in Figure 6.3 (bottom left). The difference between the central regions and the mean of the frontal and posterior regions was greater in the control group than the combined ADHD groups ($F(1,117) = 3.96, p<.05$).

Regional differences are shown for the slow/fast ratio in Figure 6.3 (bottom right). The combined ADHD groups had a higher ratio than the control group ($F(1,117) = 25.89, p<.001$) and the ADHDcom group had a greater ratio than the ADHDin group ($F(1,117) = 16.05, p<.001$). A sagittal difference between the combined ADHD groups and the control group ($F(1,117) = 9.45, p<.01$), and the ADHDcom group and the ADHDin ($F(1,117) = 23.86, p<.001$) was found, with the ratio greater at the frontal regions than the posterior regions. Laterality differences were found (Figure 6.4, bottom right), with the difference between the midline and the two hemispheres being greater in the combined ADHD groups than in the control group ($F(1,117) = 10.46, p<.01$). For the combined ADHD groups versus the control group ($F(1,117) = 9.29, p<.01$), and the two ADHD groups ($F(1,117) = 6.23, p<.05$), the difference between the midline and the two hemispheres was greater at the frontal regions than at the posterior regions. In each of these frontal midline differences, the midline had greater power than the two hemispheres. This difference was greatest in the ADHDcom group and became more equipotential in the ADHDin and the control group.
Figure 6.5 Mean frequency distributions as a function of scalp distribution, Total EEG (top left), Delta (centre), Theta (top right), Alpha (bottom left), Beta (bottom right).

**6.3.4 Frequency analysis**

Figure 6.5 (top left) shows the results for the mean frequency of the EEG. The combined ADHD groups had significantly lower mean frequency than the control group (F(1,117) = 39.52, p<.001) and the ADHDin group had significantly lower mean frequency than the ADHDcom group (F(1,117) = 9.26,
Figure 6.6 Mean frequency distributions as a function of scalp distribution for the sagittal section, Total EEG (top left), Delta (centre), Theta (top right), Alpha (bottom left), Beta (bottom right).

p<.01). A significant interaction was found (Figure 6.6, top left), with the difference between the left and right hemispheres being greater in posterior regions than frontal regions for the ADHDin group compared to the ADHDcom group (F(1,117) = 4.00, p<.05).

In the delta band (Figure 6.5, central) the combined ADHD groups had a higher mean frequency than the control group (F(1,117) = 6.68, p<.05). The
ADHDcom group had a higher mean frequency than the ADHDin group, which approached significance (F(1,117) = 3.76, p = .055).

The results for the mean frequency in the theta band are shown in Figures 6.5 and 6.6 (top right). The difference between the midline and the two hemispheres was greater at frontal regions than posterior regions in the control group, compared with the combined ADHD groups (F(1,117) = 4.54, p<.05).

In the alpha band (Figure 6.5, bottom left), the control group had a higher mean frequency than the combined ADHD groups (F(1,117) = 4.59, p<.05). The difference between the control group and the combined ADHD groups was greater in the left hemisphere than the right hemisphere (Figure 6.6, bottom left; F(1,117) = 5.8, p<.05).

The results for the mean frequency in the beta band are shown in Figure 6.5 (bottom right). The control group had a significantly higher mean frequency than the combined ADHD groups (F(1,117) = 7.92, p<.01). A group difference for laterality was found (Figure 6.6, bottom right), with relatively higher mean frequency occurring in the right hemisphere than the left hemisphere (F(1,117) = 6.34, p<.05), in the control group compared with the combined ADHD groups.

6.3.5 IQ Analysis

Due to the significant IQ difference between the control group and the two ADHD groups, two different analysis were performed to investigate the effect of IQ on the EEG results. In the first analysis the control group was split into two groups which were designated as low IQ and high IQ. The low IQ group
comprised children with IQ below the mean (110.7) and the high IQ group were children with IQ greater than the mean. These groups did not differ on age but had a significant mean difference of 19 IQ points \( F(1,38) = 32.62, p<.001 \). The EEGs of the two groups were compared using the same planned contrasts as for the other group comparisons. There were no significant differences between the low and high IQ groups for absolute or relative power in any of the bands. In the second analysis, the data for absolute and relative power described above were reanalyzed using IQ as a covariate. No changes in significance levels were found for any main effect or interaction.

6.4 DISCUSSION

A significant difference was found between the ADHD groups and the control group for IQ. Previous studies of the effect of IQ differences on EEG have found small correlations between increased IQ and EEG measures indicative of increased maturation (Gasser, Mocks et al., 1983). Chabot and Serfontein (1996) compared the EEGs of normal and lower intelligence children with ADHD. They concluded from their results that the greatest group variance was related to the diagnosis and not intelligence. The present analyses of IQ failed to find any significant EEG differences due to IQ.

Children with ADHD have been found to have more slow wave activity than normal children (Capute et al., 1968; Satterfield, Cantwell, Saul, Lesser et al., 1973; Satterfield & Cantwell, 1974; Matousek et al., 1984; Lubar, 1991; Mann et al., 1992). Chabot and Serfontein (1996) found children with ADD had
an increase in absolute and relative theta, with the greatest increase being in the frontal region and at the midline. These results were highly consistent with the findings of Mann et al. (1992), who reported an increase in absolute theta amplitude at frontal sites and a decrease in beta in the posterior region. Study 1 found ADHD subjects had increased levels of theta wave activity, especially in the frontal region, a decrease in posterior beta, and a decrease in relative alpha. Differences in the EEG were also found between the ADHDcom group and the ADHDin group in the theta, alpha and beta bands. In the present study, the ADHD groups had greater absolute and relative theta and less absolute and relative alpha and beta, compared to the control subjects. Significant topographic differences were found, with the differences between the ADHD and control groups being greater in the posterior region for relative delta and for both absolute and relative alpha.

As part of the present study, a replication of Study 1 was undertaken to determine the reliability of the significant group differences in a larger independent sample. The present results showed a high level of replication of the previous results for relative power. All relative power results that were significant in the previous study were significant in this study, both for the comparison of the two ADHD groups with the control group and for differences between the two ADHD groups. The group differences in the theta, alpha and beta bands, as well as posterior differences in the delta band, have been shown to be reliable measures of differences between the three groups.

The results were less stable in the absolute power measures. In absolute theta, the difference between the ADHD groups and the control group was
replicated. However, in the alpha and beta bands, a strengthening of the effect of group was found, with results that were approaching significance in the previous study, reaching statistical significance here. Differences in midline delta and theta remained stable over the two studies. However, the frontal midline theta and posterior beta differences failed to reach significance in the present study. Previous studies have found high levels of variability within subject groups and poor test-retest reliability for absolute compared with relative power (John et al., 1980). A number of differences were found between the two ADHD groups, which were not present in Study 1: for relative alpha in the posterior, and relative beta in the frontal region. Levels of frontal and posterior beta and alpha appear to differ between all three groups. In the previous study, small differences between the two ADHD groups were evident, with the difference between the combined ADHD groups and the control group being greater than the difference between the two ADHD groups. It is possible that these differences found in the present study represent subtle group differences between the two groups of children with ADHD, which may not have been detected in the previous study because of insufficient statistical power due to the sample size used (Baer & Ahern, 1989).

In this study, ratio coefficients between frequency bands and the mean frequency of each band were calculated in an attempt to further quantify the nature of the underlying electrophysiological differences between the two clinical groups. Previous studies have demonstrated that certain ratio coefficients between frequency bands can be used to differentiate normal children from children with ADHD (Jansen, 1995). Lubar (1991) found that the theta/beta ratio was effective in differentiating children with and without ADHD, across all sites. In the present
study, group differences were found for the theta/alpha and theta/beta ratios between normal children and children with ADHD, and also between the two ADHD groups, across all regions. The theta/alpha ratio was the only ratio to demonstrate a sagittal effect. This was able to differentiate between all three groups in the frontal region. The theta/beta ratio proved to be the most effective coefficient for differentiating midline differences between the three groups. Significant differences were found for the comparison of the midline and the two hemispheres, as well as regional differences at the frontal and central regions.

Children with ADHD have been reported to have a decreased mean frequency in the alpha and beta bands (Chabot & Serfontein, 1996). This was confirmed in the present study, with the combined ADHD groups having lower mean frequencies for these bands. In the delta band, the reverse was found, with the ADHD groups having a higher mean frequency than the control group. This would suggest a shift in the EEG towards the theta band in the ADHD groups, with the mean frequency increasing in the lower bands and decreasing in the higher bands.

Results of Study 1 suggested that the EEG differences between the patient groups was one of degree rather than providing neurological evidence of the subtypes being independent disorders. In each measure, the ADHDin group was positioned between the control group and the ADHDcom group. This was also proposed by Chabot and Serfontein (1996). Although such findings are necessary for the categorisation of a disorder as dimensional rather than categorical, it is not sufficient in itself to make such an assertion (Grayson, 1987).
Opposed to a continuum model are behavioural studies that have shown that differences other than hyperactivity exist between children with ADD/H and ADD/WO (Barkley et al., 1990; Cantwell & Baker, 1992), leading some researchers to suggest that these two subtypes may be independent disorders (Lahey et al., 1985). Neuropsychological studies of children with ADHD have also found deficits which suggest that the frontal cortex or regions projecting to the frontal cortex are dysfunctional in at least some ADHD children (Faraone & Biederman, 1998). In hyperactive children, these appear to be frontal lobe mediated, self-regulation deficits, such as in inhibition control (Rubia, Oosterlaan, Sergeant, Brandeis & Leeuwen, 1998). Neuropsychological studies of subtypes of ADHD in adults have found deficits in the area of executive control type functioning, which could be linked to dysregulation of frontal lobe systems (Gansler, Fucetola, Kengel, Stetson, Zimering & Makary, 1998). Different types of executive system deficits were found between the hyperactive/impulsive and inattentive subtypes of the disorder. This has led some researchers to postulate that the attentional differences between the subtypes may reflect dysfunctions in different neuroanatomical loci and different neurotransmitter systems (Barkley, 1990).

In this study, seven main effects of group were found that differentiated between the ADHDin and ADHDcom groups. In each of these, the ADHDin group was positioned between the ADHDcom group and the control group. However, in absolute and relative theta, and the theta/alpha ratio, group differences were found in the frontal regions that were indicative of a qualitative difference between the two ADHD groups. In these measures, the activity in the
frontal regions increased from the central to frontal regions in the ADHDcom group, but decreased in the ADHDin group. Theta activity has been identified as an electrophysiological marker of cerebral dysfunction in a number of childhood disorders. Mentally retarded (Gasser, Mocks et al., 1983), learning disabled (Lubar et al., 1985), and hyperactive children (Capute et al., 1968; Wikler et al., 1970) have all been found to have excess theta. Theta activity has also been found to be an indicator of both a maturational delay (Mann et al., 1992) and an abnormality in CNS functioning (Chabot & Serfontein, 1996). In this study, it is possible that the elevated frontal activity in the ADHDcom group (which is primarily associated with the theta band) is associated with this group having frontal lobe dysfunction, whereas children with ADHDin may have other forms of CNS dysfunction which are not primarily associated with frontal lobe functioning, or are associated with different types of frontal lobe dysfunction.

If the frontal theta excess and theta/alpha ratio are primarily associated with hyperactive/impulsive behaviour, then it is possible that the other differences may result from factors associated with inattention. In this study, such differences between the two subtypes may have resulted from two different reasons. The first is that the ADHDcom group were more inattentive than the ADHDin group and the EEG results simply reflect greater inattention. But both clinical groups met the criteria for the inattentive subtype diagnosis and thus it is unlikely that differences in inattention levels resulted in the group differences. The alternative is that there may be two different types of inattention involved, resulting in the different EEG abnormalities. Results of a number of studies have suggested that the inattention in the inattentive subtype may be a different form of impairment to
that found in the combined subtype (Barkley et al., 1990; Goodyear & Hynd, 1992; Lahey & Carlson, 1992). Research on the inattentive subtype has found that these children show symptoms of daydreaming, are easily confused, stare frequently, are lethargic, hypoactive and passive (Barkley et al., 1990; Lahey & Carlson, 1992), have deficits in speed of information processing, and in focused or selective attention (Goodyear & Hynd, 1992; Lahey & Carlson, 1992). The deficits in the combined subtype of ADHD are more a problem of sustained attention and persistence, and of ease of distraction (Barkley, 1997). That is, it appears that the inattentive symptoms found in these two subtypes are different.

From our results, it is possible that the subtypes of ADHD involve relative differences in two independent neurophysiological disorders which commonly occur together. Further research is needed in children with comorbid factors, such as behavioural problems and learning disabilities, to explore this possibility.

Within the literature, two main models of ADHD have been proposed. The first proposes that ADHD is a deviation from normal development of the CNS (Chabot & Serfontein, 1996) while the second proposes that ADHD is a maturational lag of the CNS (Mann et al., 1992). To try to evaluate the nature of the differences found in ADHD children, we examined the mean frequency in each band as well as a number of ratio coefficients calculated between frequency bands. In the analyses of absolute and relative power, there was more theta and less alpha and beta in the ADHD groups. The results for the theta/alpha and theta/beta ratios show greater levels of slow wave activity in the two clinical groups. A similar result was found for the mean frequency of the alpha and beta bands, with the ADHD groups having a lower mean frequency than controls. In
the lower frequency bands, clinical subjects had higher mean frequencies in the
delta band and higher ratio coefficients for the delta/theta ratio, which are not
consistent with the maturational lag model. From these results it would appear
that ADHD is associated with a deviation from normal development in CNS
functioning. This would better account for the existence of ADHD in adults,
which is conceptually difficult for a maturational lag model.

One problem with most of the studies that have proposed a model of
ADHD based on EEG measures is that they have used measures from children at
one point in time and then interpreted their results in terms of the developmental
literature for normal children. Few studies have investigated changes with age in
an ADHD population. Bresnahan et al. (1999) investigated differences in the
EEG of ADHD subjects who were divided into three age groups, children,
adolescents and adults. The results indicated that theta activity remained elevated
in adults, but there was a decrease in beta activity with age. An age analysis of
this type, using smaller increments between age groups, may help to clarify the
nature of the underlying EEG abnormalities found in this population.

Nine subjects were replaced in this study due to atypical excess beta
activity, with eight having a diagnosis of ADHDcom. A similar percentage of
subjects with excess beta was found in Study 1, and Chabot and Serfontein
(1996) also noted the existence of such a group. No subjects were previously
diagnosed with ADHD or had a prior history of stimulant or other psychoactive
medication use. It is possible that these children constitute a separate neurological
subtype of the disorder. Further research is needed to determine the percentage of
children with this neurological profile and to investigate whether any factors exist which differentiate them from other children with a diagnosis of ADHD.
CHAPTER 7. STUDY 3. AGE AND SEX EFFECTS IN THE EEG:

DEVELOPMENT OF THE NORMAL CHILD3

3This Study is under review for publication as: Clarke, A., Barry, R., McCarthy, R. & Selikowitz, M. EEG Differences in two Subtypes of Attention-Deficit/Hyperactivity Disorder.
7.1 INTRODUCTION

EEG studies of the maturational changes of normal children have primarily found that slow wave activity decreased with increasing age, and faster waveforms increase. Matousek and Petersen (1973) found that delta activity decreased almost linearly with age. Theta and Alpha 1 activity initially increased and then proceeded to decrease. Alpha 2 activity increased throughout childhood, and beta activity decreased slightly with age. John et al. (1980) developed 32 linear regression equations which predicted the frequency composition of the EEG as a function of age. Matthis et al. (1980) found, with normal maturation, that EEG frequencies increase as a function of age, with slow wave activity apparently being replaced by faster waveforms. Benninger et al. (1984) found that theta activity decreased as alpha increased, and that the speed of change in occipital areas was almost twice that of central areas. Variances within the EEGs were also found to be two to three times more reflective of interindividual characteristics than age differences.

Gasser, Verleger et al. (1988) found that delta, theta and alpha waves were developed earliest occipitally followed by parietal, central and frontal regions. Beta waves developed earliest in central regions, followed by parietal, occipital and then frontal regions. In the central area, the midline was found to have more low frequency power than the two hemispheres, whereas high frequency power was found more evenly distributed between the three regions. Although maturational changes in the two hemispheres have been documented (Gasser,
Jennen-Steinmetz et al., 1988), no studies have investigated the relationship between changes at the midline and the two hemispheres.

A number of studies have also used the calculation of ratio coefficients between frequency bands as measures of changes in the EEG with age. Matousek and Petersen (1973) found the theta/alpha ratio to be a good indicator of age-related changes in the EEG. Matthis et al. (1980) found theta/alpha ratios correlated best with increasing age. The theta/beta ratio has also been proposed as a measure that could be relatively free of factors which would affect single waveform band results and could be used to quantify age-related changes, as well as deviations from normal development in a number of clinical groups (Lubar, 1991).

Reports of sex differences in the normal maturation of the EEG have been mixed. Petersen et al. (1971) found girls had higher alpha frequencies until the age of 11 years. Matousek and Petersen (1973) found adolescent females had more beta activity than males. These are suggestive of earlier maturation in girls. However, Cohn et al. (1985) and Gasser, Jennen-Steinmetz et al. (1988) failed to find EEG differences between males and females, or the existence of a pubertal spurt. In contrast to this, Matthis et al. (1980) found that at age six, girls have more relative theta and less relative alpha. By age eleven, girls have surpassed males for relative slow alpha in occipital areas, but still have less alpha in frontal regions. Benninger et al. (1984) confirmed the results of Matthis et al. (1980), with girls up to six years old having greater levels of theta than boys and boys having greater alpha levels until ten years old. However, the rate of change in girls was greater, and a pubertal spurt was found from about 11 to 13 years old,
which resulted in girls catching up with boys by adolescence. Similar results have also been found with gender differences in absolute and relative alpha and for rates of change with age (Diaz De Leon et al., 1988). Harmony et al. (1990) found boys had more alpha and less delta, theta and beta than girls. This difference was greater at age six than at age 12. All of these studies used an eyes-closed resting EEG and the majority found that girls have a maturational lag in the EEG compared to boys. This lag appears to disappear about the time of adolescence, with changes occurring faster in girls.

The aim of this study was to investigate maturational changes and the effect of age and sex in the EEG of normal children, and to provide normal developmental profiles as part of this thesis, for the study of children with Attention-Deficit/Hyperactivity Disorder. A second aim of this study was to investigate the relationship between maturational changes at the midline, relative to the two hemispheres.

7.2 METHOD

7.2.1 Subjects

Eighty right-handed and right-footed children participated in this study, with 40 boys and 40 girls between the ages of 8 and 12 years. Subjects in each sex group were age matched within one year bands, with 8 subjects in each of the five bands. Subjects came from local schools and community groups and were assessed for the purpose of being a normal control group for Study 4. Inclusion
criteria in this study was the same as for the control group in Study 1.

7.2.2 Procedure

The procedure used in Study 1 (section 5.2.3) was used in this Study. The EEG was analysed in four frequency bands: Delta (0.5-2.5 Hz), Theta (2.5-7.5 Hz), Alpha (7.5-13.5 Hz) and Beta (13.5-20.5 Hz). Ratio coefficients were also calculated for the theta/alpha and theta/beta ratios by dividing the power of the slower frequency band by the power of the faster frequency band.

7.2.3 Statistical analysis

Analyses of variance were performed, examining the effects of region, sex and age for each band in absolute and relative power, for the total power, and for the theta/alpha and theta/beta ratios. The effects of region were examined using the same planned contrasts as were used in Study 1. Within the sex factor, differences in the EEGs of the male and female groups were compared, and within the age factor, the linear trend and quadratic trend were examined.
7.3 RESULTS

7.3.1 Topography

With total power (Figure 7.1, top left), greater power was found in the posterior regions than the frontal regions ($F(1,70) = 138.88$, $p<.001$). The mean of frontal and posterior power was greater than the level of power in the central regions ($F(1,70) = 109.66$, $p<.001$), and this difference was greater in the right hemisphere than the left hemisphere ($F(1,70) = 4.65$, $p<.05$), indicating a posterior maximum for total power. Greater power occurred in the right hemisphere than the left ($F(1,70) = 11.48$, $p<.001$) and the greatest power occurred at the midline ($F(1,70) = 177.65$, $p<.001$). The difference between the midline and the two hemispheres was greater at the posterior regions than the frontal regions ($F(1,70) = 7.35$, $p<.01$) and greatest at the central regions ($F(1,70) = 208.15$, $p<.001$).

In the delta band (Figure 7.1, top right), absolute power was greater in the posterior regions than the frontal regions ($F(1,70) = 51.97$, $p<.001$) and the central regions had less power than the mean of the frontal and posterior regions ($F(1,70) = 29.85$, $p<.001$). Laterally, greater power was found in the right hemisphere than the left ($F(1,70) = 7.23$, $p<.01$) and the midline had greater power than the two hemispheres ($F(1,70) = 399.68$, $p<.001$). This difference between the midline and the two hemispheres was greatest at the central regions than the mean of the frontal and posterior regions ($F(1,70) = 291.24$, $p<.001$). In relative delta (Figure 7.2, top left), more power was found in ($F(1,70) = 618.46$, $p<.001$).
Figure 7.1 Absolute power and ratio coefficients as a function of scalp region for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre left), Absolute Alpha (centre), Beta (centre right), Theta/Alpha (bottom left), Theta/Beta (bottom right).

Laterally, the midline had less relative delta overall than the two hemispheres ($F(1,70) = 40.97, p<.001$), with the reduction being greater at the frontal regions than at the posterior regions ($F(1,70) = 60.66, p<.001$), and less at the central regions than the mean reduction in the frontal and posterior regions ($F(1,70) = 58.00, p<.001$).
Figure 7.2 Relative power as a function of scalp region for Relative Delta (top left), Relative Theta (top right), Relative Alpha (bottom left), Relative Beta (bottom right).

For absolute theta (Figure 7.1, centre left), posterior regions had greater power than frontal regions ($F(1,70) = 57.8$, $p<.001$). Significantly more power was found in the right hemisphere than the left hemisphere ($F(1,70) = 11.09$, $p<.001$). Greater power was found at the midline, compared to the two hemispheres ($F(1,70) = 221.92$, $p<.001$), with the greatest difference occurring at the central regions. A greater difference between the central regions and the mean of the frontal and posterior regions occurred in the right hemisphere compared to the left hemisphere ($F(1,70) = 6.73$, $p<.05$). Relative power estimates (Figure 7.2, top right) indicated more activity in the frontal regions than the posterior regions.
(F(1,70) = 143.99, p<.001) and in the central regions compared with the mean of the frontal and posterior regions (F(1,70) = 232.47, p<.001). Laterality effects were found, with the midline having more power than the two hemispheres (F(1,70) = 305.86, p<.001). The difference between the midline and the two hemispheres was greater at the frontal than the posterior regions (F(1,70) = 90.37, p<.001) and greatest at the central regions (F(1,70) = 69.13, p<.001).

In the absolute alpha band (Figure 7.1, centre), greater power occurred in the posterior regions than the frontal regions (F(1,70) = 163.72, p<.001), and the central regions had less power compared to the mean of the frontal and posterior regions (F(1,70) = 139.66, p<.001). This indicated that alpha power showed a strong posterior maximum. Greater power was found in the right hemisphere than the left hemisphere (F(1,70) = 5.68, p<.05), with this difference being greater at the posterior regions than the frontal regions (F(1,70) = 4.51, p<.05). A significant increase in power was found at the midline compared to the two hemispheres (F(1,70) = 60.29, p<.001), with the difference being greater in the posterior regions than the frontal regions (F(1,70) = 9.88, p<.05) and greatest at the central regions (F(1,70) = 7.69, p<.01). For relative power (Figure 7.2, bottom left), posterior regions had more activity than frontal regions (F(1,70) = 820.8, p<.001) and the central regions had less activity than the mean of the frontal and posterior regions (F(1,70) = 173.87, p<.001). Laterally, the midline had more power than the two hemispheres (F(1,70) = 4.71, p<.05) except at the central regions, where the midline had less power (F(1,70) = 17.07, p<.001). Regional hemispheric differences were found, with the left hemisphere having more relative power than the right hemisphere in the frontal regions, and the reverse
occurring in the posterior regions (F(1,70) = 8.31, p<.01).

Greater absolute power for the beta band was found in the posterior regions compared to the frontal regions (F(1,70) = 71.03, p<.001) and the central regions had less power than the mean of the frontal and posterior regions (F(1,70) = 49.29, p<.001) (Figure 7.1, centre right). Laterally, the right hemisphere had greater power than the left hemisphere (F(1,70) = 21.48, p<.001), with a greater difference occurring in the frontal regions than the posterior regions (F(1,70) = 4.17, p<.05). The midline had greater power than the two hemispheres (F(1,70) = 27.75, p<.001) and this difference was greater at the frontal regions than the posterior regions (F(1,70) = 4.76, p<.05). For relative power (Figure 7.2, bottom right), the frontal regions showed greater activity than the posterior regions (F(1,70) = 260.33, p<.001) and the central regions had greater activity than the mean of the frontal and posterior regions (F(1,70) = 11.29, p<.001), indicating a non-linear change from the frontal to the posterior regions. Laterally, more power was found in the right hemisphere than the left (F(1,70) = 5.66, p<.05) and the midline had less power than the two hemispheres (F(1,70) = 321.87, p<.001). The difference between the midline and the two hemispheres was greater at frontal regions than posterior regions (F(1,70) = 8.47, p<.01) and greatest at the central regions (F(1,70) = 96.28, p<.001). Regional hemispheric differences were found, with the left hemisphere having less power than the right hemisphere at the frontal regions, and the reverse occurring at the posterior regions (F(1,70) = 12.97, p<.001).

For the theta/alpha ratio (see Figure 7.1, bottom left) greater coefficients were found for the frontal regions compared to the posterior regions (F(1,70) =
492.39, p<.001) and the central regions had higher coefficients than the mean of the frontal and posterior regions (F(1,70) = 75.93, p<.001). Laterally, the midline had greater coefficients than the two hemispheres (F(1,70) = 50.2, p<.001). This difference was greater at the frontal regions than the posterior regions (F(1,70) = 22.22, p<.001) and maximal at the central regions (F(1,70) = 36.61, p<.001). The theta/beta ratio (Figure 7.1, bottom right) was larger in the posterior regions than the frontal regions (F(1,70) = 43.4, p<.001) and in the central regions compared with the mean of the frontal and posterior regions (F(1,70) = 60.41, p<.001). At the midline, the ratio was greater than in the two hemispheres (F(1,70) = 344.22, p<.001) and this difference was maximal at the central regions (F(1,70) = 184.13, p<.05).

7.3.2 Age Related Changes

No significant results were found for total power (Figure 7.3, top left).

In absolute delta (Figure 7.3, top right), a linear decrease in power was found with increasing age (F(1,70) = 8.35, p<.01). This decrease occurred most rapidly at the midline, with the difference in power between the midline and the two hemispheres becoming less with age (F(1,70) = 4.77, p<.05). In relative power (Figure 7.4, top left), the amount of delta activity decreased linearly with age (F(1,70) = 6.2, p<.05). In the posterior regions, the amount of delta decreased faster in the younger subjects and the decrease slowed with age, whereas in the frontal regions, the rate of change was more constant (F(1,70) = 4.21, p<.05).
No significant results were found for absolute theta (Figure 7.3, centre left). In relative theta (Figure 7.4, top right), power was found to decrease linearly with age ($F(1,70) = 13.44, p<.001$). This decrease was faster in the posterior regions than the frontal regions ($F(1,70) = 7.82, p<.01$).

In the absolute alpha band (Figure 7.3, centre), the central sites had less power than the mean of the frontal and posterior sites, with the difference becoming greater with age ($F(1,70) = 4.05, p<.05$). This indicated that power
increased with age at a greater rate in the posterior regions than in the frontal regions. In relative power (Figure 7.4, bottom left), alpha activity was found to increase with age ($F(1,70) = 6.51, p<0.05$), with the increase occurring faster in the posterior regions compared to the frontal regions ($F(1,70) = 5.88, p<0.05$).

In the absolute beta band (Figure 7.3, centre right), the difference between the midline and the two hemispheres became greater with age ($F(1,70) = 4.96, p<0.05$). In relative power (Figure 7.4, bottom right), beta activity was found to increase with age ($F(1,70) = 8.74, p<0.05$).

In the theta/alpha ratio (Figure 7.3, bottom left), coefficients became smaller with age ($F(1,70) = 4.17, p<0.05$) indicating a linear shift from slow to fast
wave activity with age. Age related changes were found for the theta/beta ratio (Figure 7.3, bottom right), with the coefficient becoming smaller with age (F(1,70) = 21.5, p<.001), and this occurred faster in the posterior regions than the frontal regions (F(1,70) = 13.12, p<.001). This again indicated a linear shift from slow to fast wave activity. An effect of laterality was found, with the midline and the two hemispheres becoming more equipotential with age (F(1,70) = 10.85, p<.01), with the greatest age-related change occurring at the central regions (F(1,70) = 4.95, p<.05).

7.3.3 Sex Differences

No significant differences were found for total power (Figure 7.5, top left) or absolute delta (Figure 7.5, top right). The difference between the amount of relative delta (Figure 7.6, top left) activity in the frontal regions compared to the posterior regions was greater in males than females (F(1,70) = 6.19, p<.05). Regional hemispheric differences were found between the sexes (F(1,70) = 6.25, p<.05), with males having more relative power in the left frontal region than the right frontal region and more power in the right posterior region compared to the left posterior region. This pattern was laterally reversed in females. In the theta band, males had less absolute power (Figure 7.5, centre left; F(1,70) = 4.44, p<.05) and less relative power (Figure 7.6, top right; F(1,70) = 26.11, p<.001) than females. For relative power, this difference was significantly greater in the posterior regions than the frontal regions (F(1,70) = 9.61, p<.001). In the absolute alpha band (Figure 7.5, centre), males had more posterior alpha than females.
Figure 7.5 Sex differences in power and ratio coefficients as a function of scalp region for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre left), Absolute Alpha (centre), Beta (centre right), Theta/Alpha (bottom left), Theta/Beta (bottom right).

(F(1,70) = 3.97, p<.05). For relative power (Figure 7.6, bottom left), a significant main effect of gender was found, with males having more relative alpha activity than females (F(1,70) = 10.62, p<.01). This difference was greater in the posterior regions than the frontal regions (F(1,70) = 15.53, p<.001). In the theta/alpha ratio (Figure 7.5, bottom left), coefficients were higher in males than females (F(1,70) = 4.17, p<.05).

No significant sex differences were found for absolute or relative beta
Figure 7.6 Sex differences in relative power as a function of scalp region for Relative Delta (top left), Relative Theta (top right), Relative Alpha (bottom left), Relative Beta (bottom right).

(Figure 7.5, centre right; Figure 7.6, bottom right) or the theta/beta ratio (Figure 7.5, bottom right).

7.3.4 Sex by Age Interactions

Total power (Figure 7.7, top left) was found to increase with age in males but to decrease in females ($F(1,70) = 8.89, p<.05$). This change in power among females was not linear, with the power level remaining stable until the age of ten years and then dropping, whereas in males the increase was more linear ($F(1,70) = 5.00, p<.05$). The greater change in power occurred in posterior regions compared to frontal regions, and this was greater in males than females ($F(1,70) =$
Figure 7.7 Group changes in absolute power and ratio coefficients with age, for Frontal regions (Left Column), Central Regions (Central Column) and Posterior regions (Right Column).
6.13, p<.05). In the absolute delta band (Figure 7.7, top right), mean power across sites was found to decrease faster in females than males (F(1,70) = 6.18, p<.05). No significant results were found for relative delta (Figure 7.8, top left). Absolute theta power (Figure 7.7, top centre left) across sites was found to decrease in females but was mostly stable in males (F(1,70) = 4.44, p<.05). No significant results were found for relative theta (Figure 7.8, top right). In absolute alpha (Figure 7.7, centre), power decreased with age in females but increased in males (F(1,70) = 8.34, p<.01). This change was mostly linear for males, but in females, the alpha levels remained constant until the age of 10 years and then decreased (F(1,70) = 7.58, p<.01). For the comparison of frontal and posterior regions, greater change in power occurred in the posterior regions compared to the frontal regions, with the effect being larger for males than females (F(1,70) = 6.75, p<.05). No significant results were found for relative alpha (Figure 7.8, bottom left). No significant age by sex interactions were found for absolute or relative beta (Figure 7.7, centre right; Figure 7.8, bottom right). Theta/alpha ratio (Figure 7.7, bottom left) changes with age occurred faster in the frontal regions compared to posterior regions and this was greater in males than females (F(1,70) = 4.41, p<.05). No interactions occurred for the theta/beta ratio (Figure 7.7, bottom right).

7.4 DISCUSSION

A number of approaches have been used to assess changes in the EEG of children with normal development. This has included the analysis of waveform amplitude (Matousek et al., 1973), absolute and relative power (John et al., 1980;
Gasser, Verleger et al., 1988; Gasser, Jennen-Steinmetz et al., 1988), dominant and subordinate frequency analysis (Katada et al., 1981; Katada et al., 1990), the wave percentage time (Matsuura, et al., 1985) and ratio coefficient analysis between waveforms (Matousek et al., 1973; Mattis et al., 1980). All of these studies found that as a child becomes older, activity in the lower frequency bands decreases and faster waveform activity increases.

The present study primarily investigated changes in absolute and relative power, which have been found to be reliable EEG measures and are easily interpreted (Mattis et al., 1981). Factors of changes in bone thickness, skull resistance and impedance in young children have been given as reasons for not using absolute power in maturational research in children (Benninger et al., 1984). However, if absolute power was substantially affected by factors such as changes in cranial structure, age effects would be expected for total power, and this did not occur.

In absolute power, the delta band was the only band where a significant main effect of age was found. Absolute delta activity decreased with age. In the relative power bands, a decrease was found for the delta and theta bands and an increase in the alpha and beta bands with increasing age. These results are typical of other maturational studies with relative power estimates appearing to be more sensitive than absolute power to changes in the frequency composition of the EEG with age.

Within the literature, there are a number of conflicting results for the nature of EEG development. Matousek and Petersen (1973) found that the absolute amplitude of the delta, theta and alpha 1 frequency increased until a
certain age and then decreased. John et al. (1980) found that linear equations could be used to predict EEG composition for log transformed relative power as a function of age. In the present study linear changes were found in the theta, alpha and beta bands, but the changes in the delta band were non-linear. Relative delta reduced faster in the younger children and plateaued with further increases in age. It is likely that the differences in results are due to the differing methodologies and EEG parameters used, rather than subject differences.

Matousek and Petersen (1973) found that maturation in the EEG occurs more rapidly in posterior regions than frontal regions. Katada et al. (1981) found that the earliest changes in children take place in the occipital regions, followed by the central and frontal regions. The present study found that changes occurred faster in the posterior regions than the frontal regions, with relative delta and theta reducing and alpha increasing. Laterally, most studies (e.g. Gasser, Jennen-Steinmetz et al., 1988) have failed to detect hemispheric differences in brain maturation, which is supported by the present study. However, lateral differences were found in rates of development between the midline and the two hemispheres. In absolute delta, the midline had greater power than the two hemispheres but this difference became less with age. A similar result was found for the theta/beta ratio. At the same time, midline beta band power was found to increase at a greater rate than in the two hemispheres. These results suggest that maturational changes occur at the midline faster than in the two hemispheres.

Ratio coefficients between waveforms have also been used to quantify developmental changes in the EEG. Matousek (1968) found the theta/alpha ratio to be a reliable measure. Lubar (1991) proposed that the theta/beta ratio could be
relatively free of factors which would affect single waveform band results and could be used to quantify age-related changes as well as deviations from normal development in a number of clinical groups. The current study found decreases in both the theta/alpha and theta/beta ratios with age. The theta/beta ratio appeared to be more sensitive to regional changes, with ratio changes occurring faster in the posterior regions than the frontal regions and faster at the midline compared to the two hemispheres.

The existence of sex differences in the EEG of children has been a contentious issue in the literature. Studies have reported conflicting results from no sex differences (Gasser, Jennen-Steinmetz et al., 1988) to the existence of EEG differences which are indicative of a maturational lag in girls (Harmony et al., 1990). The present study found sex differences in absolute theta and relative theta and alpha bands. Males had less theta and more alpha than females, which is supportive of the results of Mattis et al. (1980) and Benninger et al. (1984). Regionally, there was less relative theta and more absolute and relative alpha at the posterior regions in males than in females. Studies have shown that there appears to be a complementary relationship between an increase in alpha and a decrease in theta activity with age and that the changes in these two bands occur earliest in posterior regions (Gasser, Jennen-Steinmetz et al., 1988). From the current results, females in the 8 to 12 year age group appear to have a maturational lag in EEG, compared to males. Relative maturational lag has been reported as being larger in younger children and decreasing at about the age of 11 to 12 years (Matthys et al., 1980; Harmony et al., 1990). In the present study, power was found to decrease with age in the delta, theta and alpha bands in
females, but levels remained mostly constant or rose slightly in males. These results are consistent with other findings that the rate of change with age is faster in females than males (Harmony et al., 1990). Benninger et al. (1984) found evidence of a pubertal spurt in the EEG of girls between the ages of 11 and 13 years. This was not confirmed by the present results, though it is possible that our age cut-off of 12 years prevented detection of such a spurt.

The existence of maturational sex differences in the EEG has implications for the development of normative data bases for use in the assessment of children with a number of clinical disorders. Studies of mentally retarded children (Gasser, Mocks et al., 1983), learning disabled children (Lubar et al, 1985), and children with attention deficit disorder (Mann et al., 1992; Study 1; Study 2) have reported increased slow wave activity in the EEG of these patients. The current results would support the need for normative data bases to be sex as well as age dependent, if they are to be used for the assessment of developmental abnormalities.

The present data provided normative EEG profiles for the next study of age and sex effects in ADHD subtypes.
CHAPTER 8. STUDY 4. AGE AND SEX EFFECTS IN THE EEG:
DIFFERENCES IN TWO SUBTYPES OF ATTENTION-
DEFICIT/HYPERACTIVITY DISORDER⁴

⁴This Study is under review for publication as: Clarke, A., Barry, R., McCarthy, R. & Selikowitz, M. Age and Sex Effects in the EEG: Differences in Two Subtypes of Attention-Deficit/Hyperactivity Disorder.
8.1 INTRODUCTION

In Studies 1 and 2, EEG differences between children with ADHD and a normal control group, and between the two subtypes of ADHD, were investigated. The results of these two studies presented somewhat conflicting results pertaining to the underlying electrophysiological deficits found in children with ADHD. In Study 1, the two ADHD groups had increased levels of absolute and relative theta, and decreased levels of relative alpha and beta. In posterior regions, relative delta estimates were elevated compared to the control group. All of these results are supportive of the maturational lag model of the CNS.

In Study 2, most main effects of group were replicated. Differences in absolute and relative theta, relative alpha and beta, and posterior relative delta estimates were all able to differentiate the three experimental groups. The theta/alpha, theta/beta and slow/fast ratios had greater coefficients in the two clinical groups. In the alpha and beta bands, the ADHD groups had lower mean frequencies than controls, and in the lower frequency bands, the control subjects had lower mean frequencies in the delta band, and lower coefficients for the delta/theta ratio. The results from the ratio coefficients and the mean frequency analysis suggested that in the ADHD groups there is a shift in the EEG at both ends of the spectrum towards the theta frequency range. Such results do not support a maturational lag model of ADHD, but rather indicate that the probable underlying cause of ADHD is associated with a developmental deviation in CNS functioning.
One limitation of most of the studies of ADHD is that they have investigated EEG differences between their clinical sample and a normal control group, and have proposed explanations of the underlying causes of ADHD based on what has been found in studies of normal children. Few studies have investigated actual age related changes in the EEG of children with ADHD.

Satterfield et al. (1984) studied age effects in hyperactive children between 6 and 12 years old. Results indicated a significant age effect in all frequency bands except slow beta, with changes occurring slower in the hyperactive group compared to the control subjects. From these results it was concluded that hyperactivity reflected an aberrant EEG disorder rather than a maturational lag.

A second area where inconsistent results were obtained between Studies 1 and 2 was the nature of the differences found between the two subtypes of the disorder. In Study 1, the differences between subtypes of ADHD appeared to be related to the degree of severity of the disorder. In every EEG measure where the three groups were significantly different, the ADHDin group's results were positioned between the ADHDcom group and the control group. In Study 2, seven group main effects were found that differentiated between the two clinical groups. Of these group differences, absolute and relative theta, and the theta/alpha ratio were indicative of a qualitative difference between the two ADHD groups. The activity in the frontal regions increased from the central to frontal regions in the ADHDcom group, but decreased in the ADHDin group. These results were interpreted as suggesting that the two ADHD groups may have different types of CNS dysfunction.
Another area that has not been adequately investigated within the ADHD literature is the existence of sex differences within this population. The ratio of boys to girls with ADHD has been estimated at approximately four to one for all three DSM-IV subtypes (De Quiros et al., 1994), and this sex imbalance has been viewed as the major reason for the paucity of studies of female ADHD within the literature (Arnold, 1996). Results of studies are varied, although they tend to suggest that childhood disorders are generally more prevalent among males but are more severe in females (Eme, 1992). In comparison to boys with ADHD, ADHD girls display greater intellectual impairment and lower rates of hyperactivity and other externalizing behaviours (Gaub & Carlson, 1997). No studies have investigated EEG abnormalities in girls with ADHD.

This study aimed to investigate age-related changes in the EEG of children with ADHD, and to determine 1. if such changes occur in a similar manner to normal children, and 2. if changes in the EEG of the inattentive and combined subtypes of the disorder are similar. In Studies 1 and 2, the EEG abnormalities of ADHD in children were generally similar to, but less severe than those found in ADHD com. It was of interest to determine whether these subtype similarities and differences changed with age. A second aim was to investigate whether EEG differences exist between boys and girls with ADHD, and how such differences might occur in the subtypes.

8.2 METHOD
8.2.1 Subjects

Two groups of 80 children, with 40 boys and 40 girls in each group, participated in this study. All of the boys and 24 girls in this study were drawn from subjects in Studies 1 and 2. All children were between the ages of 8 and 12 years and right handed and footed. Subjects had a full-scale WISC-III IQ score of 85 or higher. The groups used were children diagnosed with ADHDcom or ADHDin, and their data were compared with the age- and sex-matched control group described in Study 3. Inclusion criteria for all groups was the same as in Study 1 (section 5.2.2).

Within each group, subjects were matched to form five one year age bands, each containing 8 boys and 8 girls.

8.2.2 Procedure

The same procedure as Study 1 (section 5.2.3) was used in this study. The EEG was analyzed in four frequency bands: Delta (0.5-2.5 Hz), Theta (2.5-7.5 Hz), Alpha (7.5-13.5 Hz) and Beta (13.5-20.5 Hz), for both absolute and relative power, as well as the total power of the EEG (0.5-20.5 Hz). Theta/alpha and theta/beta ratio coefficients were calculated between the frequency bands by dividing the power of the slower frequency band by the power of the faster frequency band.
8.2.3 Statistical analysis

Analysis of variance was performed examining the effects of region and group for absolute and relative power in each band, total power, and the theta/alpha and theta/beta ratios. The effects of region were examined using the same planned contrasts as in Study 1. Within the group factor, planned contrasts compared the patient groups with the control group (to establish ADHD differences from normals) and the ADHDcom group with the ADHDin group. Within the sex factor, differences in the EEGs of the male and female groups were compared, and for the age factor, the linear trend and (where a significant linear result was also found) quadratic trend were examined. For the normal control group, topography, age, and sex effects for absolute and relative power were described in Study 3. The focus here is on group differences in topography, and the main effects of topography are not described because of their similarity to the results of Study 3.

8.3 RESULTS

A significant difference in total power (see Figures 8.1 & 8.2, top left) was found, with the two ADHD groups having greater power than the control group ($F(1,210) = 40.38$, $p<.01$). The difference between the midline and the two hemispheres was greater in the ADHD groups than the control group ($F(1,210) = 7.63$, $p<.01$) and this difference was maximal at the central regions ($F(1,210) =$
Figure 8.1 Power and ratio coefficients as a function of scalp region in male subjects, for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre left), Absolute Alpha (centre), Absolute Beta (centre right), Theta/Alpha (bottom left) and Theta/Beta (bottom right).

14.79, p<.001). Age related differences were found between the two ADHD groups (Figure 8.3), with changes in the posterior regions occurring faster in the ADHDcom group than the ADHDin group (F(1,210) = 5.43, p<.05). The difference between the control group and the two ADHD groups was greater in females (Figure 8.2, top left) than males (Figure 8.1, top left, F(1,210) = 3.94, p<.05). This group difference reduced faster with age in females than males (F(1,210) = 10.12, p<.01), with the magnitude of change being greater in the
posterior regions than the frontal regions ($F(1,210) = 11.41, p<.001$). The difference between the midline and the two hemispheres was found to reduce faster with age in the control group than the ADHD groups, in males compared to females ($F(1,210) = 5.07, p<.05$).

In absolute delta (Figures 8.1 and 8.2, top right), the two ADHD groups had more power than the control group ($F(1,210) = 9.83, p<.01$). With increasing
Figure 8.3 Frequency distribution as a function of scalp region, sagittal section, for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre left), Absolute Alpha (centre), Absolute Beta (centre right), Theta/Alpha (bottom left) and Theta/Beta (bottom right).

age, power decreased slower in the two females ADHD groups than the control group, but in males the rate of decrease was relatively equal for the three groups ($F(1,210) = 7.51, p<.01$). This sex x age x group interaction was greater in the posterior regions compared to the frontal regions ($F(1,210) = 6.7, p<.01$), and less at the central regions than the for the mean of the frontal and posterior regions ($F(1,210) = 4.32, p<.05$). This indicated that the effect was maximal in the
Figure 8.4 Group changes in absolute power and ratio coefficients with age, for Frontal Regions (Left Column), Central Regions (Central Column) and Posterior Regions (Right Column).
Figure 8.5 Sex differences in the combined ADHD groups with increasing age, for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre), Absolute Alpha (bottom left), Absolute Beta (bottom right).

posterior regions. With age, absolute delta decreased faster in the ADHDcom group than the ADHDin group (F(1,210) = 3.99, p<.05), with this interaction being greater in the posterior regions than the frontal regions (F(1,210) = 5.44, p<.05). With increasing age, the difference between the two hemispheres and the midline increased in the ADHDcom group, in the frontal regions, but reduced in the ADHDin group (F(1,210) = 4.6, p<.05). This indicated that power was becoming more equipotential in the ADHDin group, but in the ADHDcom group,
maturational changes were occurring faster in the two hemispheres than at the midline. For relative delta, the difference between the two ADHD groups and the control group was greater for males than females (F(1,210) = 6.24, p<.05). With increasing age, the difference between the ADHD groups and the control group became greater in the posterior regions than the frontal regions (F(1,210) = 5.59, p<.05), resulting from the power changing at a slower rate in the ADHD groups. In the ADHDin group, relative delta power at the midline was found to decrease to a level lower than the two hemispheres with increasing age, whereas in the ADHDcom group, the midline and the two hemispheres remained more equipotential (F(1,210) = 12.36, p<.001). A sex difference was also found between the two ADHD groups, with the difference between the two groups being larger in the right hemisphere in females compared with males (F(1,210) = 5.21, p<.05).

In absolute theta (Figures 8.1 and 8.2, middle left) the two ADHD groups had more power than the control group (F(1,210) = 30.15, p<.001) and the ADHDcom had more power than the ADHDin group (F(1,210) = 4.54, p<.05). The difference between the midline and the two hemispheres was greater in the ADHD groups than the control group (F(1,210) = 22.11, p<.001). Power differences between the two ADHD groups were greater in the left hemisphere than the right (F(1,210) = 8.87, p<.01) and this difference reduced faster with age in the ADHDcom group than the ADHDin group (F(1,210) = 8.43, p<.01). Sex differences were also found between the two ADHD groups, with the group differences being more posterior in males (Figure 8.1, top left) (F(1,210) = 5.98, p<.05) and more frontal in females (Figure 8.2, middle left). With increasing age,
the difference between the two ADHD groups and the control group reduced faster in males than females (F(1,210) = 4.07, p<.05). An age effect was found between the two ADHD groups, with the reduction in power occurring faster in the ADHDcom group (F(1,210) = 5.85, p<.05). This interaction was larger in the posterior regions than the frontal regions (F(1,210) = 6.36, p<.05), and smaller in the central regions than the mean of the frontal/posterior regions (F(1,210) = 10.96, p<.01). Both of these sagittal effects were larger in males than females (F(1,210) = 7.29, p<.01 and F(1,210) = 4.79, p<.05 respectively). The combined ADHD groups had greater levels of relative theta than the control group (F(1,210) = 73.77, p<.001). This difference between groups was somewhat greater in males than females (F(1,210) = 3.67, p = .057). The ADHDcom group also had more relative theta than the ADHDin group (F(1,210) = 14.75, p <.001).

In the absolute alpha band, the difference between the two ADHD groups and the control group was greater in males (Figure 8.1, centre) than females (Figure 8.2, centre) (F(1,210) = 8.58, p<.01) and increased with age more in males than females (F(1,210) = 11.31, p<.001). Power changed less with age in posterior regions compared to the frontal regions in the ADHD groups compared to the control group (F(1,210) = 4.05, p<.05). This age x group effect was less in the central regions than in the mean of frontal/posterior regions (F(1,210) = 5.64, p<.05). Both of these developmental group differences in topography were greater in males than females (F(1,210) = 10.05, p<.01, F(1,210) = 6.86, p<.01 respectively). In relative alpha, the two ADHD groups had less activity than the control group (F(1,210) = 36.75, p<.001) and the ADHDcom group had less activity than the ADHDin group (F(1,210) = 4.81, p<.05). In posterior regions,
the two ADHD groups had a less relative alpha than the control group ($F(1,210) = 15.37, p<.001$) and the difference between groups was less at the central regions, compared to that at the frontal and posterior regions ($F(1,210) = 10.46, p<.001$). The difference between the two ADHD groups was greater in the posterior regions than the frontal regions ($F(1,210) = 6.03, p<.05$). The difference between the combined ADHD groups and the control group was greater in males than females ($F(1,210) = 10.33, p<.01$), and, with increasing age, this became larger for the male groups but stayed relatively constant in the female groups ($F(1,210) = 4.69, p<.05$).

In the absolute beta band the difference between the control group and the two ADHD groups was larger in males (Figure 8.1, centre right) than in females (Figure 8.2, centre right, $F(1,210) = 4.4, p<.05$) and this difference increased with age in males at a faster rate than in females ($F(1,210) = 5.7, p<.05$). Changes occurred faster in posterior regions than frontal regions, with this effect being less in the two ADHD groups than the control group ($F(1,210) = 4.79, p<.05$). In the two ADHD groups compared with the control group, the central regions had less power than the mean of the frontal/posterior regions ($F(1,210) = 3.95, p<.05$) and this was greater in males than females ($F(1,210) = 4.04, p<.05$). The two ADHD groups had less relative beta power than the control group ($F(1,210) = 51.87, p<.001$), with the difference at the frontal regions being greater than posterior regions ($F(1,210) = 26.31, p<.001$), and less at the central regions relative to the mean of the frontal and posterior regions ($F(1,210) = 5.64, p<.001$). Laterally, the difference between the two ADHD groups and the control group was greater in
the right hemisphere than the left hemisphere ($F(1,210) = 4.74, p<.05$) and greater in the two hemispheres than at the midline ($F(1,210) = 10.63, p<.001$).

For the theta/alpha ratio (Figures 8.1 & 8.2, bottom left), the two ADHD groups had a greater coefficient than the control group ($F(1,210) = 38.76, p<.001$), and the ADHDin group had a larger ratio than the ADHDcom group ($F(1,210) = 11.08, p<.001$). A difference between the frontal/posterior regions and the central region showed a greater change with age in the ADHDcom group than the ADHDin group ($F(1,210) = 4.29, p<.05$). Laterally, greater changes occurred with age in the right hemisphere of the ADHDcom group than the ADHDin group ($F(1,210) = 6.59, p<.05$). In the theta/beta ratio (Figures 8.1 & 8.2, bottom right), the two ADHD groups had a greater coefficient than the control group ($F(1,210) = 51.11, p<.001$) and the ADHDcom group had a greater coefficient than the ADHDin group ($F(1,210) = 10.54, p<.001$). Changes in the theta/beta ratio with age occurred faster in the ADHDcom group than the ADHDin group ($F(1,210) = 6.59, p<.05$). This effect were larger in the posterior regions than the frontal regions ($F(1,210) = 4.23, p<.05$) and larger in the central regions than the mean of the frontal/posterior regions ($F(1,210) = 6.33, p<.05$). Laterally, the difference between the two hemispheres and the midline was greater in the two ADHD groups than the control group ($F(1,210) = 27.01, p<.001$).

8.4 DISCUSSION

Most studies of children with ADHD have found an increase in slow wave
activity in comparison to normal children (Satterfield Lesser, Saul & Cantwell, 1973; Capute et al., 1968; Satterfield & Cantwell, 1974). This was primarily found in the theta band, with the maximal amount of theta being found in the frontal regions (Mann et al, 1992). In posterior regions, an increase in delta has been found (Matousek et al., 1984), and decreases in both the alpha (Matsuura et al.,1993) and beta bands (Mann et al, 1992).

In Studies 1 and 2, EEG differences were found between children with ADHDcom, ADHDin and control subjects. These differences occurred across all sites in absolute and relative theta, and in relative alpha and beta. In posterior regions relative delta estimates were able to differentiate between all three experimental groups.

In the present study, the ADHD groups had greater total power, less relative alpha and beta, more absolute delta and theta, and more relative theta than the control group. Regionally, the ADHD groups had less relative alpha in posterior regions and less relative beta in the frontal areas, compared to the control group. These results are consistent with previous studies of children with ADHD (Mann et al., 1992; Lubar, 1991; Matousek et al., 1984), and the results of Studies 1 and 2.

Analysis of ratio coefficients between frequency bands has also been used to assess differences between normal children and children with ADHD (Matousek & Petersen, 1973; Lubar, 1991). In Study 2, the theta/alpha and theta/beta ratios were found to differentiate between control subjects and children with ADHD. The present study found higher ratio coefficients in the ADHD groups than control subjects, in both the theta/alpha and theta/beta ratios. These
results are again consistent with previous research, and the results of Study 2.

In the comparison of the two clinical groups, this study failed to obtain significant results in a number of group comparisons that were significant in Studies 1 and 2. The previous results for relative alpha were not significant in this study. The major difference between Studies 1 and 2, and this study, was the ratio of males to females used. The previous study used a ratio of four males to one female, which represents the approximate sex difference in clinical presentations for the disorder (De Quinos, 1994). In contrast, this study used equal numbers of males and females in each group, and this is the likely reason for the changes in results for some frequency bands. Differences between the two clinical groups were smaller in the female subjects than in the male subjects. When group comparisons were performed, both the male and female subjects were effectively combined into single experimental groups based on diagnosis. This resulted in greater variances within the groups, and the differences found between the clinical groups in Studies 1 and 2 disappeared. These results identify the need for future EEG research into ADHD, to be sex specific in the construction of experimental groups.

This is the first EEG study to investigate sex differences in children with ADHD. Sex differences were found between the combined ADHD groups and the control group for total power, absolute alpha and beta, and relative delta and alpha. The theta/alpha and theta/beta ratios were the most sensitive measures of differences between the two female clinical groups. These were the only measures where group differences were not found to be larger in males than females. With increasing age, changes occurred faster in male ADHD subjects than females,
all absolute power measures and in relative alpha. These results indicated that in most frequency bands, differences between the ADHD group and control subjects was smaller in females than males, and that changes with age occurred faster in male subjects. However, this study did find that EEG differences exist between girls with ADHD and normal girls.

These results pose the question of why the EEG differences were smaller in the female subjects than in the male subjects. Studies have suggested that childhood disorders are generally more prevalent among males, but are more severe in females (Eme, 1992). In Study 1 the data suggested that the more behavioural problems exhibited by a child, the greater the level of associated EEG abnormality. If this is true, and females generally have more severe cases of disorders in childhood, then it would be expected that the females in this study would have had greater levels of EEG anomalies than males. This was not found, as girls had lower levels of EEG abnormalities compared to the age-matched male patient groups.

One area that has been identified for further research is the effect of environmental influences on the expression and evaluation of ADHD in girls (Rhee, Waldman, Hay & Levy, 1999). Within clinical settings, sex differences have been found between children referred for treatment, with girls often being referred at younger ages (Arcia & Conners, 1998). A diagnosis of ADHD is almost always based on reports given by adults who know the child, not on objective measures taken from the child itself. Even the use of questionnaires such as the Child Behaviour Check List (Achenbach, 1991) or the Conners’ Rating Scales (Conners, 1990), which are sex-normed, rely on ratings of the
child's behaviours by people other than the person making the diagnosis. To try to compensate for this, some researchers have suggested that multiple sources of information should be obtained (Brandenburg, Friedman & Silver, 1991). However, this is confounded by the fact that there is little correlation between the ratings of a child's behaviour obtained from parents and from teachers (Achenbach, McConaughy & Howell, 1987).

From the results of this study, it appears that the differences found could reflect sex-related referral biases. In comparison to boys, girls may have to show less behavioural disturbances to be given a diagnosis of ADHD, and this could underlie the present results. Girls showed smaller differences between the clinical groups and the control group, and smaller differences between the two clinical groups, than did boys. This would suggest that the girls, despite having received the same diagnosis, were less electrophysiologically impaired than the boys. These results highlight the need for the utilisation of independent measures, distinct from observational data provided by adults, in the diagnosis of ADHD. Although some researchers have favored the use of electrophysiological measures in the initial evaluation of ADHD (Chabot, Merkin, Wood, Davenport & Serfontein, 1996), this has been criticized on the grounds of showing poor sensitivity and specificity (Rey, 1997). The utilization of electrophysiological measures in the evaluation and diagnosis of ADHD warrants further investigation, as they appear to have the potential to provide independent measures of a disorder that is becoming increasingly perceived as CNS-based.

Abnormalities in the EEG of children with ADHD have been found consistently in studies performed over the last 30 years. However, the
interpretation of what these abnormalities actually represent remains contentious. Mann et al. (1992) found an increased level of theta activity in children with ADHD and concluded that it represented a maturational lag of the CNS. Chabot and Serfontein (1996) also found an increased level of theta in children with ADHD but concluded that it represented a developmental deviation, rather than a maturational lag. The results of Study 1 suggested that ADHD was due to a maturational lag, but in Study 2, results obtained from the mean frequency analysis, and the ratio coefficient analysis, were not supportive of this model. Callaway et al. (1983) compared the EEG of hyperactive children with age-matched normal controls. Their results did not support either the developmental deviation or the maturational lag model. They concluded that these explanations were too simple to be useful. Most of the studies described above based their conclusions on maturational data from normal children rather than investigating age changes in an ADHD population. Bresnahan et al. (1999) investigated age-related changes in the EEG of ADHD children, adolescents and adults, and found that theta activity remained elevated in adult patients but that there was an increase and relative normalisation of beta activity with age.

A second area which has been debated within the ADHD literature, is whether the subtypes of ADHD are similar, or whether they are separate disorders, and should be listed as such. While there are commonalities of symptoms among ADHD children, they do not represent an homogeneous group, having a diversity of related psychiatric symptoms, family backgrounds, developmental courses and responses to treatments (Barkley, 1990a). Few EEG studies have investigated differences between subtypes of the disorder. Chabot
and Serfontein (1996) found results that suggested that the subtypes of ADHD represented different points along a continuum of severity, with children who showed more behavioural disturbances also showing greater EEG deviation compared to normal children. Results of Study 1 suggested that the EEG differences between the patient groups were one of degree rather than providing neurological evidence of the subtypes being independent disorders. In each measure where significant differences were found between the three groups, the ADHDin group was positioned between the control group and the ADHDcom group. In Study 2, three measures in the frontal regions, showed a qualitative difference between the two ADHD groups. From these results it was concluded that this EEG activity could be associated with the ADHDcom group having frontal lobe dysfunction, whereas children with ADHDin may have other forms of CNS dysfunction not primarily associated with frontal lobe functioning, or associated with different types of frontal lobe dysfunction.

In an attempt to further clarify the nature of the underlying electrophysiological abnormality in ADHD, and the nature of differences between the subtypes, this study investigated age effects in the EEG of children with ADHD, over a five year range. Results failed to find any simple effects of age which differentiated between the control group and the combined ADHD groups. Significant differences were found in the posterior regions, with maturational changes occurring slower in the ADHD groups than the control group, in absolute alpha and beta, and relative delta. In the comparison of the two ADHD groups, changes occurred faster in the ADHDcom group than the ADHDin group. The ADHDcom group levels became similar to the ADHDin with age. This was found
for total power, absolute delta and theta, and the theta/beta ratio.

These results suggest that there are two distinct components in ADHD which are quantifiable using electrophysiological measures. The first is a hyperactive/impulsive component which appears to normalise with increasing age. In total power, absolute delta and theta, and the theta/beta ratio, the power levels of the ADHDcom group reduced to a level that was similar to the ADHDin group. The second component is an inattentive component which does not appear to normalise with age. The differences between the control group and the ADHDin group were found to remain constant, even with changes in age. Both of the components changed in different ways, and although they were both present in the ADHDcom group, they appeared to be independent.

From these results, neither a model of ADHD as a maturational lag, nor a model in terms of developmental deviations, can entirely account for changes in the EEG of children with ADHD. Rather, the symptoms of ADHD appear compatible with a combination of the two models. The hyperactive/impulsive component, which was found in the ADHDcom group, normalises with age, and hence appears to result from a maturational lag in CNS development. In contrast to the hyperactive/impulsive component, the inattentive component appears to be relatively stable, and while maturational changes were found in the EEG of the inattentive children, the EEG was not normalising towards the control group. These results are consistent with the results of behavioural studies which have found that the hyperactive symptoms of ADHD diminish with age, but the inattentive symptoms remain into adulthood (Bellak & Black, 1992). This also supports the claims of Callaway et al. (1983), that neither model was complex
enough to account for all the differences found in children with ADHD.

In Study 2, the question of whether the same type of inattention is found in the ADHDcom and ADHDin subtypes of ADHD was raised. Behavioural studies have suggested that the inattention in the inattentive subtype may be a different form of impairment to that in the combined subtype (Barkley et al., 1990; Goodyear & Hynd, 1992; Lahey & Carlson, 1992). Inattentive ADHD children are often dreamy, hypoactive, and passive (Barkley et al., 1990; Lahey & Carlson, 1992), while children with the combined subtype of ADHD have a problem of sustained attention and are easily distracted (Barkley, 1997). The results of Study 2 found distinct EEG differences in the frontal regions which were associated with the hyperactive/inattentive symptoms. A number of other EEG differences between the two subtypes were found in the central and posterior regions of the scalp. It was speculated that these differences may represent a measure of differences in the inattentive component of the disorder. The present study found that maturational changes occurred in the ADHDcom groups in the posterior regions, as well as the frontal regions. As the inattentive component was found not to mature in this study, and these other EEG measures did, it is likely that the posterior differences in the ADHDcom group, from Study 2, were associated with the hyperactive/impulsive component rather than inattention.

Overall, the results of this study found that there are two independent components that constitute the present DSM-IV diagnosis of ADHD. The first is the hyperactive/impulsive component which matures with increasing age. The second is an inattentive component that appears to be more pervasive with increasing age. Both of these components can be differentiated using
electrophysiological measures. From these results, the present diagnosis of ADHD appears to be associated with both a maturational lag and a developmental deviation in CNS functioning. These results further support the splitting of ADHD into two separate disorders, based on inattention and hyperactivity/impulsivity. The results of the analysis of sex differences in ADHD found that group differences were smaller in females than in males. This was believed to result from referral biases in the sample used, and identified the need for the development of independent assessment instruments for the diagnosis of ADHD, which do not rely on perceptions, by adults in the child’s environment, of what is normal behaviour.

A limitation of most EEG studies of ADHD is that they have not investigated the effect of comorbidity on their results. Studies have shown that “pure” ADHD, without the presence of a second diagnosis is rare (Arnold & Jensen, 1995; Nottelmann & Jensen, 1995). In Studies 1, 2 and the present Study, similar criteria to other studies for the clinical groups was used, which did not exclude every other possible comorbid factor from the diagnosis, such as the presence or absence of learning disabilities. EEG research needs to be conducted comparing ADHD children with and without other comorbid conditions, as many of the disorders commonly found with ADHD also have reported effects in EEG components.
CHAPTER 9. STUDY 5. EEG ANALYSIS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND COMORBID OPPOSITIONAL DEFIANT DISORDER

5This Study is under review for publication as: Clarke, A., Barry, R., McCarthy, R. & Selikowitz, M. EEG Analysis of Children with Attention-Deficit/Hyperactivity Disorder and Comorbid Oppositional Defiant Disorder
9.1 INTRODUCTION

In Studies 1, 2 and 4 of this thesis, EEG differences were investigated between children with ADHD and normal children, as well as between two subtypes of the disorder. In Study 1, EEG differences between children with ADHDcom, ADHDin and control subjects occurred across all sites in absolute and relative theta and for relative alpha and beta. In posterior regions, relative delta estimates were able to differentiate between all three experimental groups. From these results it was concluded that ADHD resulted from a maturational lag of the CNS. The differences between the subtypes appeared to be quantitative in nature, rather than the two subtypes being independent.

Study 2 results were not supportive of some of the conclusions made in Study 1. In the theta/alpha, theta/beta and slow/fast ratios, the ADHD groups had greater coefficients than the normal group. In the alpha and beta bands, the ADHD groups had lower mean frequencies than the control group. In the lower frequency bands, the ADHD subjects had higher mean frequencies in the delta band, and higher coefficients for the delta/theta ratio. These results were indicative of a developmental deviation of the CNS rather than a maturational lag.

Study 1 also found results which suggested that the differences between subtypes were associated with the degree of severity of the disorder rather than the two subtypes being electrophysiologically independent. In Study 2, qualitative differences in the clinical groups were found in the frontal regions, in absolute and relative theta, and the theta/alpha ratio. These results suggested that two
different types of CNS functioning may be associated with the different subtypes of the disorder, which is in contradiction to the interpretation of Study 1.

In an attempt to reconcile the disparities that were found in Studies 1 and 2, an analysis of age-related changes was undertaken in Study 4. Study 4 found that total power, absolute delta and theta, and the theta/beta ratio changed at a greater rate in an ADHDcom group than in an ADHDin group, with power levels between the two groups becoming similar with age. These results suggest that ADHD has two independent components, with the hyperactive/impulsive component maturing with age, and the inattentive component remaining more stable.

Most EEG studies of ADHD have not considered the possible effects on their results of comorbidity with other disorders, even though ADHD is often found in conjunction with other disorders. ADHD often occurs with anxiety and depressive disorders (Cohen et al., 1989; Velez et al., 1989), and learning disabilities are also common among this group of children (Pliszka, 1998; Biederman et al., 1991). The most commonly occurring of all disorders found in children with ADHD, are behavioural disorders such as Conduct Disorder (CD) or Oppositional Defiant Disorder (ODD) (Jensen et al., 1997). As many as 93% of children with a DSM-III diagnosis of attention deficit disorder have been reported to have CD or ODD (Bird et al., 1993). Other studies have obtained rates of comorbidity between 47% (Anderson et al., 1987) and 42% (Offord et al., 1989).

EEG studies of behaviourally disordered children have been conducted using categories such as delinquency (Wiener, Delano & Klass, 1966; Swinton,
Fenwick & Dolimore, 1977; Hsu et al., 1985) and CD (Phillips et al., 1993). None of these studies found significant differences between their behaviourally disordered groups and non-delinquent control subjects.

Only one study has compared EEG differences in ADHD children with or without comorbid behavioural disorders. Satterfield and Schell (1984) investigated EEGs of hyperactive adolescents, both with and without signs of delinquent behaviour. The non-delinquent hyperactive group had higher total power and absolute alpha and beta, higher relative alpha and beta, and less relative theta than normal control subjects. The EEGs of the delinquent hyperactive group were similar to the control group. From these results it was concluded that the delinquent behaviour was associated with an environmental-social factor rather than a CNS dysfunction. No studies have investigated EEG differences in children with ADHD and a comorbid behavioural disorder listed in the DSM.

This study aimed to investigate EEG differences between children with ADHD, with or without comorbid ODD, and to quantify the nature of any differences. Only children with a diagnosis of ODD were included in this study, as ODD is a more common diagnosis than CD in children under the age of 12 years (APA, 1980; Lahey et al., 1992; Loeber, Lahey & Thomas, 1991; Lahey, Loeber, Quay, Frick & Grimm, 1994).

9.2 METHOD
9.2.1 Subjects

Three groups of 20 boys participated in this study. All children were between the ages of 8 and 12 years and right handed and footed. Subjects had a full-scale WISC-III IQ score of 85 or higher. This study used DSM-IV (APA, 1994) criteria for the diagnosis of all clinical groups. The groups used were children diagnosed with ADHD or ADHD with comorbid Oppositional Defiant Disorder (ADHD+ODD), and a control group. Inclusion criteria for the control and the ADHD group was the same as in Study 1 (section 5.2.2). In the ADHD+ODD group, the inclusion criteria was the same as for the ADHD group, and subjects also had to meet the DSM-IV (APA, 1994) criteria for ODD.

Across all groups, subjects were matched in one year age bands. Subjects with ADHD and comorbid ODD were independent from subjects used in earlier studies.

9.2.2 Procedure

The same procedure as Study 1 (section 5.2.3) was used in this study. The EEG was analyzed in four frequency bands: Delta (0.5-2.5 Hz), Theta (2.5-7.5 Hz), Alpha (7.5-13.5 Hz) and Beta (13.5-20.5 Hz), for both absolute and relative power, as well as the total power of the EEG (0.5-20.5 Hz). Ratio coefficients were also calculated between frequency bands by dividing the power of the slower frequency band by the power of the faster frequency band. These were calculated for theta/alpha and theta/beta frequencies.
9.2.3 Statistical analysis

Analysis of variance was performed examining the effects of region and group for each band in absolute and relative power and the total power, and ratio coefficients. The effects of region were examined using the same planned contrasts as were used in Study 1. Within the Group factor, planned contrasts compared the patient groups with the control group (to establish ADHD differences from normals) and the ADHD group with the ADHD+ODD group.

9.3 RESULTS

9.3.1 Topography Across Groups

Across all groups, total power was greater in the posterior regions compared to the frontal regions (F(1,57) = 78.72, p<.001), and the central regions had less power than the mean of the frontal and posterior regions (F(1,57) = 45.05, p<.001). The right hemisphere had significantly greater power than the left hemisphere (F(1,57) = 24.39, p<.001), and this was greater in the frontal regions compared to the posterior regions (F(1,57) = 7.76, p<.01). The midline had greater power than the two hemispheres (F(1,57) = 82.64, p<.001), and this difference was maximal at the central regions (F(1,57) = 72.88, p<.001). The difference between the frontal/posterior regions and the central region was greater in the right hemisphere than the left hemisphere (F(1,57) = 6.63, p<.05).
In absolute delta, the posterior regions had greater power than the frontal regions \( (F(1,57) = 26.98, p<.001) \), and the central regions had less power than the mean of the frontal and posterior regions \( (F(1,57) = 21.74, p<.001) \). An effect of laterality was found, with the right hemisphere having greater power than the left hemisphere \( (F(1,57) = 14.37, p<.001) \), and the midline having greater power than the two hemispheres \( (F(1,57) = 151.99, p<.001) \). The difference between the midline and the two hemispheres was greatest at the central regions \( (F(1,57) = 201.75, p<.001) \).

For relative delta, more power was found in frontal regions than posterior regions \( (F(1,57) = 206.20, p<.001) \). A significant effect of laterality was found, with the midline having less power than the two hemispheres \( (F(1,57) = 36.24, p<.001) \). This difference was greater in the posterior regions than the frontal regions \( (F(1,57) = 61.72, p<.001) \), and was smaller at the central regions compared to the mean of the frontal and posterior regions \( (F(1,57) = 21.40, p<.001) \).

In absolute theta, greater power occurred in posterior regions than frontal regions \( (F(1,57) = 24.80, p<.001) \). Laterally, the right hemisphere had more power than the left hemisphere \( (F(1,57) = 17.13, p<.001) \), and this was greater in the posterior regions compared to the frontal regions \( (F(1,57) = 5.15, p<.05) \). The midline had greater power than the two hemispheres \( (F(1,57) = 83.28, p<.001) \), and this difference was maximal at the central regions \( (F(1,57) = 38.74, p<.001) \).

In the relative theta band, more theta was found in the frontal regions compared to the posterior regions \( (F(1,57) = 60.73, p<.001) \), and the central regions had more theta than the mean of the frontal and posterior regions \( (F(1,57) = 66.52, p<.001) \). Laterally, the midline had more theta than the two hemispheres \( (F(1,57) = 245.72, p<.001) \). This difference was greater at the frontal regions than the posterior regions \( (F(1,57) = 108.60, p<.001) \), and maximal at the central regions \( (F(1,57) = 21.63, p<.001) \). The difference between the two hemispheres
was greater in the frontal regions than the posterior regions \(F(1,57) = 7.53, p<.01\).

In absolute alpha, greater power was found in the posterior regions than the frontal regions \(F(1,57) = 87.81, p<.001\), and the central regions had less power than the mean of the frontal and posterior regions \(F(1,57) = 70.67, p<.001\). An effect of laterality was found with the left hemisphere having less power than the right hemisphere \(F(1,57) = 9.96, p<.01\), and this difference was greater in the posterior regions than the frontal regions \(F(1,57) = 7.28 p<.01\). The midline had more power than the two hemispheres \(F(1,57) = 23.12, p<.001\), and this was greater in the central regions compared to the mean of the frontal and posterior regions \(F(1,57) = 12.82 p<.001\). The difference between the central region and the mean of the frontal and posterior regions was greater in the right hemisphere than the left hemisphere \(F(1,57) = 5.19, p<.05\).

For relative alpha, more power was found in the posterior regions than the frontal regions \(F(1,57) = 326.99, p<.001\), and less at the central regions than the mean of the frontal and posterior regions \(F(1,57) = 73.91, p<.001\). In the frontal regions, the left hemisphere had greater power than the right hemisphere, and this hemispheric difference was reversed in the posterior regions \(F(1,57) = 8.38, p<.01\).

For absolute beta, greater power was found in the posterior region compared to the frontal regions \(F(1,57) = 34.11, p<.001\), and the central regions had less power than the mean of the frontal and posterior regions \(F(1,57) = 42.98, p<.001\). Laterally, greater power was found in the right hemisphere compared to the left hemisphere \(F(1,57) = 13.45, p<.001\). Greater power occurred at the midline than in the two hemispheres \(F(1,57) = 21.37, p<.001\), and this was maximal at the central regions \(F(1,57) = 6.08, p<.05\).

For relative beta, more power was found in the frontal regions compared to the posterior regions \(F(1,57) = 138.63, p<.001\), and the central regions had
more power than the mean of the frontal and posterior regions (F(1,57) = 10.34, p<.01). Laterally, the midline had less power than the two hemispheres (F(1,57) = 168.78, p<.001). The difference between the midline and the two hemispheres was greater at frontal regions compared to the posterior regions (F(1,57) = 34.78, p<.001), and maximal at the central regions (F(1,57) = 71.82, p<.001). The difference between the two hemispheres was greater in the frontal regions than the posterior regions (F(1,57) = 9.79, p<.01).

A greater theta/alpha ratio occurred in the frontal regions compared to the posterior regions (F(1,117) = 108.05, p<.001), and the central regions had a higher ratio than the mean of the frontal and posterior regions (F(1,117) = 5.76, p<.05). The midline had a higher ratio than the two hemispheres (F(1,117) = 42.43, p<.001). This lateral difference was greater in the frontal regions than in the posterior regions (F(1,117) = 22.19, p<.001), and maximal at the central regions (F(1,117) = 6.16, p<.05).

A greater theta/beta ratio was found in the posterior regions than in the frontal regions (F(1,117) = 16.44, p<.001). The midline had a higher ratio than the two hemispheres (F(1,117) = 108.30, p<.001). This difference between the two hemispheres and the midline was greater in the frontal regions than in the posterior regions (F(1,117) = 22.83, p<.001), and maximal at the central regions (F(1,117) = 85.88, p<.01).

9.3.2 Group Differences

For total power (Figure 9.2, top left), the difference between ADHD groups and the control group was greater in the right hemisphere than the left hemisphere (F(1,57) = 4.11, p<.05).
Figure 9.1 Absolute power and ratio coefficients as a function of scalp region, from frontal to posterior regions, for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre left), Absolute Alpha (centre), Absolute Beta (centre right), Theta/Alpha (bottom left), and Theta/Beta (bottom right).

No significant results were found for absolute delta (Figure 9.1, top right).

In relative delta, the difference between the ADHD groups and the control group was greater in the posterior regions, compared to the frontal regions \( (F(1,57) = 8.16, p<.01) \).

In absolute theta (Figure 9.1, centre left), the ADHD groups had greater power than the control group \( (F(1,57) = 6.5, p<.05) \). Laterally (Figure 9.2, centre left), the difference between the ADHD groups and the control group, and between the two ADHD groups, was greater in the right hemisphere than the left hemisphere.
Figure 9.2 Absolute power and ratio coefficients as a function of scalp region, from left to right regions, for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre left), Absolute Alpha (centre), Absolute Beta (centre right), Theta/Alpha (bottom left), Theta/Beta (bottom right).

(F(1,57) = 6.49, p<.05 and F(1,57) = 5.08, p<.05 respectively). The ADHD groups had more relative theta than the control group (F(1,57) = 39.16, p<.001). The difference between the frontal midline and the two hemispheres was greater in the ADHD groups than the control group (F(1,57) = 5.32, p<.05).

No significant differences were found in absolute alpha (Figure 9.1, centre). The ADHD groups had less relative alpha than the control group (F(1,57) = 15.73, p<.001), and this was greater in the posterior regions compared to the
frontal regions ($F(1,57) = 6.7, p<.05$). The difference between the ADHD groups and the control group was less at the central regions than the mean of the frontal/posterior regions ($F(1,57) = 4.02, p<.05$). The difference between the midline and the two hemispheres (Figure 9.2, centre) was greater in the posterior regions compared to the frontal regions, and greater in the ADHD group than in the ADHD+ODD group ($F(1,57) = 4.06, p<.05$).

No significant differences were found in absolute beta (Figures 9.1 and 9.2, centre right). The ADHD groups had less relative beta than the control group ($F(1,57) = 5.83, p<.05$). This difference was greater in the frontal regions than the posterior regions ($F(1,57) = 5.3, p<.05$).

The two ADHD groups had a greater theta/alpha ratio (Figure 9.1, bottom left) than the control group ($F(1,57) = 12.46, p<.001$). This group difference was greater in the frontal regions than the posterior regions ($F(1,57) = 5.62, p<.05$). In the ADHD groups compared to the control group, the difference between the midline and the two hemispheres (Figure 9.2, bottom left) was greater in the frontal regions than the posterior regions ($F(1,57) = 4.18, p<.05$). The two ADHD groups had a greater theta/beta ratio (Figure 9.1, bottom right) than the control group ($F(1,57) = 12.6, p<.001$) and this difference was greater in the posterior regions than the frontal regions ($F(1,57) = 4.12, p<.05$). In the ADHD groups compared to the control group, the difference between the midline and the two hemispheres (Figure 9.2, bottom right) was greater in the frontal regions than the posterior regions ($F(1,57) = 7.62, p<.01$).

No significant group differences were found in absolute delta, alpha, or beta (Figures 9.1 and 9.2, top right, centre, centre right).
9.4 DISCUSSION

A number of studies have investigated EEG differences between children with ADHD and normal children (Capute et al., 1968; Satterfield, Cantwell, Saul, Lesser et al., 1973; Satterfield & Cantwell, 1974; Chabot & Serfontein 1996; Mann et al., 1992). These studies have typically found that ADHD children have an increase in theta activity which is greatest in the frontal regions. Decreased alpha and beta activity have also been found in ADHD children (Callaway et al., 1983; Matsuura et al., 1993). In Studies 1, 2 and 4, EEG differences were found between children with ADHDcom, ADHDin and control subjects. Significant group differences were found in absolute and relative theta and for relative alpha and beta. In Studies 1 and 2, relative delta estimates in the posterior regions were able to differentiate between all three experimental groups.

In the present study, the ADHD groups had less relative alpha and beta than the control group. The ADHD groups also had more absolute and relative theta than the control group. Regionally, the ADHD groups had less relative alpha and more relative delta in posterior regions and less relative beta in the frontal regions, than the control group. These results are consistent with those obtained in Studies 1, 2 and 4.

An analysis of ratio coefficients between frequency bands was conducted in Study 2. This found that the theta/alpha and theta/beta ratios were able to discriminate between the three experimental groups. These ratio coefficients have been used to discriminate between children with ADHD, and normal children in
other studies (Matousek et al., 1973), with the theta/beta ratio being proposed as a more sensitive measure of group differences than the individual frequency bands. This assertion was supported by the results of Study 4, where the theta/alpha and theta/beta ratios were able to quantify group differences in the female subjects, although individual frequency band analysis could not. The results of the present study found that the theta/alpha and theta/beta ratios differentiated between the ADHD groups and the control group, which is consistent with Studies 2 and 4.

Most studies of children with a diagnosis of CD or ODD have failed to find any EEG differences between their clinical groups and normal children (Satterfield & Schell, 1984; Hsu et al., 1985; Phillips et al., 1993). From these results, CD or ODD was not viewed as having an electrophysiological component, and probably resulted from a social-environmental factor rather than abnormal CNS functioning (Satterfield & Schell, 1984). Although this study did not investigate children with a diagnosis of ODD without ADHD, the results are supportive of the view that there is not an electrophysiological component in ODD. The ADHD+ODD group had differences in their EEG when compared to normal children. However, these differences appeared to be specific to the ADHD component of the diagnosis, rather than the ODD component. No significant main effects of group were found between the two ADHD groups. Only two regional differences were found between ADHD and ADHD+ODD children. In absolute theta, the difference between the two groups was greater in the right hemisphere than the left hemisphere, with the ADHD+ODD group having less power than the ADHD group. The second difference was in relative alpha, with the difference between the midline and the two hemispheres, in the posterior regions, being
greater in the ADHD group than the ADHD+ODD group. In both of these differences, in comparison to the control group, the results for the ADHD group were more extreme than those obtained for the ADHD+ODD group. From these results, the EEG differences found between the ADHD+ODD group and the control group appear to be specific to the ADHD diagnosis.

Phillips et al. (1993) investigated EEG abnormalities in children with CD with the hope that characteristic abnormalities in such patients could be identified and that these could aid in objective diagnosis. They concluded that routine EEG screening may be of limited value in childhood behaviour problems. This assertion is not totally supported by the present results. Where the presence of ODD is suspected in the absence of other behavioural disorders, the resultant EEG is likely to be the same as in normal children. However, if a dual diagnosis of ADHD and ODD is being considered, the EEG has the potential to be of use, as any deviations in the EEG of these children are likely to be specific to the ADHD diagnosis, and not the ODD diagnosis.

In clinical assessments, it can be difficult to obtain accurate information to make a diagnosis of comorbid ADHD and ODD, as the primary source of information comes from adults who know the child, rather than from independent measures of behaviour. To improve the quality of information available to clinicians, it is recommended that behavioural information is obtained from a number of sources (Achenbach et al., 1987). This is confounded by the fact that there is little correlation between the reports of parents and teachers in relation to a child's behaviour (McGee & Feehan, 1991). EEG measures are independent of biases in what different people consider to be normal behaviour, and since the
EEG abnormalities appear to be specific to the ADHD component of the diagnosis, this procedures has the potential to aid in differentiating the two disorders.

This study found group differences between the clinical groups which were under investigation. For this procedure to be reliable in clinical assessments, these EEG differences need to demonstrate reliability and specificity in individual patients. This needs to be further investigated.

In Study 2, a qualitative difference was found between the two ADHD group. This was in the frontal regions, for absolute and relative theta, and the theta/alpha ratio. These EEG differences between the two ADHD groups was further investigated in Study 4. Total power, absolute delta and theta, and the theta/beta ratio changed at a greater rate with increasing age, in the ADHDcom group compared to the ADHDin group, with power levels between the two groups becoming similar with age. These results suggested that ADHD has two components, with the hyperactive/impulsive component maturing with age, and the inattentive component remaining more stable. This was interpreted as supporting a two component model of ADHD, involving two types of abnormalities in CNS functioning. From the present results, ODD is a disorder independent of ADHD, and does not appear to have an electrophysiological component associated with it.

Behavioural studies of ODD have found that ADHD is a significant predictor of the future development of ODD (Biederman et al., 1987). This poses the question of how are these two disorders linked? There are two possible explanations for such an association. The first is that ODD results from some
form of CNS dysfunction, but that the EEG is not sensitive enough to detect and quantify the underlying dysfunction. If this is true, then the CNS dysfunction found in ADHD might simply alter in some subtle fashion, resulting in the symptoms of ODD. This explanation might be better investigated using other electrophysiological assessment techniques, such as ERPs or fMRI.

A second explanation might be that ODD occurs as a result of secondary factors associated with ADHD. Hyperactive children are often socially rejected by their peers (Lahey et al., 1984). This rejection is not a primary component of ADHD, such as hyperactivity or impulsivity, but this secondary level of associated problems may facilitate the development of the antisocial problems found in ODD. This link between the two disorders needs to be further investigated.

Overall, this study found that children with a diagnosis of comorbid ADHD+ODD had EEG differences from normal children. However, the differences appeared to be specific to the ADHD component of the disorder. These results further supported the conclusions of other studies that have proposed that ADHD is associated with a CNS dysfunction, but that ODD is associated more with an environmental-social factor. They also support the specificity of the EEG anomalies reported here to be associated with ADHD, and hence encourage their use as diagnostic aids.
CHAPTER 10. STUDY 6. EEG ANALYSIS OF CHILDREN WITH
ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND COMORBID
LEARNING DISABILITIES

This Study is under review for publication as: Clarke, A., Barry, R.,
McCarthy, R. & Selikowitz, M. EEG Analysis of Children with Attention-
Deficit/Hyperactivity Disorder and Comorbid Learning Disabilities.
10.1 INTRODUCTION

Studies 1, 2 and 4 of this thesis investigated EEG differences between children with ADHD and normal children, and between two subtypes of ADHD. Collectively, these studies found EEG differences between all three experimental groups. Study 2 identified three measures in the frontal regions where the EEG of the two ADHD groups were qualitatively different. These group differences were further investigated in Study 4. Results indicated that changes occurred faster in the ADHDcom group than the ADHDin group, with the ADHDcom group’s power levels becoming similar to the ADHDin with age. These results suggested that there are two distinct components in ADHD which are quantifiable using electrophysiological measures. The first is a hyperactive/impulsive component which appears to normalise with increasing age. In total power, absolute delta and theta, and the theta/beta ratio, the power levels of the ADHDcom group reduced to a level that was similar to the ADHDin group. The second component is an inattentive component which does not appear to normalise with age. The magnitude of the differences between the control group and the ADHDin group were found to remain stable, even with changes in age.

Few EEG studies have investigated the impact of the presence of other comorbid factors on the EEG of children with ADHD. ADHD is often found in conjunction with language and communication disorders, learning disorders, conduct and oppositional defiant disorder, anxiety disorders, mood disorders, and Tourette's syndrome or chronic tics (Cantwell, 1994).
In Study 5, effects in the EEG of children with ADHD, with or without comorbid ODD, were investigated. Only two regional differences were found between ADHD and ADHD+ODD children. The results for the ADHD group were more extreme from the control group than was the ADHD+ODD group from the control group. From these results it was concluded that ODD was possibly associated with an underlying environmental-social factor rather than being associated with a CNS dysfunction.

Learning disabilities (LD) have been found in between 20% and 25% of children with ADHD (Pliszka, 1998), although figures within the literature vary from 10% to 92% (Biederman et al., 1991). Even though high levels of comorbidity have been found for ADHD and LD, a number of researchers have suggested that the two disorders are distinct (Shaywitz & Shaywitz, 1991; Pliszka, 1998).

EEG studies of children with LD have found that 87% of such children had QEEGs which were statistically different from normal children (John, Corning, Easton, Brown, Ahn, John, Harmony, Princhep, Toro, Gerson, Bartlett, Thatcher, Kaye, Valdes. & Schwartz, 1977). Excessive delta and theta wave activity has been found in the parieto-occipital regions, along with deficiencies in relative alpha (John et al., 1980). Excessive levels of posterior delta have also been found in other studies (Chabot & Serfontein, 1996). Harmony et al. (1990) found greater relative theta and increased left hemisphere delta in LD subjects. Lubar et al. (1985) reported that LD children had excessive levels of theta activity in the 4 to 8 Hz range.
Studies of EEG differences between children with ADHD and LD have found group differences in the low beta band, with the ADHD group having greater power at the parietal and midline sites (Ackerman et al., 1994). The LD group also had increased levels of delta and alpha in the right parietal sites, and greater low frequency beta in the left temporal area. Chabot et al. (1996) performed a discriminant analysis using 9 EEG measures to study differences between children with ADHD and a second group with LD. The discriminant function analysis classified the ADHD group with 93.1% accuracy and the LD group with 89.7% accuracy. From these results, it was concluded that EEG differences existed between the two clinical groups.

No studies have investigated EEG differences in ADHD children with and without comorbid LD. The aim of this study was to investigate whether EEG differences could be found between children with ADHD with comorbid LD and ADHD without LD, and to quantify the nature of any such differences.

10.2 METHOD

10.2.1 Subjects

Three groups of 20 children, with 18 boys and 2 girls in each group, participated in this study. All children were between the ages of 8 and 12 years and right handed and footed. Subjects had a full-scale WISC-III IQ score of 85 or higher. The groups used were children diagnosed with ADHD+LD, or ADHD,
and a control group. Twelve of the ADHD+LD subjects had not been used in any of the previous studies. The same inclusion criteria as Study 1 (section 5.2.2) was used in this study, with additional criteria. Here, subjects in the ADHD group had to score in the normal range on the measures of accuracy and comprehension on the Neale Analysis of Reading and have a standard score of 90 or above on the Wide Range Achievement Test (Spelling). Inclusion in the ADHD+LD group was based on also meeting DSM-IV (APA, 1994) criteria for LD. Subjects had to score at two years below their chronological age for accuracy and comprehension of reading, and have a standard score of 75 (5th percentile) or less for spelling.

Across all groups, subjects were matched in one year age bands and by sex.

10.2.2 Procedure

The same procedure was used in this study as in Study 1 (section 5.2.3). The EEG was analyzed in four frequency bands: Delta (0.5-2.5 Hz), Theta (2.5-7.5 Hz), Alpha (7.5-13.5 Hz) and Beta (13.5-20.5 Hz), for both absolute and relative power, as well as the total power of the EEG (0.5-20.5 Hz). The mean frequency was calculated for each band and for the total EEG. Ratio coefficients were also calculated between frequency bands by dividing the power of the slower frequency band by the power of the faster frequency band. These were calculated for theta/alpha and theta/beta ratios.
10.2.3 Statistical analysis

Analysis of variance was performed examining the effects of region and group for each band in absolute and relative power, total power, and the theta/alpha and theta/beta ratios. The effects of region were examined using the same statistical procedures as were used in Study 1. Within the Group factor, planned contrasts compared the patient groups with the control group (to establish ADHD differences from normals) and the ADHD+LD group with the ADHD group.

10.3 RESULTS

10.3.1 Topography Across Groups

Across all groups, total power was greater in the posterior regions compared to the frontal regions (F(1,57) = 59.43, p<.001) and the central regions had less power than the mean of the frontal and posterior regions (F(1,57) = 36.14, p<.001). The right hemisphere had significantly greater power than the left hemisphere (F(1,57) = 18.36, p<.001), and this was greater in the frontal regions than the posterior regions (F(1,57) = 5.48, p<.05). The midline had greater power than the two hemispheres (F(1,57) = 120.32, p<.001), and this difference was maximal at the central regions (F(1,57) = 98.97, p<.001). This indicated that across the scalp, power was maximal at the central midline region.

In absolute delta, the posterior regions had greater power than the frontal regions (F(1,57) = 23.17, p<.001), and the central regions had less power than the
mean of the frontal and posterior regions ($F(1, 57) = 15.13, p<.001$). An effect of laterality was found, with the right hemisphere having greater power than the left hemisphere ($F(1, 57) = 11.13, p<.001$), and the midline having greater power than the two hemispheres ($F(1, 57) = 276.85, p<.001$). The difference between the midline and the two hemispheres was greatest at the central regions ($F(1, 57) = 262.59, p<.001$). These results indicated that across the scalp, power was maximal at the central midline region.

For relative delta, more power was found in frontal regions than posterior regions ($F(1, 57) = 208.32, p<.001$), and the central regions had more power than the mean of the frontal and posterior regions ($F(1, 57) = 3.99, p<.05$). A significant effect of laterality was found with the midline having less power than the two hemispheres ($F(1, 57) = 29.20, p<.001$). This difference was greater at the frontal regions than the posterior regions ($F(1, 57) = 58.79, p<.001$) and was smaller at the central regions compared to the mean of the frontal and posterior regions ($F(1, 57) = 42.36, p<.001$).

In absolute theta, greater power occurred in posterior regions than frontal regions ($F(1, 57) = 21.94, p<.001$), and the central regions had less power than the mean of the frontal and posterior regions ($F(1, 57) = 4.01, p<.05$). Laterally, the right hemisphere had more power than the left hemisphere ($F(1, 57) = 12.67, p<.001$). The midline had greater power than the two hemispheres ($F(1, 57) = 125.47, p<.001$), and this difference was maximal at the central regions ($F(1, 57) = 160.04, p<.001$). The difference between the frontal/posterior regions and the central region was greater in the right hemisphere than the left hemisphere ($F(1, 57) = 3.99, p<.05$). A significant frontal/posterior by laterality interaction was found with the maximum power occurring at the central midline region ($F(1, 57) = 101.64, p=.001$).

In the relative theta band, more theta was found in the frontal regions than the posterior regions ($F(1, 57) = 61.25, p<.001$), and the central regions had more
theta than the mean of the frontal and posterior regions \(F(1,57) = 91.80, p<.001\). Laterally, the midline had more theta than the two hemispheres \(F(1,57) = 180.79, p<.001\). This difference was greater at the frontal regions than the posterior regions \(F(1,57) = 107.09, p<.001\), and maximal at the central regions \(F(1,57) = 16.80, p<.001\). The difference between the two hemispheres was greater in the posterior regions than the frontal regions \(F(1,57) = 7.53, p<.01\). The difference between the central regions and the mean of the frontal and posterior regions was greater in the left hemisphere than the right hemisphere \(F(1,57) = 4.17, p<.05\).

In absolute alpha, greater power was found in the posterior regions than the frontal regions \(F(1,57) = 71.59, p<.001\), and the central regions had less power than the mean of the frontal and posterior regions \(F(1,57) = 58.90, p<.001\), indicating a strong posterior source. An effect of laterality was found where the left hemisphere had less power than the right hemisphere \(F(1,57) = 5.70, p<.05\), and this difference was greater in the posterior regions than the frontal regions \(F(1,57) = 4.45 p<.05\). The midline had more power than the two hemispheres \(F(1,57) = 36.44, p<.001\), and this was greater in the posterior regions than the frontal regions \(F(1,57) = 7.55 p<.01\). Together, these results indicate that power became more equipotential from the posterior regions, to the frontal regions.

More relative alpha power was found in the posterior regions than the frontal regions \(F(1,57) = 355.37, p<.001\), and less at the central regions than the mean of the frontal and posterior regions \(F(1,57) = 89.18, p<.001\), indicating a strong posterior source. The difference between the midline and the two hemispheres was greater in the posterior regions compared to the frontal regions \(F(1,57) = 6.02, p<.05\), and less at the central regions than the mean of the frontal and posterior regions \(F(1,57) = 9.59, p<.01\).

Greater absolute beta power was found in the posterior regions than the frontal regions \(F(1,57) = 31.88, p<.001\), and the central regions had less power
than the mean of the frontal and posterior regions (F(1,57) = 28.48, p<.001). Laterally, greater power was found in the right hemisphere than the left hemisphere (F(1,57) = 18.36, p<.001), and the greatest power occurred at the midline (F(1,57) = 19.60, p<.001). The difference between the central regions and the mean of the frontal and posterior regions was greater in the right hemisphere than the left hemisphere (F(1,57) = 4.28, p<.05).

More relative beta power was found in the frontal regions than posterior regions (F(1,57) = 93.77, p<.001), and the central regions had more power than the mean of the frontal and posterior regions (F(1,57) = 7.06, p<.01). Laterally, more power occurred in the right hemisphere than the left hemisphere (F(1,57) = 6.27, p<.05) and the midline had less power than the two hemispheres (F(1,57) = 159.16, p<.001). The difference between the midline and the two hemispheres was greater at frontal regions than the posterior regions (F(1,57) = 12.21, p<.001), and the central regions had less power than the mean of the frontal and posterior regions (F(1,57) = 60.50, p<.001), indicating a strong maximal posterior source. The difference between the two hemispheres was greater in the frontal regions than the posterior regions (F(1,57) = 14.91, p<.001).

A greater theta/alpha ratio occurred in the frontal regions than the posterior regions (F(1,117) = 165.81, p<.001), and the central regions had a higher ratio than the mean of the frontal and posterior regions (F(1,117) = 11.67, p<.001). The midline had a higher ratio than the two hemispheres (F(1,117) = 56.34, p<.001). This was greater in the frontal regions than the posterior regions (F(1,117) = 22.78, p<.001), and maximal at the central regions (F(1,117) = 7.94, p<.01). The difference between the central regions and the mean of the frontal and posterior regions was greater in the right hemisphere than the left hemisphere (F(1,57) = 4.04, p<.05).

For the theta/beta ratio, a greater value occurred in the posterior regions than the frontal regions (F(1,117) = 9.5, p<.01). The midline had a higher ratio
than the two hemispheres ($F(1,117) = 97.38, p<.001$). The difference between the two hemispheres and the midline was greater in the frontal regions compared to the posterior regions ($F(1,117) = 18.31, p<.001$), and maximal at the central regions ($F(1,117) = 93.74, p<.01$). The difference between the mean of the frontal and posterior, and the central region was greater in the left hemisphere compared to the right hemisphere ($F(1,117) = 7.02, p<.01$).

### 10.3.2 Group Differences

As expected from the group inclusion criteria, significant differences were found between the two ADHD groups (Table 10.1) on the measures of reading accuracy ($F(1,38) = 73.33, p<.001$), reading comprehension ($F(1,38) = 39.27, p<.001$) and spelling ($F(1,38) = 149.55, p<.001$). No significant differences were found between the ADHD and control group for any of these measures.

<table>
<thead>
<tr>
<th>Group</th>
<th>Accuracy (Months)</th>
<th>Comprehension (months)</th>
<th>Spelling (Standard Score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>138.65</td>
<td>138.05</td>
<td>107.95</td>
</tr>
<tr>
<td>ADHD</td>
<td>136.95</td>
<td>134.05</td>
<td>104.4</td>
</tr>
<tr>
<td>ADHD+LD</td>
<td>90.65</td>
<td>96.75</td>
<td>71.75</td>
</tr>
</tbody>
</table>
EEG group differences are shown in Figures 10.1 (sagittal view) and 10.2 (lateral view).

No group differences were found in total power.

In absolute delta (Figures 10.1 & 10.2, top right), a hemispheric difference was found between the two ADHD and ADHD+LD groups, with the difference being maximal in the left posterior regions ($F(1,57) = 5.94, p<.05$). For relative delta, the two ADHD groups had more activity than the control group ($F(1,57) = 5.65, p<.05$). This was more pronounced in the posterior regions than the frontal regions ($F(1,57) = 7.28, p<.001$). The ADHD+LD group had more power than the ADHD group in the posterior regions compared to the frontal regions ($F(1,57) = 5.41, p<.05$). Hemispheric differences were also found, with the difference between the control group and the two ADHD groups being greater in the left hemisphere than the right hemisphere ($F(1,57) = 4.20, p<.05$) and the difference between the ADHD+LD and ADHD groups being greater in the right hemisphere than the left ($F(1,57) = 8.57, p<.01$).

The two ADHD groups had significantly more absolute theta power than the control group (see Figures 10.1 & 10.2, centre left; $F(1,57) = 3.99, p<.05$). Significant differences were also found in the relative theta band, with the ADHD groups having more theta than the control group ($F(1,57) = 47.16, p<.001$), and the ADHD+LD group more theta than the ADHD group ($F(1,57) = 7.17, p<.01$). The two ADHD groups had a greater difference between the midline and the two hemispheres at frontal compared with posterior regions, than did the control
Figure 10.1 Frequency distribution and ratio coefficients as a function of scalp region, from frontal to posterior regions, for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre left), Absolute Alpha (centre), Absolute Beta (centre right), Theta/Alpha (bottom left), Theta/Beta (bottom right).

group (F(1,57) = 4.61, p<.05). This indicated that power differences across the scalp, between the midline and the two hemispheres, were more equipotential in the control group than the ADHD groups.

In the absolute alpha band (Figure 10.1, centre), the control group had greater power than the two ADHD groups (F(1,57) = 7.27, p<.01). This group
Figure 10.2 Frequency distribution and ratio coefficients as a function of scalp region, sagittal section, for Total Power (top left), Absolute Delta (top right), Absolute Theta (centre left), Absolute Alpha (centre), Absolute Beta (centre right), Theta/Alpha (bottom left), Theta/Beta (bottom right).

The difference was greater in posterior regions than frontal regions ($F(1,57) = 7.27$, $p<.01$). The difference between central regions and the mean of the frontal and posterior regions was also greater in control subjects than the two ADHD groups ($F(1,57) = 6.72$, $p<.05$), as was the difference between the midline and the two hemispheres ($F(1,57) = 6.65$, $p<.05$). A hemispheric difference was found between the two ADHD groups (Figure 10.2, centre), with the difference between groups being greater in the right hemisphere than the left hemisphere ($F(1,57) = $
5.97, p<.05), and this hemispheric difference was greater in the posterior regions than the frontal regions (F(1,57) = 4.98, p<.05). For relative alpha, the control group had more activity than the two ADHD groups (F(1,57) = 35.93, p<.001) and the ADHD group had more alpha than the ADHD+LD group (F(1,57) = 4.33, p<.05). The difference between the control group and the two ADHD groups was greater in posterior than frontal regions (F(1,57) = 11.61, p<.001). In the ADHD groups, the midline had less power than the two hemispheres in frontal regions, and greater power than the two hemispheres in the posterior regions, whereas, in the control group, midline power was greater than the two hemispheres in all regions (F(1,57) = 4.79, p<.05). The difference between the two ADHD groups was greater in the left hemisphere than the right hemisphere (F(1,57) = 4.19, p<.05).

The control group had greater levels of absolute beta power than the two ADHD groups (Figures 10.1 & 10.2, centre right; F(1,57) = 4.41, p<.05), with this difference being greater in the posterior regions than the frontal regions (F(1,57) = 5.04, p<.05). For relative beta, the control group had more power than the ADHD groups (F(1,57) = 5.00, p<.05) and this was greater in the frontal regions than the posterior regions (F(1,57) = 9.7, p<.01). Laterally, the difference between the control group and the two ADHD groups was greater in the right hemisphere than the left (F(1,57) = 4.11, p<.05).

Significant differences were found in the theta/alpha ratio (Figure 10.1, bottom left), with the patient groups having a higher ratio than the control group (F(1,57) = 22.16, p<.001), and the ADHD+LD group having a higher ratio than the ADHD group (F(1,57) = 6.12, p<.05). Both of these differences were greater
in the frontal regions than the posterior regions ($F(1,57) = 9.09, p<.01$ and $F(1,57) = 16.65, p<.001$ respectively). The difference between the midline and two hemispheres (Figure 10.2, bottom left), was greater in the ADHD groups than the control group ($F(1,57) = 12.04, p<.001$), and this group difference was greater in the frontal regions than the posterior regions ($F(1,57) = 6.87, p<.05$).

The patient groups had a greater theta/beta ratio (Figure 10.1, bottom right) than the control group ($F(1,57) = 10.35, p<.01$). The difference between the midline and two hemispheres (Figure 10.2, bottom right), was greater in the ADHD groups than the control group ($F(1,57) = 8.18, p<.01$), and this group difference was greater in the frontal regions than the posterior regions ($F(1,57) = 4.41, p<.05$).

10.4 DISCUSSION

In Studies 1, 2, 4 and 5, the two clinical groups were compared to a normal control group. In each study, the clinical groups had more absolute and relative theta, and less relative alpha and beta than the control group. The ADHD groups also had less relative alpha in the posterior regions, and less relative beta in the frontal regions. In Studies 2, 4 and 5, ratio coefficients were calculated for the theta/alpha and theta/beta ratios. These ratios have been found to be sensitive measures of maturational changes in the EEG (Matousek et al., 1973), and for differentiating between normal children and children with ADHD (Lubar, 1991), and this was found to be the case in the current series of studies.
In the present study, the ADHD groups had less absolute and relative alpha and beta, more absolute theta, and more relative delta and theta than the control group. Regionally, the ADHD groups had less absolute alpha, relative alpha, and absolute beta in posterior regions, and less relative beta in frontal areas, than the control group. In the posterior regions, the ADHD groups had greater levels of relative delta and theta than the control group. The ADHD groups also had greater theta/alpha and theta/beta ratios compared to the control group. All of these results are consistent with the results of the earlier studies in this thesis.

EEG studies of children with LD have found excessive delta and theta wave activity in the parieto-occipital regions, along with deficiencies in relative alpha (John et al., 1980; Chabot & Serfontein, 1996). Greater relative theta and increased left hemisphere delta has also been documented (Harmony et al., 1990; Lubar et al., 1985).

The present study found that the ADHD+LD group globally had more relative theta, less relative alpha and a higher theta/alpha ratio than the ADHD group. Regionally, the ADHD+LD group had more posterior relative delta and a higher theta/alpha ratio in frontal regions, when compared with the ADHD group. Note that these differences were in EEG frequency bands that were found to differ between the ADHD group and the control group. Some researchers have suggested that the EEG differences between ADHD subtypes is only quantitative in nature, and that children with the greatest level of impairment also have the greatest level of deviation in their EEGs (Chabot & Serfontein, 1996; Study 1). Since the ADHD+LD group have the same inattentive and behavioural problems
as the ADHD group, as well as the addition of LD, the greater level of EEG
deviance in these frequency bands could be considered as an enhancement of the
electrophysiological abnormalities found in the ADHD children.

A number of studies have identified hemispheric differences, primarily
located in the posterior region, in the EEGs of LD children. Rebert, Wexler and
Sproul (1978) found greater theta power in the left parietal region compared to
the right parietal region during an eyes-open resting condition. Duffy et al. (1979)
found differences between dyslexic and normal control subjects, primarily in the
left posterior regions. Harmony et al. (1990) found increased absolute delta and
theta in the LD groups which were primarily in the left hemisphere. The results
are supportive of those from other studies that used other imaging techniques to
investigate brain functioning in LD children. PET studies involving language
tasks have found differences in the left hemisphere of learning-disabled subjects
compared with non-LD subjects (Flowers, 1993). CBF studies (Flowers, 1993)
have shown that there is an inferior left parietal component associated with word
meaning in LD children. Galaburda et al. (1985), and Kaufman and Galaburda
(1989) also found that the brains of reading-disabled individuals had significantly
more focal dysplasias, particularly in the language regions that border the sylvian
fissure, than those of normal controls.

In the present study, a number of hemispheric differences between the two
ADHD groups were also found. Group differences were greater in the right
hemisphere than the left hemisphere in the delta and alpha bands, with the
ADHD+LD group having more absolute alpha in the right hemisphere,
particularly in the right posterior region, than the ADHD group. The ADHD+LD
group also had greater left posterior absolute delta than the ADHD group, which is consistent with other studies that used absolute power measures. These results suggest that there is a distinct electrophysiological component associated with the LD diagnosis in the left posterior region.

A number of researchers have suggested that, although LD is often found in children with ADHD, the disorders are independent (Shaywitz & Shaywitz, 1991; Pliszka, 1998). In the context of the results of Studies 2 and 4, it appears that the greater EEG abnormalities found in the ADHD+LD group represent a third electrophysiological component that is distinct for LD, and independent of the ADHD diagnosis. This would account for the fact that the differences found between the two clinical groups in this study are similar to the EEG abnormalities found in other studies that compared children with LD and normal children. This independence of these disorders is further supported by the number of hemispheric differences found between the ADHD and ADHD+LD groups. In Studies 1, 2 and 4, few hemispheric differences were found between the ADHD groups. However, with the LD group, the number of hemispheric differences increased, especially in the posterior regions. These results support the identification of ADHD and LD as two distinct disorders that are electrophysiologically independent. That is, each disorder has distinct EEG components.

From these results it appears that when a child has multiple comorbid factors, the EEG results obtained represent an accumulation of these different components, with each component overlaying a further level of EEG abnormality. This indicates that EEG measures have the potential for use in the diagnosis of
some of these disorders. The reliability and specificity of these factors needs to be further examined at an individual level for the clinical use of this to be properly evaluated.

In conclusion, this study found EEG differences between children with ADHD and ADHD+LD. Widespread differences were found in relative theta and alpha, and a higher theta/alpha ratio, as well as posterior differences in relative delta. Hemispheric differences were also found in relative delta and alpha, and in absolute delta in the left posterior region. These results suggested that LD is a distinct disorder from ADHD, although the two disorders commonly occur together. The resultant EEGs from these children present as an accumulation of the EEG anomalies associated with each component of the disorders that are present. The specificity of these EEG associates of ADHD and LD may support the diagnostic use of EEG in this field.
CHAPTER 11. STUDY 7. EXCESS BETA IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: AN ATYPICAL ELECTROPHYSIOLOGICAL GROUP

This Study is under review for publication as: Clarke, A., Barry, R., McCarthy, R. & Selikowitz, M. Excess Beta in Children with Attention-Deficit/Hyperactivity Disorder: An Atypical Electrophysiological Group.
11.1 INTRODUCTION

Most EEG studies of children with ADHD have found these children have increased slow wave activity compared to normal children (Capute et al., 1968; Wikler et al., 1970; Satterfield Lesser, Saul & Cantwell, 1973). Matousek et al. (1984) found increased relative delta in posterior regions in children with minimal brain dysfunction. Mann et al. (1992) found children with ADHD had an increase in frontal absolute theta, during an eyes-open resting condition. Chabot and Serfontein (1996) found children with ADHD had an increase in absolute and relative theta, with the greatest increase being found in frontal regions and at the midline, during an eyes-closed resting condition. Lazzaro et al. (1998) found increased absolute theta in frontal regions and reduced relative beta in the posterior regions, during an eyes open condition. These results have been interpreted as ADHD representing either a maturational lag (Mann et al., 1992) or a developmental deviation (Chabot & Serfontein, 1996) in CNS functioning.

In Studies 1 and 2, a subset of the ADHD groups were identified with excessive levels of beta activity. In both of these studies, this group constituted approximately 20% of children with a diagnosis of ADHDcom. One subject with a diagnosis of ADHDin was also identified in Study 2. Chabot and Serfontein (1996) are the only other group to document the existence of this subset of children with ADHD. In their study, approximately 13% of ADHD children were found to have excess beta activity.
Studies of clinical chart recordings of EEGs have found that beta activity is not common in children and adolescents, and that this activity does not normally exceed 25μV in amplitude (Fisch, 1994). In normal awake children, Kellaway (1990) found beta activity was less than 20μV in 98% of subjects, and less than 10μV in 70%. When increased levels of beta activity have been found, they usually are associated with drug usage (Kozelka & Pedley, 1990), with beta being increased by the use of drugs such as benzodiazepines (Pichlmayr & Lips, 1980; Glaze, 1990).

EEG studies of psychiatric patients have found increased beta activity in a number of clinical groups (Gibbs & Gibbs, 1950). Increased beta has been found in schizophrenic patients (Morihisa et al., 1983), major depressive disorders (Pollock & Scheider, 1990) and associated with anxiety (Kiloh et al., 1981).

The aim of this study was to ascertain the percentage of children diagnosed as having ADHD who have excess levels of beta activity in their EEG, and to examine how their EEGs differ from other children with ADHD. A second aim was to determine if ADHD children with excess beta activity have behavioural profiles different from other children with ADHD.

11.2 METHOD

11.2.1 Subjects

298 children diagnosed with ADHD and 80 control subjects participated in this study. 208 subjects were diagnosed as ADHDcom and 90 were diagnosed as having ADHDin. All children were between the ages of 8 and 12 years and
right handed and footed. Subjects had a full-scale WISC-III IQ score of 85 or higher. The inclusion criteria used in Study 1 (section 5.2.2) was used in this study for both ADHD groups and the control group.

11.2.2 Procedure

The same procedure as Study 1 (section 5.2.3) was used in this study. The EEG was analyzed in four frequency bands: Delta (0.5-2.5Hz), Theta (2.5-7.5Hz), Alpha (7.5-13.5Hz) and Beta (13.5-20.5Hz), for both absolute and relative power, as well as the total power of the EEG (0.5-20.5Hz).

11.2.3 Statistical analysis

The analysis of this data set was conducted in three stages. In stage one, the control subjects was divided into two groups based on sex. Means and standard deviations were calculated for both groups of control subjects, in relative delta, theta, alpha and beta bands. The EEGs of each of the ADHD subjects were then compared to the means of the same sex control group. For each frequency band, the ADHD subject was deemed to have an excess or deficiency of relative power if the calculated value for the electrode site was greater than two standard deviations above or below the control mean.

In stage two, ADHD subjects with excess beta were matched on age, sex and diagnosis with a comparison group of subjects with ADHD, but without excess beta, and an age and sex matched control group. An analysis of variance
was performed examining the effects of region and group for each band in absolute and relative power. The effects of region were examined using the same planned contrasts that were used in Study 1. Within the Group factor, planned contrasts compared the ADHD without excess beta activity with the control group (to establish ADHD differences from normals and to provide a ‘typical’ ADHD comparison group) and the ADHD group with the ADHD excess beta group.

In stage three, only subjects diagnosed with ADHD combined subtype were included due to numbers being too small to allow accurate analysis of the ADHD inattentive subtype. The behavioural profile that was used in the diagnosis of ADHD was compared between the typical ADHD group and the excess beta group. This included behaviours listed in the DSM-IV (APA, 1994) for the diagnosis of ADHD combined type, as well as any other problem behaviours reported in the initial assessment.

11.3 RESULTS

11.3.1 Prevalence of ADHD with Excess Beta

The percentages of ADHD subjects with excess beta are presented in Table 11.1. From the total sample, excess beta was found in approximately 15% of ADHDcom subjects and 2% of subjects with a diagnosis of ADHDin. Excess beta was more common among male ADHDcom subjects than female ADHDcom subjects ($\chi^2 = 6.29, df=1, p<.05$); no female ADHDin subjects were found with excess beta.
Table 11.1

Percentage of Beta subjects by sex and diagnostic category.

<table>
<thead>
<tr>
<th></th>
<th>Total Sample</th>
<th>Male Subjects</th>
<th>Female Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ADHDcom</td>
<td>ADHDin</td>
<td>ADHDcom</td>
</tr>
<tr>
<td>Group</td>
<td>(N=208)</td>
<td>(N=90)</td>
<td>(N=159)</td>
</tr>
<tr>
<td>ADHD</td>
<td>84.6%</td>
<td>97.8%</td>
<td>81.2%</td>
</tr>
<tr>
<td>Beta Group</td>
<td>15.4%</td>
<td>2.2%</td>
<td>18.8%</td>
</tr>
</tbody>
</table>

A review of the EEGs found that the excess beta activity was primarily located in frontal and central electrode sites. The mean frequency ranged from 16.7 Hz to 19.3 Hz in frontal sites and 15.8 Hz to 17.7 Hz in the posterior sites. Beta spindles were apparent in 10% of the excess beta group (Figure 11.1).

11.3.2 Topography Across Groups

Across all groups, total power was greater in the posterior regions compared to the frontal regions (F(1,99) = 109.9, p<.001), and the central regions had less power than the mean of the frontal and posterior regions (F(1,99) = 75.49, p<.001). The right hemisphere had significantly greater power than the left hemisphere (F(1,99) = 25.23, p<.001), and this was greater in the posterior regions compared to the frontal regions (F(1,99) = 4.56, p<.05). The midline had greater power than the two hemispheres (F(1,99) = 217.74, p<.001), and this
Figure 11.1 Epoch (2.5 sec) from subject with frontal beta spindles.
difference was maximal at the central regions \( (F(1,99) = 233.59, p<.001) \). The difference between the frontal and posterior regions, and the central region was greater in the right hemisphere compared to the left hemisphere \( (F(1,99) = 5.46, p<.05) \).

In absolute delta, the posterior regions had greater power than the frontal regions \( (F(1,99) = 41.63, p<.001) \), and the central regions had less power than the mean of the frontal and posterior regions \( (F(1,99) = 17.86, p<.001) \). An effect of laterality was found, with the right hemisphere having greater power than the left hemisphere \( (F(1,99) = 13.56, p<.001) \), and the midline having greater power than the two hemispheres \( (F(1,99) = 347.18, p<.001) \). The difference between the midline and the two hemispheres was greatest at the central regions \( (F(1,99) = 237.40, p<.001) \).

For relative delta, more power was found in frontal regions than posterior regions \( (F(1,99) = 309.84, p<.001) \), and the central regions had more delta than the mean of the frontal and posterior regions \( (F(1,99) = 18.54, p<.001) \). A significant effect of laterality was found with the midline having less power than the two hemispheres \( (F(1,99) = 27.69, p<.001) \). This difference was greater at the frontal regions compared to the posterior regions \( (F(1,99) = 33.84, p<.001) \), and was smaller at the central regions compared to the mean of the frontal and posterior regions \( (F(1,99) = 67.70, p<.001) \). The difference between the central regions and the mean of the frontal and posterior regions was greater in the left hemisphere than the right hemisphere \( (F(1,99) = 7.43, p<.05) \).

In absolute theta, greater power occurred in posterior regions compared to the frontal regions \( (F(1,99) = 33.22, p<.001) \), and the central regions had less theta than the mean of the frontal and posterior regions \( (F(1,99) = 4.24, p<.05) \). Laterally, the right hemisphere had more power than the left hemisphere \( (F(1,99) \)
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= 14.70, p<.001), and this was greater in the posterior regions compared to the frontal regions (F(1,99) = 4.51, p<.05). The midline had greater power than the two hemispheres (F(1,99) = 247.10, p<.001), and this difference was maximal at the central regions (F(1,99) = 267.40, p<.001). The difference between the central regions and the mean of the frontal and posterior regions was greater in the right hemisphere than the left hemisphere (F(1,99) = 7.19, p<.01).

For relative theta band, more theta was found in the frontal regions compared to the posterior regions (F(1,99) = 69.85, p<.001), and the central regions had more theta than the mean of the frontal and posterior regions (F(1,99) = 165.04, p<.001). Laterally, the midline had more theta than the two hemispheres (F(1,99) = 329.34, p<.001). This difference was greater at the frontal regions than the posterior regions (F(1,99) = 180.47, p<.001), and maximal at the central regions (F(1,99) = 46.78, p<.001). An effect of laterality was found with the left hemisphere had more power than the right hemisphere (F(1,99) = 8.17, p<.01), and this difference was greater in the frontal regions compared to the posterior regions (F(1,99) = 4.43 p<.05).

In absolute alpha, greater power was found in the posterior regions than the frontal regions (F(1,99) = 149.34, p<.001), and the central regions had less power than the mean of the frontal and posterior regions (F(1,99) = 137.67, p<.001). An effect of laterality was found with the left hemisphere having less power than the right hemisphere (F(1,99) = 12.41, p<.01), and this difference was greater in the posterior regions than the frontal regions (F(1,99) = 9.81 p<.01). The midline had more power than the two hemispheres (F(1,99) = 55.54, p<.001). This was greater in the posterior regions compared to the frontal regions (F(1,99) = 7.81, p<.01), and maximal in the central regions (F(1,99) = 8.86 p<.01). The difference between the central regions and the mean of the frontal and posterior regions was greater in the right hemisphere than the left hemisphere (F(1,99) = 7.33, p<.01).
For relative alpha, more power was found in the posterior regions compared to the frontal regions ($F(1,99) = 760.05, p<.001$), and less power at the central regions than the mean of the frontal and posterior regions ($F(1,99) = 230.65, p<.001$). An effect of laterality was found with the difference between the two hemispheres being greater in the posterior regions compared to the frontal regions ($F(1,99) = 12.24, p<.001$). The difference between the midline and the two hemispheres was greater at the posterior regions compared to the frontal regions ($F(1,99) = 5.06, p<.05$), and maximal at the central regions ($F(1,99) = 33.82, p<.001$).

For absolute beta, the central regions had less power than the mean of the frontal and posterior regions ($F(1,99) = 53.95, p<.001$). Laterally, greater power was found in the right hemisphere compared to the left hemisphere ($F(1,99) = 31.04, p<.001$), and this was greater in the posterior regions compared to the frontal regions ($F(1,99) = 10.95, p<.01$). Greater power occurred at the midline compared to the two hemispheres ($F(1,99) = 13.15, p<.001$), and this was maximal at the central regions ($F(1,99) = 8.96, p<.01$).

For relative beta, more power was found in the frontal regions compared to the posterior regions ($F(1,99) = 201.47, p<.001$). Laterally, the midline had less power than the two hemispheres ($F(1,99) = 241.84, p<.001$). The difference between the midline and the two hemispheres was greater at frontal regions compared to the posterior regions ($F(1,99) = 22.34, p<.001$), and maximal at the central regions ($F(1,99) = 51.87, p<.001$). The difference between the two hemispheres was greater in the posterior regions compared to the frontal regions ($F(1,99) = 29.00, p<.01$).

11.3.3 Typical ADHD versus control group
Figure 11.2 Absolute power from frontal to posterior regions: Total Power (top left), Absolute Delta (top right), Absolute Theta (centre), Absolute Alpha (bottom left), Absolute Beta (bottom right).

In absolute delta (Figure 11.2, top right), the ADHD group had more power than the control group (F(1,99) = 7.35, p<.01). Laterally (Figure 11.3, top right), the difference between the midline and the two hemispheres was greater in the ADHD group than the control group (F(1,99) = 5.55, p<.05), with maximal power occurring at the midline. In relative delta (Figure 11.4, top left), the difference between the control group and the ADHD group was greater in the frontal regions than the posterior regions (F(1,99) = 6.31, p<.05).
Figure 11.3 Absolute power from frontal to posterior regions, sagittal section for: Total Power (top left), Absolute Delta (top right), Absolute Theta (centre), Absolute Alpha (bottom left), Absolute Beta (bottom right).

In absolute theta (Figure 11.2, centre), the ADHD group had more activity than the control group (F(1,99) = 15.88, p<.001) and this difference was greater in the posterior regions, than the frontal regions (F(1,99) = 5.45, p<.05). Laterally (Figure 11.3, centre), the difference between the midline and the two hemispheres was greater in the ADHD group than the control group (F(1,99) = 16.7, p<.001).
The ADHD group had more relative theta (Figure 11.4, top right) than the control group (F(1,99) = 86.11, p<.001). The difference between the midline and the two hemispheres (Figure 11.5, top right) was greater in frontal regions than posterior regions, in the ADHD group than the control group (F(1,99) = 8.38, p<.01).

The ADHD group had less relative alpha (Figure 11.4, bottom left) than the control group (F(1,99) = 31.25, p<.001). This difference was greater in the posterior regions, compared to the frontal regions (F(1,99) = 12.88, p<.001) and less at the central regions than the mean of the frontal/posterior regions (F(1,99) =
Figure 11.5 Relative power for the Left Hemisphere, Right Hemispheres, and the Midline: Relative Delta (top left), Relative Theta (top right), Relative Alpha (bottom left), Relative Beta (bottom right).

5.46, p<.05). In relative beta (Figure 11.4, bottom right), the control group had greater power than the ADHD group (F(1,99) = 12.49, p<.001). No significant difference were found in total power, absolute alpha or absolute beta (Figures 11.2 and 11.3, top left, bottom left and bottom right).

11.3.4 Excess beta versus ADHD group

No significant group differences or interactions were found in total power or absolute delta (Figures 11.2 and 11.3, top left and top right).
The excess beta group had less relative delta (Figure 11.4, top left) than the ADHD group (F(1,99) = 8.42, p<.01) and this difference was greater in the frontal regions, in comparison with the posterior regions (F(1,99) = 8.87, p<.05).

Laterally (Figure 11.5, top left), the difference between the midline and the two hemispheres was less in the beta group (F(1,99) = 5.12, p<.05), and this difference between the midline and the two hemispheres was greater in the frontal regions than the posterior regions (F(1,99) = 8.15, p<.01).

For absolute theta (Figure 11.2, centre), the excess beta group had less power than the ADHD group (F(1,99) = 86.11, p<.001) and this difference was greater in the posterior regions, compared to the frontal regions (F(1,99) = 6.69, p<.05). Laterally (Figure 11.3, centre), the difference between the midline and the two hemispheres was less in the beta group (F(1,99) = 8.88, p<.01).

In relative theta (Figure 11.4, top right), the excess beta group had less theta than the ADHD group (F(1,99) = 7.98, p<.01). Laterally (Figure 11.5, top right), the difference between the left and right hemispheres was greater in the excess beta group (F(1,99) = 5.26, p<.05).

No significant group differences or interactions were found in absolute alpha (Figures 11.2 and 11.3, bottom left). The excess beta group had more relative alpha (Figure 11.4, bottom left) than the ADHD group (F(1,99) = 7.54, p<.01) and this effect was greater in the posterior regions, compared to the frontal regions (F(1,99) = 11.14, p<.001).

The excess beta group had greater absolute beta (Figure 11.2, bottom right) than the ADHD group (F(1,99) = 60.15, p<.001). This difference was greater in the frontal regions than the posterior regions (F(1,99) = 23.4, p<.001).
and less at the central regions than the mean of the frontal/posterior regions (F(1,99) = 14.32, p<.001). Laterally (Figure 11.3, bottom right), the difference between groups was greater in the right hemisphere than the left hemisphere (F(1,99) = 19.28, p<.001) and this difference was greater in the frontal region than the posterior regions (F(1,99) = 9.5, p<.01). The excess beta group also had more relative beta (Figure 11.4, bottom right) than the ADHD group (F(1,99) = 164.66, p<.001) and this was greater at the frontal regions, compared to the posterior regions (F(1,99) = 109.13, p<.001). Laterally (Figure 11.5, bottom right), the difference between groups was greater in the right hemisphere compared to the left hemisphere (F(1,99) = 4.62, p<.05). The difference between the midline and the two hemispheres was greater in the excess beta group (F(1,99) = 21.27, p<.001) and this group by laterality interaction was greater at the frontal regions than the posterior regions (F(1,99) = 8.68, p<.01).

11.3.4 Symptom Profile Differences

No significant differences were found between the two ADHD groups on their behavioural profiles in regard to the DSM-IV Hyperactive/Impulsive or Inattentive checklists. Five behaviours, other than those in the DSM-IV checklists were noted in the initial assessments. These were poor self esteem, moody or prone to temper tantrums, situationally aggressive at home (not sufficient to be diagnosed as having a conduct or oppositional defiant disorder), easily frustrated and socialisation problems. The only behaviour where a significant difference was found between the typical ADHD and excess beta groups was moody/prone
to temper tantrums. Typical ADHD children’s files noted this in 23.5% of cases, compared with 76.5% of cases for the children with excess beta ($\chi^2 = 6.48$, df=1, p<.05).

11.4 DISCUSSION

Children with ADHD have been found to have elevated slow wave activity when compared with normal children (Capute et al., 1968; Satterfield, Cantwell, Saul, Lesser et al., 1973; Satterfield & Cantwell, 1974). Mann et al. (1992) found that ADHD subjects had an increase in absolute amplitude in the theta band in frontal regions and a decrease in beta in posterior regions. This was confirmed by Lazzaro et al. (1998) who found that the ADHD group had increased absolute theta and alpha 1 activity in frontal regions and reduced relative beta in posterior regions. Matsuura et al. (1993) found that children with ADHD had a higher average amplitude of delta, higher percentage time of delta and slow theta, and lower percentage time of alpha than normal control subjects. Janzen et al. (1995) found that ADHD children had a significantly higher theta amplitude than control subjects. In the ADHD groups, Chabot and Serfontein (1996) found an increase in absolute and relative theta, with the greatest increase being found in frontal regions and at the midline, in comparison to normal control subjects.

Studies 1 and 2 found EEG differences between children with ADHDcom, ADHDin and control subjects. These differences occurred across all sites with the ADHD groups having greater absolute and relative theta and less relative alpha
and beta than control subjects. In posterior regions the ADHD groups had more relative delta than the control group. In each of these measures, the ADHDin group was positioned between the ADHDcom group and the control group. In Study 4, the differences between the clinical groups and the control group that were found in Studies 1 and 2 were still present, although some of the differences between the two clinical groups were not replicated.

In Studies 1 and 2 a subset of the ADHD children was identified who had excessive levels of beta activity, constituting approximately 20% of children with ADHDcom. Chabot and Serfontein (1996) found that approximately 13% of children with ADHD had excess beta activity. These children were excluded from the group analyses in Studies 1, 2 and 4.

The present study found that approximately 15% of children with ADHDcom and 2% of children with ADHDin had excess beta activity, which is consistent with these other studies. The beta activity was often high amplitude and in the frontal regions, and varied from 16 to 19 Hz. Beta in the 18 to 25 Hz range is often viewed as a medication effect (Fisch, 1994). However, in this study, no subjects had a history of medication for ADHD and were not prescribed any other form of medication at the time of assessment. For this reason, the beta levels cannot be seen as the result of medication. Beta levels in children of up to 60 μV have also been found in stage 1 and 2 sleep (Kellaway & Fox, 1952). All subjects were constantly checked for drowsiness during the recording of the EEG, and for this reason, the results are not believed to be associated with the subjects’ state of alertness.
Sex differences were also found in this group, with excess beta activity occurring more often in male subjects. Within clinical settings, sex differences have been found between children referred for treatment, with girls often being referred at younger ages (Arcia & Conners, 1998). In Study 4, the difference between the clinical groups, and the ADHD groups was smaller in female subjects than in the male subjects. This was considered to have resulted from a referral bias within the clinical group sample. It is also possible that this referral bias resulted in the lower numbers of females with excess beta activity being identified in the sample rather than excess beta being sex linked.

To quantify exactly how the excess beta group differed from typical ADHD subjects, a sex and age-matched ADHD comparison group was used to compare both EEG and behavioural differences. The ADHD comparison group was first compared to normal control subjects, to determine whether this group had EEGs which were consistent with other ADHD studies. The ADHD group had more absolute delta and frontal relative delta, greater absolute relative theta, and less relative alpha and beta than control subjects. The ADHD group also had an increase in frontal midline theta. These results are consistent with the results of Studies 1, 2 and 4.

The excess beta group had EEG profiles which were different from both normal subjects and typical ADHD subjects. In absolute power, the excess beta group had less theta and more beta than the typical ADHD group. The excess beta group also had more fast wave activity in the relative alpha and beta bands. In comparison to this, the ADHD group was found to have more slow wave activity, with significant group differences being found in relative delta and theta. No
group differences were found in total power, which would suggest that there was a replacement of theta activity by beta in the EEG of the excess beta group.

In both absolute and relative beta, maximal group differences were found in the frontal regions. Studies of children with ADHD have found neuropsychological deficits which suggest that the frontal cortex or regions projecting to the frontal cortex are dysfunctional in at least some ADHD children (Faraone & Biederman, 1998). In hyperactive children, these appear to be frontal lobe mediated self-regulation deficits, such as in inhibition control (Rubia et al., 1998). Neuropsychological studies of subtypes of ADHD in adults have found deficits in the area of executive control type functioning, which could be linked to dysregulation of frontal lobe systems (Gansler et al., 1998). Study 2 found three EEG measures in the frontal regions, in the ADHDcom group that were not present in the ADHDin group. These were most likely to be associated with frontal lobe dysregulation in the ADHDcom group. Most of the subjects in the excess beta group had a hyperactive component to their diagnosis, and as the excess beta activity predominated in the frontal regions, it would appear that frontal lobe functioning is also involved in the behavioural disorders found in this group of ADHDcom subjects. The only diagnostic behavioural difference between the two ADHD groups was that the excess beta group were more prone to temper tantrums and were more moody. All other behavioural symptoms were the same in both groups. Both mood and temper problems could be associated with dysfunction in the frontal lobe systems associated with self-regulation and inhibition control, although more research is needed to determine why these
systems are functioning in such a different way in two groups of children who are behaviourally very similar.

Although EEG studies of children with ADHD have typically found increased levels of slow wave activity, the interpretation of what these results represent has been contentious. Some researches have proposed that ADHD is the result of a developmental lag in the CNS (Kinsbourne, 1973a; Mann et al., 1992), while others have viewed these results as representing a developmental deviation of the CNS (Chabot & Serfontein, 1996). Bresnahan et al. (1999) investigated changes in the EEG of ADHD subjects who were divided into three age groups, children, adolescents and adults. The results indicated that theta activity remained elevated in adults but there was a decrease in beta activity with age. From these results, it was concluded that beta activity may be linked to hyperactivity and increased theta activity to impulsivity, though this needed further investigation.

Study 4 found that with increasing age, power changed at a greater rate in the ADHDcom group than in the ADHDin group, with power levels between the two groups becoming similar with age. These results suggest that ADHD has two components, with the hyperactive/impulsive component maturing with age and the inattentive component remaining more stable. The excess beta group in this study would have to be viewed as having an EEG profile that represents a developmental deviation of the CNS, rather than a maturational lag. This EEG profile could not be seen as normal for a person at any age. If the assumption in this study is correct, and the beta is being generated by the same systems that are normally associated with excess theta in ADHDcom subjects, then this poses the question of, do these systems mature with age as has been found in typical
ADHDcom subjects? If maturation does occur in this group, and the beta normalised with age, then these two groups of ADHDcom children are probably neuroanatomically similar. If maturation does not occur, then it is possible that this group of children represent a separate subgroup of the disorder. It is also not known whether the behaviour symptoms found in this group change with age, as is found in other groups with ADHD, or how well this group responds to medication.

This study found that children with excess beta represent a small independent subset of children diagnosed with ADHD, primarily males with a diagnosis of ADHDcom. Behaviourally, this group was similar to other children with ADHD, although more prone to temper tantrums and moodiness. The excess beta activity was primarily found in the frontal regions and is probably associated with systems associated with self-regulation and inhibition control in the frontal lobes, although it is not known why these systems are functioning in such a different manner.
CHAPTER 12. DISCUSSION
12.1 OVERVIEW OF STUDIES

A number of studies have investigated EEG differences between children with ADHD and normal children. These studies primarily have focused on hyperactive children, with few studies investigating EEG differences between the subtypes of the disorder. Study 1 aimed to replicate the generally-reported findings of differences between children with ADHD and normal children. This study also aimed to expand the knowledge of ADHD by examining EEG differences between two subtypes of the disorder. Three groups of 20 children participated in this study. These consisted of two groups of children with ADHD and a control group. Results indicated that absolute and relative theta, and relative alpha and beta, differentiated between children with ADHDcom, ADHDin and control subjects. In posterior regions, relative delta estimates were able to differentiate between all three experimental groups. These results confirmed that EEG differences existed between children with ADHD and normal children, as well as indicating EEG differences between the two subtypes of the disorder. The differences between the two subtypes appeared to be a quantitative difference, with the ADHDcom group exhibiting the greatest level of behavioural problems of the two subtypes, and also having the greatest degree of EEG deviation from normal children. The results of this study also suggested that ADHD resulted from a maturational lag in CNS functioning.

In Study 2, a replication of Study 1 was conducted to test the reliability of the group differences found between the ADHD groups and the control group, as well as those between the two ADHD groups. This study also aimed to extend the
investigation of electrophysiological differences between the two subtypes of ADHD by using calculations of ratio coefficients between frequency bands, and the mean frequency in each band, to determine the nature of the underlying neurological differences in this disorder. Forty subjects were used in each of the three groups. These children were independent of those used in Study 1. The results showed a high level of replication of Study 1 results for relative power. All relative power results for the comparison of the two ADHD groups with the control group that were significant in the Study 1 were also significant in Study 2. The group differences in relative theta, alpha and beta bands, as well as posterior differences in the delta and alpha bands, and frontal differences in the beta band, were all replicated.

The results were less stable in the absolute power measures. In absolute theta, the difference between the ADHD groups and the control group was replicated. In the alpha and beta bands, a strengthening of the effect of group was found, with results that were approaching significance in Study 1 reaching statistical significance in Study 2. Differences in midline delta and theta remained stable over the two studies. However, the previously-noted differences in theta at the frontal midline, and in posterior beta, failed to reach significance in Study 2. These results were again largely consistent with previous studies of ADHD conducted using other clinical group criteria.

Group differences were found in the theta/alpha, theta/beta and slow/fast ratios between normal children and the two groups of children with ADHD. The results for the theta/alpha and theta/beta ratios indicated greater levels of slow wave activity in the two clinical groups. A similar result was found for the mean
frequency of the alpha and beta bands, with the ADHD groups having a lower mean frequency than controls. In the lower frequency bands, clinical subjects had higher mean frequencies in the delta band and higher ratio coefficients for the delta/theta ratio. These results suggested that ADHD is associated with a deviation from normal development in CNS functioning, which is in contradiction to the conclusions drawn in Study 1.

In regard to the differences between the subtypes of ADHD, Study 2 found seven main effects that differentiated the ADHDin and ADHDcom groups. In each of these, the ADHDin group was positioned between the ADHDcom group and the control group. Additionally, however, group differences were found in the frontal regions in absolute and relative theta, and the theta/alpha ratio, that were indicative of a qualitative difference between the two ADHD groups. In these measures, the activity in the frontal regions increased from the central to frontal regions in the ADHDcom group, but decreased in the ADHDin group. It was concluded that the elevated frontal activity in the ADHDcom group indicated frontal lobe dysfunction, whereas children with ADHDin may have other forms of CNS dysfunction which are not primarily associated with frontal lobe functioning, or are associated with different types of frontal lobe dysfunction.

In Study 3, maturational changes and sex differences were investigated in normal children. This was conducted to establish a comparison group for an analysis of age-related change in the EEG of the two ADHD groups used in this series of studies. This study also investigated age effects in the relationship between EEG activity in the two hemispheres and at the midline, which have not
been reported previously. Forty normal boys and forty normal girls between the ages of 8 and 12 years participated in this study. Results indicated that absolute delta activity decreased with age. In the relative power bands with increasing age, a decrease was found for the delta and theta bands, and an increase in the alpha and beta bands. Relative delta and theta reduced and alpha increased faster with increasing age, in the posterior regions than the frontal regions. Laterally, the midline had greater power than the two hemispheres but this difference became less with age in absolute delta and in the theta/beta ratio. At the same time, midline absolute beta band power was found to increase at a greater rate than in the two hemispheres. These results indicated that maturational changes occur at the midline regions faster than in the two hemispheres.

Study 3 found sex differences in the absolute theta and relative theta and alpha bands. Males had less theta and more alpha than females. Regionally, there was less relative theta and more absolute and relative alpha at the posterior regions in males than in females. These results indicated that females in the 8 to 12 year age group appear to have a maturational lag in the EEG, compared to males.

Study 4 investigated age and sex effects in the two subtypes of ADHD. Eighty children were used in each of the ADHDin and ADHDcom groups, and the subjects of Study 3 were used as the control group. This study used 80 male ADHD subjects from Studies 1 and 2, and 56 additional female ADHD subjects that were not used in the previous studies. This is the first EEG study to investigate sex differences in children with ADHD and one of only three studies that have investigated age changes in people with ADHD.
Age changes in the EEG of children with ADHD were investigated over a five year range. Results failed to find any simple effects of age which differed between the control group and the combined ADHD groups. Significant differences in absolute alpha and beta, and relative delta, were found in the posterior regions, with maturational changes occurring faster in the control group than the ADHD groups. In the comparison of the two ADHD groups, changes occurred faster in the ADHDcom group than the ADHDin group. The ADHDcom group power levels became similar to those of the ADHDin group with age. This was found for total power, absolute delta and theta power, and the theta/beta ratio.

These results indicated that there are two distinct components in ADHD. The first one is a hyperactive/impulsive component which normalises with increasing age. In total power, absolute delta and theta, and the theta/beta ratio, the power levels of the ADHDcom group reduced to a level that was similar to the ADHDin group. The second component is an inattentive component which does not appear to normalise with age. The differences between the control group and the ADHDin group were found to remain constant with changes in age. These results indicated that ADHD consists of both a maturational lag and a developmental deviation in CNS functioning.

Sex differences in the EEG profiles were found between the two ADHD groups and the control group in total power, absolute alpha and beta, and relative delta and alpha. The theta/alpha and theta/beta ratios were the most sensitive measures of differences between the two female clinical groups. With increasing age, changes occurred faster in male ADHD subjects than females, in all absolute power measures, and in relative alpha. These results indicated that, in most
frequency bands, differences between the ADHD group and control subjects was smaller in females than males, and that changes with age occurred faster in male subjects. This was interpreted as representing a referral bias within the females patients, and identified the need for independent measures of ADHD, that do not rely on reports from adults who know the child, to be developed.

Most studies have investigated the EEG of children with ADHD without accounting for the possible effects of other comorbid disorders. Research has shown that ADHD commonly occurs with a number of other behavioural and learning disorders (Arnold & Jensen, 1995). Study 5 investigated EEG differences between children with a diagnosis of ADHDcom with and without comorbid ODD. Twenty children with a diagnosis of ADHDcom+ODD were used in this study, who had not been previously used in any other studies. In the Study 5, the ADHD groups had less relative alpha and beta than the control group. The ADHD groups also had more absolute and relative theta than the control group. Regionally, the ADHD groups had less relative alpha and more relative delta in posterior regions and less relative beta in the frontal regions, than the control group. This study also found that the theta/alpha and theta/beta ratios differentiated between the ADHD groups and the control group. These results are the consistent with those found in Studies 1, 2 and 4, except for the posterior increase in relative delta which was not found in Study 4.

In the comparison of the two clinical groups, only two regional EEG differences were found. In absolute theta, the difference between the two groups was greater in the right hemisphere compared to the left hemisphere, with the ADHD+ODD group having less power than the ADHD group. The second
difference was in relative alpha, with the difference between the midline and the
two hemispheres, in the posterior regions, being greater in the ADHD group than
in the ADHD+ODD group. In both of these differences, the results for the ADHD
group were more extreme in comparison with the control group, than were those
obtained for the ADHD+ODD group. This suggests that the group differences
found between the ADHD+ODD group and the control group appear to be
specific to the ADHD diagnosis. These results support a model of ODD based on
social-environmental factors rather than resulting from CNS functioning, and
indicate the specificity of the ADHD EEG anomalies.

In Study 6, the effects of comorbid LD on the EEG of children with
ADHD were examined. Twelve new subjects with ADHD+LD who had not been
used in any previous studies, were included. This study found that the
ADHD+LD had more relative theta, less relative alpha, and a higher theta/alpha
ratio than the ADHD group. Regionally, the ADHD+LD group had more
posterior relative delta and a higher theta/alpha ratio in frontal regions, than the
ADHD group. A number of hemispheric differences were also found. In absolute
delta, the difference between groups was greater in the left posterior, than the
right posterior regions. In absolute alpha, the difference between groups was
greater in the right hemisphere than the left hemisphere, and this hemispheric
difference maximal in the posterior regions. For relative power, group differences
were greater in the left hemisphere than the right hemisphere for the delta band,
and this was reversed for the alpha band.

These results suggested that LD is a disorder distinct from ADHD,
although the two disorders commonly occur together. LD children have an EEG
abnormality in the two hemispheres, in the posterior regions, which appears to be unique to the LD diagnosis. The resultant EEGs in these children appear to be an accumulation of the EEG anomalies of each of the disorders that are present.

In Studies 1 and 2, a small group of children were identified, primarily in the ADHDcom groups, with exceptionally high levels of beta activity in their EEG. These were excluded as outliers, and replaced in the data of those studies. In Study 7, the EEGs of 298 children with ADHD were reviewed. Results indicated that 15% of the ADHDcom group, and 2% of the ADHDin group, had exceptionally high levels of beta. This EEG profile was more common in males than in females. The excess beta activity was found mostly in the frontal regions. An analysis of the behavioural symptoms found that children in the excess beta group were more moody and more prone to temper tantrums than typical children with ADHD. This group represented an electrophysiologically independent sample of children with ADHD.

12.2 NORMAL DEVELOPMENT

Within the EEG literature for ADHD, the majority of studies have considered their results in terms of what is known about EEG maturation in normal children. Researchers have proposed a number of neurodevelopmental models of ADHD which conceptualise the disorder as being predominately a maturational lag or developmental deviation in CNS functioning. The problem with these studies is that they have not investigated age related maturational changes within the clinical population. These models have had a further
limitation in that they are not able to adequately explain changes in the
behaviours of children with ADHD as they age, or the existence of ADHD in
adults.

In Studies 1 and 2 of this thesis, the results obtained for the ADHD groups
were compared to normal control groups. These two studies produced
contradictory results pertaining to the underlying electrophysiological
abnormality in ADHD. To evaluate the maturational changes in the ADHD
groups, it was necessary to conduct a study to identify EEG development in
normal children. Study 3 aimed to investigate maturational changes in the EEG of
normal children between the ages of 8 and 12 years.

Most of the normal developmental EEG literature has been influenced by
two major studies. The first of these was conducted by Matousek and Petersen
(1973), who studied the mean EEG amplitudes in six frequency bands, and ratio
coefficients between frequency bands, in 401 normal children and 160 normal
adolescents between the ages of 1 and 21 years. The results of this study indicated
that delta activity decreased almost linearly with age. Theta activity increased
until a child was approximately 4 years old, when it reached maximum amplitude,
and then decreased. Alpha 1 activity increased until approximately 8 years of age
and then proceeded to decrease. Alpha 2 activity increased throughout childhood,
with amplitude levels remaining mostly stable during adolescence. For beta
activity, the amplitudes decreased slightly with age. The total amplitude over all
six frequency bands was found to decrease significantly with age during
childhood, but not significantly during adolescence.
In the second study, John et al. (1980) developed 32 linear regression equations that predicted the frequency composition of the EEG for four bilateral regions of the scalp, as a function of age. Relative power data from an eyes closed, resting condition was used in this study, and the data were log transformed before the equations were developed. Since its publication, the methodology of this study has been used in most studies of normal development, where relative power measures have been used.

These two studies found slightly contradictory results. In the Matousek and Petersen (1973) study, development was not linear in every frequency band. In both the theta and alpha 1 bands, amplitudes were found to increase until a given age, and then to decrease. In contrast to these findings, John et al. (1980) claimed that EEG development was linear. The major difference between these two studies was the level of transformation performed on the data. By log transforming their data, John et al. (1980) altered their data to such an extent that they could make claims only about such log transformed data, and to extrapolate their results to raw data, as is often done in the interpretation of their findings, could be problematic.

This thesis study of normal development has added to what was already known about the nature of normal development in children. Normal development was examined in children between the ages of 8 and 12 years of age, and both males and females were included in the data set. This study did not use a transformation of the data before analysis which has the strength that the results can be more easily conceptualised. The results of this study indicated, that in general terms, frequency changes in absolute and relative power were linear in
nature. These results are not in contradiction with those of Matousek and Petersen (1973), as the present data set commenced at age 8, which is older than where non-linear changes were reported by Matousek and Petersen (1973). This study also examined topographic differences in the development of the EEG, and extended the results of previous studies by examining the relationship between the midline and the two hemispheres. The results indicated that in absolute delta, differences between the midline and the two hemispheres became more equipotential with increasing age, whereas in absolute beta, power increased at a greater rate at the midline than in the two hemispheres. This would indicate that maturational changes occurred faster at the midline than the two hemispheres.

12.3 SEX DIFFERENCES IN NORMAL CHILDREN

Within the literature there has been some debate as to whether sex differences exist in the EEGs of normal children. This has resulted from a number of conflicting studies that have reported results ranging from no sex differences (Gasser, Jennen-Steinmetz et al., 1988) to the existence of EEG differences indicative of a maturational lag in girls (Harmony et al., 1990). The present study found sex differences in absolute theta and the relative theta and alpha bands. Males had less theta and more alpha than females, which is supportive of the results of Matthis et al. (1980) and Benninger et al. (1984). Regionally, there was less relative theta and more absolute and relative alpha at the posterior regions in males than in females. Studies have shown that there appears to be a complementary relationship between an increase in alpha and a decrease in theta activity with age, and that the changes in these two bands occur earliest in
posterior regions (Gasser, Jennen-Steinmetz et al., 1988). From the current results, females in the 8 to 12 year age group appear to have a maturational lag in EEG, compared to males. Relative maturational lag has been reported as being larger in younger children and decreasing at about the age of 11 to 12 years (Matthis et al., 1980; Harmony et al., 1990). In the present study, power was found to decrease with age in the delta, theta and alpha bands in females, but levels remained mostly constant or rose slightly in males. These results are consistent with other findings that the rate of change with age is faster in females than males (Harmony et al., 1990). Benninger et al. (1984) found evidence of a pubertal spurt in the EEG of girls between the ages of 11 and 13 years. This was not confirmed by the present results, though it is possible that the age cut-off of 12 years prevented detection of such a spurt.

12.4 ADHD VERSUS NORMAL CHILDREN

ADHD has undergone considerable change in conceptualisation during the period of time that EEG has been used as a tool to investigate the disorder. Associated studies have used the criteria of minimal brain damage or disorder, hyperkinesis, or hyperactivity, and there have been four changes in criteria in the last four editions of the DSM (APA, 1968, 1980, 1987, 1994). This has resulted in the EEG literature for ADHD being fragmented, as few studies have used the same diagnostic criteria. This series of studies used DSM-IV (APA, 1994) criteria for ADHD. At the time of conducting Study 1, no EEG studies of ADHD had been published which used DSM-IV criteria. In Study 1, the aim was to
investigate whether children with a DSM-IV diagnosis of ADHD differed from normal controls in their EEG. To do this, the two ADHD groups were clustered together as a single group and compared to the control group. This was done to allow an estimation of how congruent the current results may be with other studies of ADHD which used other diagnostic criteria.

Previous studies of Hyperactive children have found an increase in slow wave activity and an increase in amplitude in the 0 to 8 Hz frequency range in the EEG compared with normal controls (Capute et al., 1968; Satterfield, Cantwell, Saul, Lesser et al., 1973; Satterfield & Cantwell, 1974). Similar findings were obtained in Study 1, with the ADHD subjects having greater levels of both absolute and relative theta over all regions. Most previous studies have found an increase in theta, primarily located in the frontal derivations (Mann et al., 1992, Chabot & Serfontein, 1996). However, this study found significantly more frontal midline theta in absolute power. The ADHD groups in Study 1 had a significant increase in relative delta in the posterior regions, which is consistent with the results of Matousek et al. (1984), who found that the greatest correlation of MBD and EEG abnormalities occurred in the relative delta band at posterior sites. Mann et al. (1992) reported that subjects with ADHD had a decrease in absolute amplitude of the beta band in posterior regions. This was also found in Study 1, with the ADHD groups having less posterior beta than the control group. Chabot and Serfontein (1996) found an increase in alpha activity in children with ADHD. This was not found in Study 1, where the ADHD groups had decreased relative alpha across all sites, with the greatest difference occurring in the posterior regions. From these comparisons, the obtained data are largely consistent with the
majority of previous studies of ADHD where an eyes closed, resting condition was used.

In Studies 2, 4, 5 and 6, the clinical groups were again clustered together and compared to the control group, to further investigate general group differences between normal children and the ADHD groups which were under investigation.

In stage one of Study 2, a replication of the first study was conducted with a larger independent sample. This was done to attempt to determine the reliability of the group differences found in Study 1.

The results of Study 2 showed a high level of replication of Study 1 results for relative power. All relative power results for the comparison of the two ADHD groups with the control group that were significant in the Study 1 were significant in Study 2. The group differences in relative theta, alpha and beta bands, as well as posterior differences in the delta and alpha bands, and frontal differences in the beta band, were all replicated.

The results were less stable in the absolute power measures. In absolute theta, the difference between the ADHD groups and the control group was replicated. However, in the alpha and beta bands, a strengthening of the effect of group was found, with results that were approaching significance in Study 1 reaching statistical significance in Study 2. Differences in midline delta and theta remained stable over the two studies. However, the differences in theta at the frontal midline, and in posterior beta, failed to reach significance in Study 2. These results were again largely consistent with previous studies of ADHD, which were conducted using other clinical group criteria.
Maturation of the normal EEG in children involves a process whereby delta and theta activity decrease and alpha and beta increase. A number of studies have calculated ratio coefficients between frequency bands to quantify these normal maturational changes, and also as a measure of EEG differences between clinical groups. Matousek et al. (1984) found the theta/alpha ratio was a good discriminator of children with different levels of severity in their diagnosis of MBD. Corning et al. (1986) used the theta/alpha ratio to evaluate changes in the EEG of children with behavioural or learning disabilities. The theta/beta ratio has also been used to evaluate the EEG of children with ADHD (Janzen et al., 1995; Lubar, 1991).

In Study 2, ratio coefficients were calculated between frequency bands, to further quantify the group differences found in Study 1. In this study, group differences were found for the theta/alpha, theta/beta and slow/fast ratios between normal children and children with ADHD. The slow/fast ratio produced the same significant between-groups results as the theta/alpha ratio, and did not provide any information which could not be obtained from the theta/alpha ratio. The theta/alpha and slow/fast ratios were the only ratios to demonstrate group differences in the frontal regions. The theta/beta ratio proved to be the most effective coefficient for differentiating the clinical group at the midline. Significant differences were found for the comparison of the midline and the two hemispheres, as well as regional differences at the frontal and central regions. These results are consistent with previous studies that have used ratio coefficients to differentiate between children with ADHD and normal children (Jansen, 1995; Lubar, 1991).
In Study 4, the experimental groups were increased to 80 subjects per group, and the ratio of males to females was changed from 4:1, to 1:1, to allow an investigation of sex differences. This study found that the ADHD groups had greater total power and less relative alpha and beta than the control group. The ADHD groups also had more absolute delta and theta, and more relative theta than the control group. Regionally, the ADHD groups had less relative alpha in posterior regions and less relative beta in frontal areas than the control group. Higher ratio coefficients were found in the ADHD groups than in control subjects, for both the theta/alpha and theta/beta ratios.

All the relative power differences found in this study were also found in Studies 1 and 2. The posterior group difference in relative delta that was found in Studies 1 and 2 was not found in this study. As was found in Study 2, absolute power measures between groups were less consistent. The only absolute measure to be found to discriminate ADHD and normal children in all three studies was theta power. The total power and absolute delta differences between ADHD and normal groups found in this study had not been found in the previous two studies. Also, the differences found in absolute alpha and beta in Study 2, were not found in this study.

The major difference between Studies 1 and 2, and Study 4, was the ratio of males to females used in the experimental groups. Study 4 found that the differences between the ADHD groups and the control group was greater in males than females, in most frequency bands. The inclusion of an equal number of females thus probably contributed to these changes in between-group results.
From this, it may be advantageous to use single sex groups in the investigation of differences between children with ADHD and normal children.

In Study 5, twenty subjects with comorbid ADHD and ODD were included. The ADHD groups had less relative alpha and beta than the control group. The ADHD groups also had more absolute and relative theta than the control group. Regionally, the ADHD groups had less relative alpha and more relative delta in posterior regions and less relative beta in the frontal regions, than the control group. The theta/alpha and theta/beta ratios differentiated the ADHD groups and the control group.

Study 6 included ADHD children with and without LD. The ADHD groups had less absolute and relative alpha and beta than the control group. The ADHD groups also had more absolute theta, and more relative delta and theta than the control group. Regionally, the ADHD groups had less absolute and relative alpha, and absolute beta in posterior regions and less relative beta in frontal areas, than the control group. In the posterior regions, the ADHD groups had greater levels of relative delta and theta than the control group. An increase in relative theta and a decrease in relative alpha were found at the frontal midline compared to the two hemispheres. The theta/alpha and theta/beta ratios differentiated between the ADHD groups and the control group.

In the results of these five studies, eight EEG measures were found that consistently differentiated normal children and the ADHD groups. These differences appear to exist irrespective of the sex of the child, or the presence of comorbid LD or ODD. The ADHD groups had more absolute and relative theta, and less relative alpha and beta than the normal children. Regionally, the ADHD
groups had less relative alpha in posterior regions and less relative beta in the frontal regions, than the normal children. The theta/alpha and theta/beta ratios were also able to differentiate between the ADHD groups and the normal children. Five of the six measures which used single frequency bands to calculate group differences were relative power measures, which is consistent with previous studies that have found high levels of variability within subject groups and poor test-retest reliability for absolute power compared with relative power (John et al., 1980). Only absolute theta was found to consistently differentiate between groups in these studies.

Most of these differences were also main effects across all sites, with only two regional differences occurring in either the frontal or posterior regions. A number of regional differences were found in some studies, but not in all. These included group differences at the midline and especially at frontal midline regions, differences in the comparison of the central regions with the mean of the frontal and posterior regions and differences between the two hemispheres. These results could possibly be interpreted in two ways. Firstly, the smaller regional differences could simply be the result of large variability in the EEGs of the different samples used in each study. Benninger et al. (1984) found that the variability in the EEGs of children in a single one year age band was greater than between age bands, and this may be what is being seen in a number of these comparisons. A second possibility is that these differences represent distinct features of the EEG profile of the various clinical populations being studied and as such, they were not present in all studies. These differences were found in relative power and in the ratio coefficients, both of which have been proposed as
more reliable measures than absolute power (John et al., 1980; Lubar, 1991). Absolute power was found to have substantial variability in nearly half of the regional comparisons between Studies 1 and 2 but relative power estimates were more consistent over the two studies. It thus appears possible that a proportion of the regional differences found may have resulted from a degree of heterogeneity among the clinical groups that were investigated in this series of studies.

12.5 DIFFERENCES IN SUBTYPES OF ADHD

A second objective of this research program was to investigate the existence and nature of EEG differences between two subtypes of children with ADHD. Most studies of the EEG in ADHD have used only children with a single global diagnosis, even though the DSM-III (APA, 1980), DSM-III-R (APA, 1987) and DSM-IV (APA, 1994) have listed multiple subtypes. Thus these studies did not address whether the ADHD groups studied were homogeneous, or whether the defined subtypes might be distinct disorders, which was questioned in the DSM-III (APA, 1980) and by other researchers (Lahey et al., 1985).

Only two studies have investigated EEG differences in subtypes of ADHD. Chabot and Serfontein (1996) investigated EEG differences in 407 children who were diagnosed as meeting the DSM-III criteria for ADHD. The children with ADHD were found to have an increase in absolute and relative theta compared with normals, with the greatest increase being found in frontal regions and at the midline. A slight elevation in relative alpha was also noted, and an increase in beta was found in a small group of subjects. The differences between
their two ADHD subtype groups were mainly differences in the degree of abnormality, rather than in the type of abnormality.

Kuperman et al. (1996) used DSM-III-R criteria to study quantitative EEG differences between children with ADHD, UADD and normal children. For relative power, the control group had more delta than the UADD subjects and less beta than both groups of children with ADHD. Only the UADD group had hemispheric differences, with decreased delta and increased beta in the left hemisphere. This study investigated topographic effects only where a significant main effect was found for the band, and this may have resulted in significant regional differences being overlooked. An eyes open condition was also used, making comparison with most other EEG studies of ADHD difficult.

The present study expanded on this limited foundation by examining EEG differences in children with a DSM-IV (APA, 1994) diagnosis of ADHDcom or ADHDin. In Study 1, significant differences between patient groups across all regions were found in the relative theta and alpha bands. The ADHDcom group had greater relative theta than the ADHDin group. In the alpha band, the reverse was found, with the ADHDin group having greater alpha than the ADHDcom group. A similar finding for relative delta in posterior regions was noted, with the ADHDcom group having greater relative delta than the ADHDin group. A difference approaching significance (p=.054) was also found for an increase in frontal midline theta, compared to the two hemispheres, with the ADHDcom group showing a greater difference than the ADHDin group. As with previous studies of subtypes of ADHD, this study demonstrated that EEG can be used to differentiate children with subtypes of ADHD. From the data obtained, the
subtypes appeared to differ in severity rather than in the nature of the underlying neurological impairment. This conclusion was drawn from the fact that the EEG results for the ADHDin group were positioned between the control group and the ADHDcom group, in every frequency band where there were significant differences between the two clinical groups, and these results were consistent with other studies (Chabot & Serfontein, 1996).

In Study 2, all significant differences between the two subtypes which were found in Study 1 were replicated. In addition to these, a number of regional differences were also found. A strengthening of absolute theta differences was found across all sites. Frontal differences in relative beta and posterior alpha were found, as well as differences between the mean of the frontal and posterior regions and the central regions, for both absolute and relative theta. While most measures again placed the ADHDin group between the ADHDcom group and the control group, the data no longer supported a simple continuum model as an explanation of the group differences.

A difference at the frontal regions was found, with the ADHDcom group having an enhancement in power which was not present in the ADHDin group. The nature of this difference was such that it could not be considered to be just a more extreme result indicative of the greater behavioural impairment found in this subtype, but rather, was suggestive of a qualitative difference.

Neuropsychological studies of children with ADHD have found deficits which suggest that the frontal cortex, or regions projecting to the frontal cortex, are dysfunctional in at least some ADHD children (Faraone & Biederman, 1998). In hyperactive children, these appear to be frontal-lobe mediated, self-regulation
deficits, such as in inhibition control (Rubia et al., 1998). Neuropsychological studies of subtypes of ADHD in adults have found deficits in the area of executive control type functioning, which could be linked to dysregulation of frontal lobe systems (Gansler et al., 1998). Different types of executive system deficits were found between the hyperactive/impulsive and inattentive subtypes of the disorder. This has led some researchers to postulate that the attentional differences between the subtypes may reflect dysfunctions in different neuroanatomical loci and different neurotransmitter systems (Barkley, 1990). In this context, it is possible that the elevated frontal theta activity in the ADHDcom group is associated with this group having frontal lobe dysfunctions as one component of the disorder, whereas children with ADHDin may have other forms of CNS dysfunction which are either less associated with frontal lobe functioning or associated with other frontal lobe systems.

The involvement of the frontal lobes in the ADHDcom group is further supported by the results of Study 7. In Studies 1 and 2, a small group of children, primarily with a diagnosis of ADHDcom were identified as statistical outliers. These children had excessive levels of beta activity rather than the expected excess of theta. This group has only been documented in one other study of ADHD (Chabot & Serfontein, 1996). Study 7 further investigated the occurrence of excess beta in a sample of 298 children with ADHD. Approximately 15% of ADHDcom subjects, and 2% of subjects with a diagnosis of ADHDin, had excess beta. The excess beta group had EEG profiles which were different from both normal subjects and typical ADHD subjects. In both absolute and relative beta, maximal group differences were found in the frontal regions. No differences were
found in total power between the two ADHD groups. This suggests that the theta activity in the typical ADHD group was replaced by beta activity in the EEG of the excess beta group. Since the profile appears to be similar, except for changes in the dominant frequency band, these results suggest that the same frontal lobe or prefrontal systems are involved in both ADHD groups, but that they are functioning in different ways. It is also important to note that this excess beta activity was primarily found in children with a diagnosis of ADHDcom, which would again suggest that two different neuroanatomical systems are operating in the combined and inattentive subtypes of ADHD.

In Study 4, age effects were investigated. This was done to determine if the EEGs of the ADHDcom and ADHDin groups matured in similar ways, which would allow an estimation of whether the two subtypes represent a continuum of a single disorder or whether there are independent components that were evidenced in the EEGs.

In the comparison of the two ADHD groups, changes occurred faster in the ADHDcom group than the ADHDin group. The ADHDcom group power levels became similar to the ADHDin with increasing age. This was found in total power, absolute delta and theta, and the theta/beta ratio. These results are highly consistent with Bresnahan et al. (1999), who found in their child and adolescent groups, that differences between an ADHDcom group and normal control group became less with age for all of these frequency bands. Between their adolescent and adult groups, the difference in power in the ADHD group persisted in the lower frequency bands, but not in the higher frequencies.
Study 4 found that power levels in the ADHDin group were deviant from normal control subjects but matured in parallel to the control subjects with increasing age. In the ADHDcom group, power levels were found to be even more extreme than the ADHDin group. With increasing age, the power levels in the ADHDcom group approached those of the ADHDin group, but did not normalise further towards the control group. These results suggest that there are two distinct components in ADHD which are quantifiable using electrophysiological measures. The first is a hyperactive/impulsive component which appeared to normalise with increasing age. In total power, absolute delta and theta, and the theta/beta ratio, the power levels of the ADHDcom group reduced to a level that was similar to the ADHDin group. The second component is an inattentive component which does not appear to normalise with age. The differences between the control group and the ADHDin group were found to remain stable, even with changes in age. There was no reduction in the magnitude of the EEG abnormalities found between the ADHDin group and the control group.

These results suggest that the two components of hyperactivity/impulsivity and inattention are electrophysiologically independent. Measures associated with the hyperactive/impulsive component were found to change at a greater rate with increasing age than the inattentive component. In contrast, the inattentive component was found to mature in parallel to normal development, but the EEG deviation was not found to "catch up" to normal children. The existence of two distinct components is supported by studies that have investigated this issue using other measures between the groups.
Behavioural studies of the two subtypes of ADHD have found differences other than hyperactivity. Children with ADHDcom are more impulsive (Lahey et al., 1985, 1987; Hynd et al., 1991; Cantwell & Baker, 1992), have more conduct disorder problems (Barkley et al., 1990; Cantwell & Baker, 1992; Edelbrock et al., 1984; Hynd et al., 1991; King & Young, 1982; Lahey et al., 1984, 1987) and are less anxious (Lahey et al., 1984, 1987) than ADHDin children. ADHDin children are more socially withdrawn and shy (Edelbrock et al., 1984; Lahey et al., 1984), are more unpopular (Edelbrock et al., 1984; Lahey et al., 1984; Lahey & Carlson, 1991) and less socially competent (Barkley et al., 1990; Cantwell & Baker, 1992; Hynd et al., 1991). Neuropsychological studies of ADHD in adults have found different types of executive system deficits between the hyperactive/impulsive and inattentive subtypes, which are associated with different types of executive control functioning (Gansler et al., 1998).

From these results, the two principal components of hyperactive/impulsive and inattentive behaviour are independent, although commonly comorbid, disorders.

12.6 MATURATIONAL LAG VERSUS DEVELOPMENTAL DEVIATION OF THE CNS IN ADHD

Within the literature, two main models of ADHD have been proposed using electrophysiological data. These have conceptualised ADHD as either a maturational lag of the CNS or a developmental deviation. These models have been investigated through the use of behavioural studies (Kinsborne, 1973), cognitive assessment techniques (Grodzinsky & Diamond, 1992; Reitan &
Wolfson, 1985), as well as electrophysiological measures (Satterfield, Cantwell, Saul, Lesser et al., 1973).

EEG studies of children with ADHD have typically found an increase in slow wave activity, compared to normal control subjects (Capute et al., 1968; Wikler et al., 1970; Satterfield, Lesser, Saul & Cantwell, 1973), but the interpretation of what these results actually represent is disputed within the literature. Mann et al. (1992) found children with ADHD had an increase in absolute amplitude in the theta band, which occurred primarily in frontal regions during a resting condition. During cognitive tasks, ADHD children showed a greater increase in theta activity in frontal and central regions, and a decrease in beta activity in posterior and temporal regions. These children had EEG frequency distributions that resembled profiles typical of younger children, and Mann et al. (1992) concluded that ADHD reflects a maturational delay in the systems that subserve attention. Matsuura et al. (1993) found that the ADHD group had a higher average amplitude of delta, a higher percentage time of delta and slow theta, and a lower percentage time of alpha, than normal control subjects. In the ADHD group, mean maximum amplitude was found in the 8 Hz band, whereas in control subjects, this was in the 9 Hz band. Hypothetical EEG age was calculated for the clinical groups, which indicated that the children with ADHD showed signs of a maturational lag in brain functioning. Lazzaro et al. (1998) found increased absolute theta in frontal regions and reduced relative beta in the posterior regions, during an eyes open condition. All of these results have been considered supportive of the maturational lag model.
Similar results have been found in a number of other studies, but the conclusions drawn from these was that the EEG profiles found in children with ADHD represent a deviation from normal development. Chabot and Serfontein (1996) found children with ADHD had an increase in absolute and relative theta, with the greatest increase being found in frontal regions and at the midline. They concluded that the EEG patterns represented a deviation from normal development, rather than a maturational lag.

The major limitation of most of these studies is that they used data from a single time point and extrapolated from the normal developmental literature, to estimate whether their ADHD data fitted one particular model. Few studies have investigated changes in the EEG of ADHD children with increasing age, using DSM criteria for diagnosis. Bresnahan et al. (1999) investigated age-related changes in the EEG of ADHD children, adolescents and adults, and found that theta activity remained elevated in adult patients but that there was an increase and normalisation of beta activity with age.

In Study 4, the second aim was to investigate whether maturational changes did occur in the two clinical group, which could be used to determine if the underlying EEG abnormalities are associated with a maturational lag or a developmental deviation in CNS functioning. When the two ADHD groups were combined and compared to the control group, significant differences were found in the posterior regions. Maturational changes in relative delta, and absolute alpha and beta, occurred faster in the control group than the ADHD groups. Maturation has been found to occur earliest in posterior regions (Benninger et al., 1984; Gasser, Verleger et al., 1988), and these results indicated that maturation was
delayed in the ADHD groups. In all other measures, no age by group effects were found, which indicated that maturation was occurring in parallel to the control group. However, there was no evidence that the discrepancies between the ADHD groups and the control group were reducing with age.

In the comparison of the two ADHD groups, as age increased, the power levels in the ADHDcom group approached those of the ADHDin group, but did not normalise further towards the control group. These results suggest that there are two distinct components in ADHD which are quantifiable using electrophysiological measures. The results of this study have found that the hyperactive/impulsive and inattentive components change in different ways. The hyperactive/impulsive component was found to mature with age, which is consistent with a maturational lag model. In contrast to this, the inattentive component was found to mature in parallel, but at a level deviant from normal children, which supports the existence of a developmental deviation in the inattentive component of the disorder. These results support a two component model of ADHD, with the hyperactive/impulsive component resulting from a maturational lag, and the inattentive component being associated with a developmental deviation. A two component model of ADHD is better able to explain some of the behavioural changes found in people with ADHD. In children, the predominant features of ADHD which lead to a referral for treatment are the hyperactive behaviours such as restlessness and being fidgety. In adults, the hyperactive symptoms diminish, but the inattentive symptoms remain (Bellak & Black, 1992). Study 4 found that the hyperactive/impulsive component of the EEG matured and normalised with increasing age, which would explain the
reduction in the overt behavioural component of ADHD found in adults. The inattentive component of the EEG was found to be more stable with increasing age, which also accounts for the finding of predominantly inattentive features of ADHD in adults.

12.7 SEX DIFFERENCES IN ADHD

This study is the first to investigate the existence of sex differences in the EEG of children with ADHD. Study 4 found sex differences between the control group and the two ADHD groups for total power, absolute alpha and beta, and relative delta, theta and alpha. In all of these frequency bands, except total power, the difference between the control group and the combined ADHD groups was larger in males than females. With increasing age, maturational changes also occurred faster in male ADHD subjects than female ADHD subjects, for absolute delta, theta, alpha and beta, and relative alpha. All male and female subjects met the criteria for the group they were included in, which means that the observed effects were due only to the sex of the subjects.

Studies have shown that girls are often referred for treatment at younger ages than boys because their behaviour is considered more abnormal (Arcia & Conners, 1998). However, in boys, that same level of behavioural symptomatology is considered relatively normal, and results in later referrals being made for assessment and treatment. As the female subjects in this study did meet the criteria for ADHD, the most plausible explanation for the lower level of EEG deviance in the female group is that results were affected by a sex-related
referral bias within the sample. If this is true, then the traditional method of diagnosing childhood behavioural problems, which relies primarily on reports from adults who have contact with the child, must be viewed as having limitations. An adult may perceive a girl's behaviour to be more deviant than a boy's behaviour. However, the lower level of electrophysiological deviance found in the female groups would suggest that these perceptions may be subjective and inaccurate. This indicates the need for other independent measures of childhood psychopathology to be developed for use in the diagnosis of psychological disorders in children. As electrophysiological indices have been found that differentiate at a group level between children with ADHD and normal children, these may have utility in the assessment and treatment of individual children with behavioural disorders. This needs to be investigated in future research.

12.8 COMORBIDITY

Within the electrophysiological literature, the issue of comorbidity of ADHD with other disorders, and their effects on EEG results, has not been considered in detail. ADHD commonly has been found to occur with other conditions. As many as two thirds of elementary school-age children with ADHD, who have been referred for clinical evaluation, have at least one other diagnosable psychiatric disorder (Arnold & Jensen, 1995; Cantwell, 1994b; Nottelmann & Jensen, 1995). Three of the most commonly co-occurring disorders are either CD or ODD, and LD. Rates of comorbid LD have been estimated at between 10% and 92% (Biederman et al., 1991) depending on the population studied, and
CD/ODD at between 43% (Offord et al., 1987, 1989) and 54% (Cohen et al., 1993).

Study 5 investigated EEG differences between children with ADHDcom and ADHDcom+ODD. Previous EEG studies of children with CD/ODD have typically found no EEG abnormalities in comparison to normal children (Satterfield & Schell, 1984; Hsu et al., 1985; Phillips et al., 1993). In this study, no significant main effects of group were found between the two ADHD groups. Only two regional differences were found between ADHD and ADHD+ODD children. In absolute theta, the difference between the two groups was greater in the right hemisphere compared to the left hemisphere, with the ADHD+ODD group having less power than the ADHD group. The second difference was in relative alpha, with the difference between the midline and the two hemispheres, in the posterior regions, being greater in the ADHD group than the ADHD+ODD group. In both of these differences, the results for the ADHD group were more extreme in comparison to the control group, than those obtained for the ADHD+ODD group. The ADHD+ODD group did have abnormal EEGs, but these were sufficiently similar to those of the ADHD group for the abnormalities to be considered to be associated with the ADHD component of the diagnosis and not the ODD component. Satterfield and Schell (1984) viewed delinquent behaviour as possibly associated with an underlying environmental-social factor rather than being associated with a CNS dysfunction. This conceptualisation of ODD is supported by the present results. However, it is possible that the ODD diagnosis is associated with factors which are not measurable using EEG. This poses the question that if environmental-social factors are responsible for
delinquent and antisocial behaviour, what are the processes that take place in the person, to produce these behaviours? This needs further research to determine these processes and how these may work.

In Study 6, children with ADHDcom were compared to a sample of children with ADHDcom and comorbid LD. This study found that the ADHD+LD children had more relative theta, less relative alpha and a higher theta/alpha ratio than the ADHD group. Regionally, the ADHD+LD group had more posterior relative delta, and a higher theta/alpha ratio in frontal regions, than the ADHD group. A number of hemispheric differences were also found between the two ADHD groups. In absolute delta, the difference between groups was greater in the left posterior region than the right posterior region. In absolute alpha, the difference between groups was greater in the right hemisphere than the left hemisphere, and this difference was maximal in the posterior regions. For relative power, group differences were greater in the left hemisphere than the right hemisphere in the delta band, and this was reversed in the alpha band. These differences between the ADHD+LD group and the ADHD group are similar to those found in other studies that have investigated differences between LD and normal children (John et al., 1980; Chabot et al., 1996; Harmony et al., 1990; Lubar et al., 1985). Differences in the frontal regions, as well as posterior hemispheric differences, were found between the two clinical groups. These results suggest that an additional level of dysfunction has been added to those usually attributed to the ADHD diagnosis. Whereas hyperactivity appears to have a strong association with frontal lobe functioning (Faraone & Biederman, 1998; Rubia et al., 1998; Gansler et al., 1998), the LD component of the diagnosis is
associated with differences in hemispheric function, often in posterior regions.

From the results of these studies, a number of the behavioural problems found in children appear to be independent disorders which commonly occur together. Lahey et al. (1985) proposed that the two subtypes of ADHD are substantially dissimilar and should not be considered as subtypes of the same disorder. This thesis identified two distinct EEG components in children with ADHD. The first was found to mature with increasing age, and was associated with hyperactive/impulsive behaviour. This was primarily associated with frontal lobe functioning, although other group differences were identified. The second component was more stable with increasing age and was associated with symptoms of inattention. These results are supportive of Lahey et al.’s (1985) assertion that the hyperactive/impulsive and inattentive subtypes of ADHD should be considered as substantially distinct disorders.

This research also investigated the effects of comorbid oppositional defiant disorder and learning disabilities on the EEGs of ADHD children. In the study of comorbid ADHD+ODD, EEG components were identified that were attributable to the diagnosis of ADHD. However, no EEG component could be found that was associated exclusively with the ODD diagnosis. This suggests that ODD is an independent, but commonly occurring disorder with ADHD, although ODD cannot be measured by electrophysiological measures such as EEG. In the study of comorbid ADHD+LD, EEG results were obtained in children with ADHD+LD which were qualitatively different to those in children with ADHD alone. These results further support claims that although ADHD and LD or commonly occurring, they are independent disorders (Shaywitz & Shaywitz,
1991; Pliszka, 1998). From these results, hyperactivity/impulsivity, inattention and learning disabilities are three independent disorders with measurable electrophysiological components. ODD constitutes a fourth independent disorder which cannot be detected by the electrophysiological measures used in this thesis.

12.9 FUTURE RESEARCH

This study found mean group differences which differentiated between normal children and children with ADHD. Group differences were also found between the two subtypes of ADHD, and between groups of ADHD children with and without learning disabilities. It is clear that there are a number of EEG characteristics which are specific to ADHD and which appear independently of comorbid diagnoses of ODD and LD. Future research should investigate the reliability and specificity of these differences in individual children.

The diagnosis of childhood behavioural disorders is almost always based on descriptions from adults who have regular contact with the child. This allows for considerable variance in what is considered a normal behaviour. This is further confounded by the fact that there is little correlation between the reports of parents and teachers on many behavioural checklists that are used as diagnostic tools (Achenbach et al., 1987). These studies also identified a number of areas where an independent measure of functioning would be advantageous. The sex differences in the ADHD groups appeared to be associated with a referral bias in the sample of female subjects. Similarly, the results of Study 5 identified a possible use of EEG in the diagnosis of ADHD and ODD and possibly CD. Due
to the behavioural symptoms found in ODD/CD, a reliable diagnosis of ADHD can be hard to make, as the reported symptoms may only be the person’s perception of the child, and this may result from the ODD/CD. If EEG measures, or some other form of electrophysiological measures such as ERPs, could be demonstrated to be a reliable and specific measure of diagnostic differences at the individual level, then these measures have the potential to make a substantial contribution to the diagnosis of behavioural disorders in children.
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APPENDIX 1. PARENT INFORMATION LETTER AND PARENT CONSENT FORM
A student in the Master of Arts degree at The University of Wollongong, who is also employed as a full time member of staff of this medical practice, is presently conducting research into differences between BrainMaps of children who have been diagnosed as having an Attention Deficit Disorder. A BrainMap is the summary of information obtained after computer analysis of an electroencephalogram (EEG). The aim of this study is to see if differences exist between the BrainMaps of different groups of children with ADD. The information needed for the study is the result of the BrainMap, the intelligence testing and the reading and spelling tests that are performed as a normal part of your child’s assessment at this practice. This information will be kept totally confidential, with no one outside the practice being allowed to see the individual results. The information collected will be pooled for statistical analysis, with no individual results being used.

Participation in this study is totally voluntary and you can discontinue your involvement at any time. If you wish to participate in this study, please sign the consent part of this form below. If you decide not to participate in this study, this will not affect your child's further treatment at this practice.

If you have any enquiries regarding the conduct of the research please contact the Secretary of the University of Wollongong Human Research Ethics Committee on (042) 213079.
THE UNIVERSITY OF WOLLONGONG

DOCTOR OF PHILOSOPHY RESEARCH

PARENTAL CONSENT FORM.

I hereby consent to the use of my child's BrainMap, IQ and reading and spelling tests in this study. I understand that participation is voluntary and that I may withdraw at any stage.

Signed. ................................................................. Date .................

Parent/ Guardian
APPENDIX 2. PUBLICATIONS FROM THIS THESIS
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B. LIST OF PUBLICATIONS AND CONFERENCE PRESENTATIONS

Publications


Conference Presentations


APPENDIX 3. CD ROM. STATISTICAL ANALYSES FOR ALL STUDIES