# ELECTROPHYSIOLOGICAL AND BEHAVIOURAL CORRELATES OF DYSLEXIA IN PERCEPTUAL AND COGNITIVE TASKS

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# ABSTRACT

Despite recent extensive research in the field of dyslexia, the causal links between various behavioural symptoms and underlying neural mechanisms of this developmental disorder proposed by different theories are still hotly debated. In this project I aimed to combine behavioural and neurophysiological tests of global coherent motion (magnocellular), visual word from recognition and lexical decision (phonological), as well as attention deficits in English speaking dyslexic adolescents.

Three studies are described in this thesis. In the first study 10 dyslexic participants (ages 15.5-17.4) and 10 control participants (ages 14.4-18.3) were tested during the Continuous Performance Task (CPT), an established test of attentional performance. In the second study the 9 dyslexic and 10 control participants (from the same set as in the first study) were tested for the magnocellular deficit hypothesis, with low contrast and low coherence level random dot kinematograms (RDK) presented in a coherent motion detection test. In the final study the participants (9 dyslexics, 9 controls) had to decide whether they saw a word or a pseudoword (lexical decision task). In all three studies the event related potentials (ERPs) were recorded simultaneously with the behavioural measures, such as reaction time (RT) and error rate.

According to the results of the first study, no between-group differences in behavioural performance on CPT were found, whereas the late ERP components were delayed, attenuated and atypically symmetrical in the dyslexic group. The results of the second study showed magnocellular impairment only in one dyslexic participant, according to both ERP and behavioural data. Thus, the latency of the N1 and P2 ERP components was delayed and sensitivity of the performance was poorer in this participant when compared to the rest of the group average. In the third study, the lexical decision task, dyslexics performed significantly worse than controls in terms of accuracy and response latency. The early ERPs related to the pre-lexical visual word form recognition were atypically symmetrical, and the later ERP peaks were significantly delayed and attenuated for the dyslexic group.

The behavioural and electrophysiological results of these studies suggest that abnormal attentional performance is not a 'core' feature of dyslexia, as well as confirm previous findings of impaired magnocellular function in a small subset of dyslexic population. The atypically symmetrical early and later ERP components highlight the potential explanatory value of altered interhemispheric function in dyslexia, whereas the attenuated and delayed later ERP components highlight the deficits at later, cognitive stages of processing among dyslexics. Brain-behaviour cross-study correlational analysis showed that speed and amplitude of the early and late ERP components consistently associated across the tasks, the poor literacy scores and larger error rates associated with attenuated and delayed ERPs, whereas individual participant effect sizes showed that magnocellular impairment associated with larger error rate and delayed ERPs in the CPT and lexical decision tasks.

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# 1. INTRODUCTION

## 1.1. Background to Developmental Dyslexia

Traditionally developmental dyslexia is defined as 'a disorder in children who, despite conventional classroom experience, fail to attain the language skills of reading, writing and spelling commensurate with their intellectual abilities' (1968). It is a specific and significant impairment in reading abilities that cannot be explained by any kind of deficits in general intelligence, socioeconomic disadvantage, general motivation or sensory acuity (World Health Organisation, 1993). These definitions are based on a criterion of discrepancy between the reading performance as expected from measures of IQ and the reading performance actually observed. This learning disorder has lifelong persistence with reading deficits being just one of its manifestations. It is estimated to occur in approximately 5-10% of school age children (Shaywitz et al., 1992). Developmental dyslexia, hereafter referred to as dyslexia, should be distinguished from acquired dyslexia, which is usually caused by pathological or accidental focal brain damage (Price and Mechelli, 2005). Given the large numbers involved, dyslexia has major implications, both financial and political, as well as social significance with the need for the extra support for dyslexic children, adults and their families. It causes particular concern in English-speaking countries that may have more dyslexic population due to the deep and irregular orthography of the English language (Lindgren et al., 1985; Paulesu, 2001). One notable aspect of dyslexia that puzzles theorists is the variety of symptoms that are consistently associated with it and are not specifically related to reading *per se*. These include visual and auditory sensory skills, visuo-motor control and more (Nicolson and Fawcett, 1990; Tallal et al., 1993; Stein and Walsh, 1997). As a consequence, whatever aspect of function and behaviour is investigated – be it reading, writing, spelling, hearing, vision or learning skills – dyslexic children always show interesting deviations. Another great

challenge in theoretical research of dyslexia is that children with this condition often have associated deficits in related domains and show comorbidity with other developmental disorders such as Specific Language Impairment (SLI) (e.g., McArthur et al., 2000), Attention Deficit Hyperactivity Disorder (ADHD) (Shaywitz et al., 1994; Willcutt and Pennington, 2000; Kadesjo and Gillberg, 2001) or dyspraxia (Kadesjo and Gillberg, 1999).

It is well established now that dyslexia is a disorder of a neurobiological origin. This notion was initially and independently mentioned by British physician Pringle Morgan and Scottish ophthalmologist James Hinshelwood in the end of the 19th century. They both emphasized the similarity of symptoms in dyslexic children with a neurological syndrome of 'visual word blindness' (Hinshelwood, 1895; Morgan, 1896). As first reported by French neurologist Jules Dejerine (1891), in adults a damage to left inferior parietal-occipital area causes significant impairment in reading and writing, suggesting that this region may play an important role in processing of the 'optic images of letters' (Dejerine, 1891). Therefore, Hinshelwood and Morgan reasoned that impaired writing and reading in dyslexic children could be due to impairment in the same region as in adult alexic patients (Hinshelwood, 1917). About 20 years later American neurologist Samuel Orton (1937) advocated the use of the term 'strephosymbolia' that indicates the problem was not one of word blindness per se but of 'symbol twisting'. Orton's work with over 1000 children inspired many, including the neurologist Norman Geschwind, and eventually led to the foundation of the Orton Dyslexia Society (now the International Dyslexia Association).

In the early 1960's a Word Blind Centre was established in the UK in order to study the diagnosis and teaching of dyslexic children. The first researcher in this centre to publish quantified differences between dyslexic boys and controls was Sandhya Naidoo. He identified a specific pattern within a group characterised by 'exclusionary' criteria, i.e., a 'difficulty in learning to read and spell in physically normal intelligent children' (Naidoo, 1972). A decade later similar theoretical work was carried out by a group of researchers at Aston University who developed the

'Aston Index', a comprehensive diagnostic battery for dyslexia (Newton et al., 1976). Another decade later Tim Miles published a similar research derived from his clinical case studies of 223 children in the early 1970's that formed the basis of the Bangor Dyslexia Test (Miles, 1983). According to a large scale study by Rutter and Yule (1975), around 4% in the normal distribution of low achievers showed specific retardation in reading despite adequate intelligence. This general incidence level of 4% still provides a representative estimate of the prevalence of dyslexia in general population.

At present the major aims for dyslexia research are to identify the full range of symptoms (whether or not they are related to reading) and to consider the possible neural mechanisms that might underlie these symptoms. And despite many decades of intensive research, the underlying neurobiological and cognitive causes of dyslexia are still hotly debated. The plurality of symptoms in dyslexia and its heterogeneous nature has led to no less than four major theories trying to explain the underlying causes of this developmental disorder. Among currently most influential are the phonological deficit hypothesis, the automatisation deficit hypothesis, the cerebellar deficit hypothesis and the magnocellular deficit hypothesis, which are briefly outlined below.

## 1.2. The major theories of developmental dyslexia

### 1.2.1. The phonological deficit hypothesis

The phonological deficit hypothesis (Vellutino, 1979; Snowling, 1987; Stanovich, 1988) is currently the dominant explanatory framework for dyslexia. It postulates that difficulties experienced by dyslexics are caused by specific impairments in the representation, storage and/or retrieval of speech sounds. It explains dyslexics' reading impairment by appealing to the fact that learning to read requires learning of the grapheme-phoneme correspondence, i.e., the correspondence between letters and constituent sounds of speech. If these sounds are poorly represented, stored or retrieved, the phonological awareness skills would be affected accordingly (Bradley and Bryant, 1978).

Usually skilled reading depends on two component processes: word identification and language comprehension (Gough and Tunmer, 1986). Word identification involves visual recognition of an array of letters as a familiar word and implicit (or explicit) retrieval of the meaning of that word from memory (Vellutino et al., 2004). Language comprehension requires understanding of the meaning of spoken or written words and their integration within a sentence and a text. According to the phonological deficit hypothesis, the reading difficulties experienced by dyslexic children are manifested in inadequate printed word recognition and phonological (letter-sound) decoding that may or may not be accompanied by deficient language comprehension (Vellutino, 1979; Snowling, 2000). There is much evidence showing that children who have difficulties in mapping the alphabetic symbols to sounds also have difficulties in learning to read and spell (Snowling, 1980; Stanovich and Siegel, 1994). This ability in learning alphabetic symbol mapping, in turn, depends on acquisition of *phonological awareness*, defined as conceptual grasp and explicit awareness that spoken words

are comprised of individual speech sounds (phonemes) and combinations of speech sounds (syllables, onset-rimes) (Vellutino et al., 2004). According to many researchers, the difficulties that dyslexic children experience in phonological awareness tasks contribute to their deficient word recognition skills (e.g., Bruck, 1993a; Snowling, 1995).

According to Goswami and Bryant (1990), phonological awareness is awareness of the sounds that make up words. There are three ways of breaking up a word into constituent sounds and therefore three types of phonological awareness. Firstly, words can be divided up into syllables. Most children have little difficulty in separating words 'daddy', 'bungalow' and 'magnificent' into two, three and four syllables respectively (Liberman et al., 1974) At this simpler, syllabic, level awareness is measured by a variety of tasks, including tapping out the number of syllables, counting syllables, and deleting syllables. Usually awareness of this type is well developed by the time children start learning to read. The second type of phonological awareness is by phonemes, that is the smallest units of sound in words. The development of awareness at the phonemic level (e.g., that cat is /c/ /a/ /t/) is far more difficult to acquire (Adams, 1990), and is measured by counting phonemes, dividing words up into a series of phonemes, deleting phonemes, and substituting phonemes. Young children are not usually aware of these sound units. The third type of phonological awareness looks at units larger than phonemes but smaller than syllables. Each syllable can be divided into opening and closing sections. These units are referred to as the onset and the rime. Thus, the ability to divide words into onsets and rimes (e.g., that cat may be broken down into /c/, the onset, and /at/, the rime) falls midway in difficulty between syllabic and phoneme awareness. The use of the term 'rime' for the end units makes obvious reference to the fact that words that finish with similar rimes do rhyme. Young children's sensitivity of and experience with rhymes seems to be closely related to their fluency in reading in later years (Bryant et al., 1990). The ability to count the phonemes in a word develops around first grade for normal readers, but the ability to manipulate these phonemes is developing up to secondary school level (Adams,

1990). A typical progression would be, first, syllable recognition at around three or four years; then an intermediate stage based on recognition of onsets and rimes; and finally recognition of individual phonemes after the age of 6 (Goswami & Bryant, 1990). It is no coincidence that these skills develop at this time, in that early phonological awareness skills provide the foundations for the acquisition of higher levels of metaphonological skill.

Thus, most children are able to perform tasks requiring segmenting words in smaller units, i.e., syllables and (partly) phonemes well before reading age. For dyslexic children, however, these skills are not achievable even after several months of reading and writing (Bradley and Bryant, 1983). Subsequent training and intervention designed to improve phonological awareness and letter-sound mapping provided consistent evidence of improvement in word identification, spelling and reading ability in general (Lundberg et al., 1988; Foorman et al., 1998).

In addition to phonological awareness another component that plays an important role in acquiring reading ability is *orthographic awareness*, i.e., the child's sensitivity to constraints of how the letters in written words are organised (Vellutino et al., 2004). It is argued that orthographic knowledge is acquired only after the initial phoneme-letter encoding phase and that it is primarily derived from developing reading skill and experience with print (Ehri, 1995); that is, much of the learning will occur implicitly, over and above any explicit instructions about spelling rules. It was found that children's exposure to literacy at home, e.g., shared reading, magnetic letters, was more significantly related to phonological sensitivity than passive literacy exposure, such as parental leisure reading (e.g., Burgess et al., 2002). Further studies have shown that exposure to alphabet books is more efficient in the development of phonological sensitivity than exposure to picture books (e.g., Murray et al., 1996). These findings support the central role of letter knowledge in phonological awareness development. In a year longitudinal study of 4- and 5-year-olds Burgess et al. (2002) found that early print letter knowledge and home shared reading were significant predictors of phonological sensitivity growth, whereas speech perception and age were not significant predictors. It was reported by

Treiman et al. (1998) that children as young as 4 years old can benefit from print letter exposure in development of their phonological sensitivity.

However, in languages with many inconsistent letter-sound relations, such as English and French, children become sensitive to certain statistical properties of the orthography, such as positional constraints and word frequency, even when their own spelling production is only partially phonologically correct (Caravolas et al., 2005). According to these authors, the development of orthographic representations in spelling is shaped from the earliest stages by a complex combination of information about the properties of the lexical and orthographic input, acquired to some extent through implicit learning. There is much evidence that dyslexic children and adults who have limitations in phonological awareness and alphabetical mapping skills would also have limitations in orthographic awareness and orthographic knowledge (e.g., Bruck, 1992; Snowling, 2000). In transparent orthographies, children's reading speed and accuracy are usually equivalent for nonsense words with familiar and unfamiliar rimes, whereas in non-transparent orthographies (e.g., English or French) children show reduced speed and accuracy while reading 'unfamiliar' (zoin) as compared to 'familiar' (dake) nonsense words (Goswami, 2000). This supports the notion that children who are learning to read transparent orthographies rapidly develop orthographic representations that the present phoneme-level information, whereas children learning less transparent orthographies take longer to represent phoneme-level information (Wimmer and Goswami, 1994). There is a considerable evidence of limited knowledge of print in children with early reading difficulties that can contribute to early reading and language problems. However, limitations in such knowledge are probably not the main cause of specific reading difficulties and are usually caused 'by experiential and instructional deficits rather than biologically based cognitive deficits' (Vellutino et al., 2004). It has been shown, for example, that sometimes children with extreme reading difficulties have reasonable knowledge of print concepts and conventions (Vellutino et al., 1996).

Dyslexics are known to perform poorly on other phonological awareness tasks, particularly on nonword repetition tasks (Snowling, 1981) that provide a measure of their ability to assemble articulatory instructions (Snowling et al., 1991). A specific difficulty in finding and retrieving verbal labels in response to familiar pictures was found in dyslexic children as well (e.g., Swan and Goswami, 1997). In addition, the theorists also argue that there is evidence for poor short-term verbal memory that is possibly caused by a more basic phonological deficit in representation of quality of phonological units, their access and retrieval (Snowling, 2000).

According to Lundberg and Hoien (2001) the following phonological deficits are the characteristic symptoms of dyslexia across the lifespan:

- reading and writing even short nonwords
- repeating back long nonwords
- playing word-games where the point is to manipulate phonemes
- a slower rate of speech, sometimes with indistinct pronunciation
- segmenting words into phonemes
- keeping linguistic material (strings of sounds or letters) in short-term memory
- slow naming of colours, numbers, letters and objects in pictures

An important argument of the phonological processing theory is that there is a deficit at the level of phoneme representation itself. For example, it has been shown that in the tasks that require processing and differentiation of phonemes that are acoustically similar to each other, e.g., 'ba' or 'da', dyslexics performed worse compared to their age-matched controls (Godfrey et al., 1981; Manis et al., 1997). Hulme and Snowling (1991) suggested that two broad classes of processes should be distinguished: *input phonology* (speech perception processes) and *output phonology* (speech production processes). They have argued that particularly impairments in output phonology may be crucial in dyslexia that involve inability to sound-out novel words and errors in accurate portray of sound structure of the word.

They have studied a dyslexic boy J.M. for 6 years (Snowling et al., 1986b; Snowling and Hulme, 1989) and found a range of errors in output phonology in addition to his reading problems. These included mispronunciations of polysullabic words in his spontaneous speech and difficulties in repeating words and nonwords. He also had naming difficulties and impaired verbal short-term memory. However, he was similar to reading-age matched controls in his performance on input tasks such as auditory discrimination of nonwords and auditory lexical decision. There is evidence from other works that dyslexic children experience problems in speech production processes such as word finding, nonsense word repetition and vowel distinctiveness measures (Snowling et al., 1986a; Stackhouse and Wells, 1997; Goswami, 2000). It was suggested by Goswami (2000) that it could be the process of phonological representation itself that is compromised in dyslexia. However, the author also mentioned that there is a possibility that current measures of input phonology are not adequate and may fail to tap into main processing deficits that cause the phonological representations of dyslexic children to be underspecified and to lack segmental information. It is also possible, according to Goswami (2000), that some compensation for early processing deficits has already taken place in some children following remediation. According to Manis et al. (1997) speech perception in dyslexic children is usually examined via two major paradigms: categorical perception of stop consonants, such as /b/, /d/, /g/, and /p/, and repetition of speech with and without noise. It was found that in categorical perception dyslexic children were less able to differentiate words that differed only in initial phoneme compared to age-matched controls (e.g., Reed, 1989). Snowling et al. (1986a) found differences in monosyllabic non word and low frequency real word repetition tasks in noise. However, differences of speech perception deficits in the dyslexic population tend to be small and not always statistically robust (Joanisse et al., 2000). According to these authors, different behavioural patterns of dyslexia may have different underlying causes. For example, phonological dyslexia may be caused by deficits in both speech perception and other aspects of phonology, whereas dyslexics with the delay pattern of development exhibited performance on

the reading, phonology, morphology, and speech perception tasks that was like that of younger normal readers. They suggested that children who exhibit similar patterns of impaired reading may not necessarily have the same underlying deficits and that additional measures that assess other aspects of language and experience are needed.

The phonological deficit hypothesis was established in the dyslexia research community following a seminal analysis by Frank Vellutino (1979), who argued that the deficit was mainly in processing of language. Following this work the researchers refined the concept of a linguistic deficit, developing the 'phonological deficit' theory. The pre-eminent status of the phonological deficit hypothesis derives from findings in the early 1980s that dyslexic children had particular difficulty in hearing the individual sounds in words. For instance, at the age of 5 years, children who would later turn out to be dyslexic had considerable difficulty in hearing that, say, 'cat', 'mat' and 'bat' rhyme. In general, they seem to have limited 'phonological awareness' (sensitivity to the sound structure in words). This 'phonological deficit' leads to difficulties in learning to read and spell because one of the early stages in learning to spell is to split a word into its component sound chunks, each of which then has to be spelled in order.

By the late 1980s the prevailing view was that phonological deficits might well prove a causal explanation of reading difficulties in dyslexia. In an influential analysis, Stanovich (1988) argued that the cognitive problems characteristic to dyslexia are usually specific to the reading task and do not involve other domains of cognitive functioning. He also developed the argument that one key to fluent reading is the development of an 'autonomously functioning module at the word recognition level', and that failure to develop such a module might derive from impairments in phonological processing. He proposed that children with dyslexia suffered from a specific deficit in phonological skills, whereas when moving down the IQ continuum towards 'garden variety poor readers', deficits in phonological processing will remain, but the specificity will diminish, with deficits showing up in more and more skills, even those not related to reading. Stanovich discounted any

deficits in non-phonological skills and suggested that the mechanism by which the deficits have their effect on reading and spelling is via an early lack of phonological awareness. This phonological-core variable-difference model was the first causal explanation for dyslexia. As suggested by Sally Shaywitz (1996), the key assumption of the phonological deficit hypothesis is that a deficit in the language areas of the brain leads to specific problems in learning to read (and in remembering linguistic information), without otherwise affecting higher level reasoning. She illustrated the fundamental paradox of dyslexia – the discrepancy between reading ability and other skills - via the example of Gregory, a dyslexic medical student who "excelled in those areas requiring reasoning skills. More problematic for him was the simple act of pronouncing long words ... perhaps his least well-developed skill was rote memorization" and went on to outline an impressive range of multidisciplinary evidence consistent with the phonological deficit hypothesis. She concluded (p.84) "The phonological model crystallizes exactly what we mean by dyslexia: an encapsulated deficit often surrounded by significant strengths in reasoning, problem solving, concept formation, critical thinking and vocabulary." However, this assumption of specificity has been somewhat threatened by the diverse difficulties established for children with dyslexia. As noted by Nicolson (1996), the mode of scientific progress is in terms of increasing rather than decreasing specificity.

There is also a debate over whether problems repeating nonsense words should be seen as a phonological problem or a memory problem (Gathercole, 1995). A similar issue arises for Pig Latin and spoonerisms. Slow performance on rapid naming tasks is in fact now considered a different dimension from phonology, reflecting fluency. Not all researchers accept the view that name retrieval deficits are due to phonological deficits and phonological memory problems. Thus, in the earliest demonstrations using the 'Rapid Automatized Naming' (RAN) technique (Denckla and Rudel, 1976), the child has to say the name of each picture in turn on a page full of simple pictures (or colours). Dyslexic children usually show robust deficits in speed of their performance on these tasks. It was also reported that

dyslexic children needed a longer exposure time to read a known word than their reading age matched controls (van der Leij and van Daal, 1999). In a synthesis of phonological and speed problems, Wolf & Bowers (1999) proposed an alternative conceptualization of the developmental dyslexias, the *double-deficit hypothesis*. According to this hypothesis, phonological deficits and naming-speed deficits represent two separable sources of reading dysfunction, and that developmental dyslexia is characterized by both phonological and naming speed 'core' deficits. Wolf identified three major subtypes of reading disability: one caused by deficiencies in phonological skills such as phonological awareness and letter-sound decoding; a second caused by slow naming speed; and a third caused by a combination of both speed and phonological deficits. The latter group, with a 'double deficit', proved to be the most severely impaired and the most resistant to remediation (Torgesen et al., 1994). The incidence of double deficit varies with the characteristics of the language under examination. In a large sample of severely impaired English speaking poor readers, Lovett et al. (2000) reported that around half were double-deficit, 25% naming speed deficit, and 25% phonological deficit, whereas 96% of a similar sample of Hebrew children were double deficit and only 4% showed just a single phonological deficit (Wolf and O'Brien, 2002). The authors suggested that it is necessary to consider the role of fluency in reading development, an area that had been under-stressed in the 1990s. They also suggested an alternative approach to phonological support in which the sub-skills of reading are broken down further and practiced until fluent.

As concluded by Ramus (2003), 'phonology does not reduce to awareness, naming and memory; consequently many aspects of dyslexics' phonology remain to be investigated'. According to Nicolson and Fawcett (2007), the 'phonological deficit' hypothesis has been extended to include both speed of processing and verbal working memory, both of which are normally considered as fundamental cognitive attributes rather than derivatives of phonology.

At a *neurological level*, the phonological deficit hypothesis is usually linked with the findings of anatomical abnormalities in the language areas of the brain. The

first attempts to link dyslexia to specific parts of the brain were undertaken by Geschwind, who investigated a set of brains of 100 (dead) dyslexic and control people (Geschwind, 1968). His examinations showed that planum temporale, a small triangular part of the superior surface of the temporal lobe, was often larger in the left than in the right hemisphere. Galaburda and his colleagues completed Geschwind's plan and undertook painstaking neuroanatomical studies of the dyslexic and control brains in the Orton collection. They found "a uniform absence of left-right asymmetry in the language area and focal dysgenesis referable to midgestation ... possibly having widespread cytoarchitectonic and connectional repercussions. ... Both types of changes in the male brains are associated with increased numbers of neurons and connections and qualitatively different patterns of cellular architecture and connections" (Galaburda et al., 1989). Thus, the early anatomical works by Galaburda and Geschwind involving post-mortem examinations revealed differences in the structure of the brains of dyslexic individuals from those of non-dyslexic individuals, particularly in the language areas. They found specific cortical malformations including ectopias (small neuronal congregations in an abnormal superficial layer locations), mostly in frontal areas and in the left language brain regions of four dyslexic males (Galaburda et al., 1985). They have reported an absence of the usual left > right asymmetry (as found in earlier work by Geschwind) in dyslexic brains. Since this area in the left hemisphere supports language functions, its unusual symmetry in dyslexic brains was viewed as a partial cause of language deficiencies and, consequently, a cause of reading problems. Although the developmental mechanisms leading to such atypical symmetry are still under debate (e.g., Eckert, 2004), these findings could be considered a good evidence of developmental deviancies in brain maturation being at the source of learning difficulties experienced by dyslexics (Habib, 2000).

New technologies such as positron emission tomography (PET) and magnetic resonance imaging (MRI) have enabled researchers to identify differences in the brain structure and function of dyslexics from those of controls. In a recent review of brain imaging studies, Eckert (2004) summarised that anomalies in the

parietal and inferior frontal regions are most frequently associated with dyslexia. According to the majority of these studies, the disconnections between phonological and orthographic representation centres in the left perisylvian brain areas (see Fig. 1.1) are at the basis of problems in dyslexia that was also called a 'disconnection syndrome' (Shaywitz, 1998a; Pugh et al., 2000; Paulesu et al., 2001). According to some authors, abnormalities in the left hemisphere language areas are compensated by higher activation of right hemisphere and inferior frontal regions (e.g., Demonet et al., 2004).

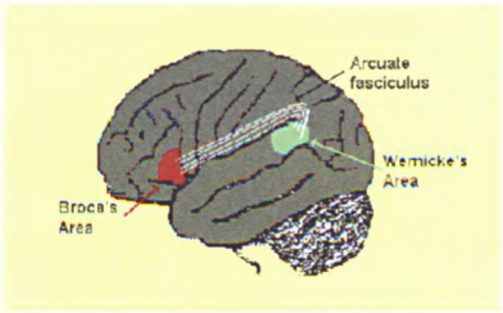


**Figure 1.1. Disconnections in the language areas**
Schematic diagram of disconnections between Wernicke's and Broca's areas through Sylvian fissure.

In a recent study using diffusion tensor imaging (DST) Klingberg et al. (2000) reported that the white matter in the left hemisphere was less developed in the group with dyslexia suggesting reduced myelination of the neurons. Richards et al. (2000) used magnetic resonance spectroscopy (MRS) to evaluate changes in brain chemistry as part of three-week phonologically oriented intervention. Before intervention MRC showed a higher metabolic rate of lactate in the left hemisphere of dyslexic children during completion of a reading task. After intervention, measures of lactate metabolism taken during reading were not different among dyslexic and non-dyslexic children. According to Vellutino et al. (2004) these results may suggest that instruction may be necessary for the neural networks that take part in word recognition ability to establish in dyslexia and that environmental factors may be important in establishing these networks.

A schematic view of the causal connections at neurological and behavioural levels in dyslexia according to phonological deficit hypothesis has been suggested by Ramus (2003) and is shown in Fig. 1.2.

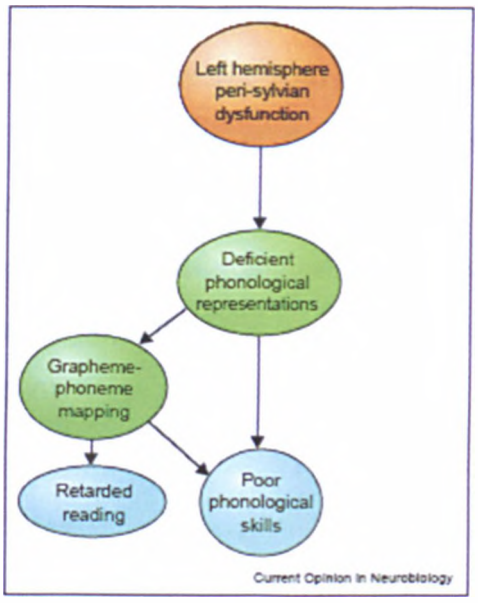


**Figure 1.2. Phonological deficit hypothesis**
A diagram representing the phonological hypothesis according to Ramus (2003). It shows the proposed causal connections at neurological (upper), cognitive (middle) and behavioural (lower) levels.

The phonological deficit hypothesis has made major contributions to understanding of dyslexia. However, there are limitations in this explanatory framework. The reliance on symptom rather than cause is unsatisfactory for an approach to a 'constitutional' disability. Additionally, the approach to diagnosis and support could be achieved more effectively if an earlier intervention, based on the presumed precursors of the phonological deficits, were undertaken (e.g., Richardson et al., 2000). The issue of phonology and reading is also related to the transparency of the language in question. For example, in more transparent languages such as German and Italian phonological and orthographic errors in reading are much less frequent than in English, so diagnosis depends upon reading speed rather than reading accuracy. The original phonological hypothesis suggested that there was a 'phonological core' deficit in dyslexia. It is currently known, that the phonological deficits are not specific to dyslexia and the discrepancy criterion should be relaxed

when diagnosing dyslexia. The phonological core domain needs to be enhanced by inclusion of naming speed and perhaps even verbal working memory, neither of which is unique to the phonological module.

The phonological hypothesis has been criticised on the grounds of its inability to explain the co-occurrence of sensory (for a review, see Stein, 2001) and motor (for a review, see Nicolson et al., 2001) deficits in dyslexic individuals (Ramus et al., 2003a). The supporters of the phonological hypothesis usually dismiss these deficits as not being part of the core features of dyslexia. They consider their co-occurrence with phonological deficit as potential markers of dyslexia that do not seem to be playing a causal role in the origins of reading difficulties (Snowling, 2000).

### 1.2.2. The automatisation and cerebellar deficits hypotheses

An alternative explanatory framework of dyslexia is represented by automatisation deficit hypothesis (Nicolson and Fawcett, 1990; Nicolson et al., 2001). It is generally known that dyslexic children and adults have a lack of reading automaticity (e.g., Stanovich, 1980). In the early 90s Nicolson and Fawcett aimed to investigate whether dyslexic children will show lack of automaticity in skills unrelated to reading. They found a deficit for balance – a highly automatic skill with no language component (Nicolson and Fawcett, 1990). The authors suggested that dyslexic children have difficulty automatising skills, which means they need to make more effort and concentrate harder, i.e., 'consciously compensate', to achieve normal levels of performance. They have also established that dyslexic children have severe deficits in a range of skills, including balance, motor skills, phonological skills and rapid processing (Nicolson and Fawcett, 1990, 1994a, 1994b). Although dyslexic children were able to normally balance compared to their age and IQ matched controls, their performance significantly deteriorated

when they had to undertake counting (Nicolson and Fawcett, 1990) or blindfolding (Fawcett and Nicolson, 1992) as a secondary task, while trying to balance. Ability to balance is a highly automatic skill that is unrelated to reading performance. These studies provided a support that dyslexic children have deficits in automatising their skills which may take up more of their concentration and efforts in order to perform at the same levels with non-dyslexic children. Nicolson and Fawcett (1995) concluded that '*the dyslexic children showed deficits in most of the skills, with fundamental deficits (worse performance than reading age controls) on phonological skill, naming speed, bead threading, and on some balance tasks. Furthermore, there was no evidence of sub-types of dyslexia, with all dyslexic children showing deficits in at least two skill modalities.*" The authors have also used the analogy of driving in a foreign country – 'one can do it, but it requires continual effort and is stressful and tiring over long periods'. They made this analogy to describe that life for a dyslexic child is like always living in a foreign country.

According to Nicolson and Fawcett (1990), impairments in automatised naming and automatisation of phonological coding in dyslexics would cause severe disruption to the development of fluency in word identification and comprehension, as well as phonological awareness, all of which would severely affect the development of reading skills. Lack of automaticity in basic skills such as literacy and numeracy could mean that dyslexic people are more likely to experience processing overload when they are required to carry out new and complex tasks. They may need far more practice at any skill before they can achieve automaticity. In a long-term training study Nicolson and Fawcett (2000) investigated the time course of combining two separate simple reactions (hand and foot) into a choice reaction to two stimuli (tone and flash). Participants were trained until their performance, i.e., the speed and accuracy of the responses, stopped improving. There were no initial between-group differences on simple reactions, whereas in choice reaction tasks dyslexics were significantly worse compared to controls. The final choice reaction performance was significantly worse among dyslexics both for

hand and foot responses. Nicolson and Fawcett (2001) established a 'square root law', according to which the amount of time needed for a dyslexic child to master a skill increases with a square root of the time needed for a non-dyslexic child. For example, if a non-dyslexic child needs 25 trials to learn a skill, it would take 5 times more time for a dyslexic child, i.e., 125 trials, and so on. Thus, according to automatisation deficit hypothesis the problems in reading and phonological skills of dyslexic individuals are caused by their inability to automatise these skills. A weak capacity to automatise would affect the learning of grapheme-phoneme correspondence.

It may be seen that the automatisation deficit provides a cognitive level (Morton and Frith, 1995) explanation of deficits in dyslexia, and may even be seen to subsume the phonological deficit hypothesis. Nonetheless, it does not attempt to explain why there are deficits in automaticity. Thus, at a *neurological* level, the lack of automaticity is explained by abnormalities in cerebellum (Nicolson et al., 1995). The *cerebellar* deficit theory predicts that the neurological substrate of the deficits described in the automatisation deficit theory of dyslexia is the cerebellum. Therefore, this theory may be seen as a 'biological level' explanation of the automatisation deficit theory.

The cerebellum is a densely packed and deeply folded subcortical brain structure. In humans, it accounts for about 10-15% brain weight, 40% of brain surface area and 50% of the brain neurons. It was considered in the past as an important regulator of reflex and voluntary movements only, it is now recognised important in many aspects of sensorimotor functions and learning. Damage to different parts of the cerebellum could cause various abnormalities like disturbances in posture and balance, lack of coordination and impaired planning of automatic movements. However, the cerebellar system has great plasticity which helps recovery and almost normal performance after only a few months of damage (Fawcett and Nicolson, 2001). There is extensive evidence that the cerebellum is involved in motor control and coordination, acquisition of motor skills via its rich connections with the motor cortex, the skeleton-muscular system and the sensory

cortex (Ito, 1990). On the other hand, it has been recently established that the cerebellum also plays an important role in a variety of cognitive skills, including abstract reasoning, working memory, verbal fluency, visuospatial memory (e.g., Schmahmann and Sherman, 1998). Patients with lesions in cerebellum have demonstrated impairments in the procedural learning of cognitive tasks leading to an emergence of newly defined clinical entity, the 'cerebellar cognitive affective syndrome' (Schmahmann and Sherman, 1998). These clinical observations have been reinforced in neuroimaging studies showing cerebellar activation in a variety of non-motor skills (Allen et al., 1997)

Administering clinical tests of cerebellar function established marked deficits among dyslexic children (Fawcett and Nicolson, 1999), as did behavioural tests with eye blink conditioning (Nicolson et al., 2000) and adaptation to visually displacing prisms (Brookes et al., 2007). As it was found in a PET study, when performing a previously learned sequence and learning a new sequence, the dyslexic group showed only 10% of increase in activation of the right cerebellar hemisphere and vermis when compared to the controls (Nicolson et al., 1999). The study showed a direct link between abnormal cerebellar function and behavioural deviations in performance of dyslexics on these cerebellar tasks. Thus, the results of the brain regional cerebral blood flow (rCBF) activation showed significantly greater increase in the right cerebellum for the controls compared to dyslexics during both learning a new sequence and performing a pre-learned sequence. By contrast, dyslexics showed greater CBF activation in large areas of the frontal lobes when learning a new sequence. Nicolson and co-authors (2001) further elaborated their causal hypothesis linking cerebellar problems, phonological difficulties and, eventually, reading problems.

Anatomical studies also support the notion of involvement of the cerebellum in dyslexia. In a recent post-mortem analysis of the cerebellum of brains of dyslexic and control people, it was found, that dyslexics had larger mean cell areas in the medial posterior cerebellar cortex, anterior lobe and inferior olive, and the cell size distribution showed larger numbers of large neurones and fewer number of smaller

neurones (Finch et al., 2002). Rae et al. (2002) reported that dyslexic children failed to exhibit rightward grey matter asymmetry, due in part to reduced volume of right cerebellar grey matter, whereas a greater asymmetry (right > left) was found in the control group. The authors interpreted this lack of asymmetry in the cerebellar volumes of the dyslexic group as a reflection of their increased cerebral symmetry (Rae et al., 2002). They concluded that people with developmental dyslexia show a wide variety of differences in multifaceted systems of the brain including changes in the cerebellum and particularly its right hemisphere. According to Rae et al. (2002), *'such changes can be expected to occur in an evolutionarily highly complex task that requires the integration of functions of language and cognition, motor and visual skills'*. Other studies also establish direct independent evidence of functional and anatomical abnormality of the cerebellum in dyslexia, such as smaller right cerebellar anterior lobe (Leonard et al., 2001; Eckert et al., 2003), reduced amount of grey matter in the left (Eckert et al., 2003) or both left and right semilunar lobules (Brown et al., 2001).

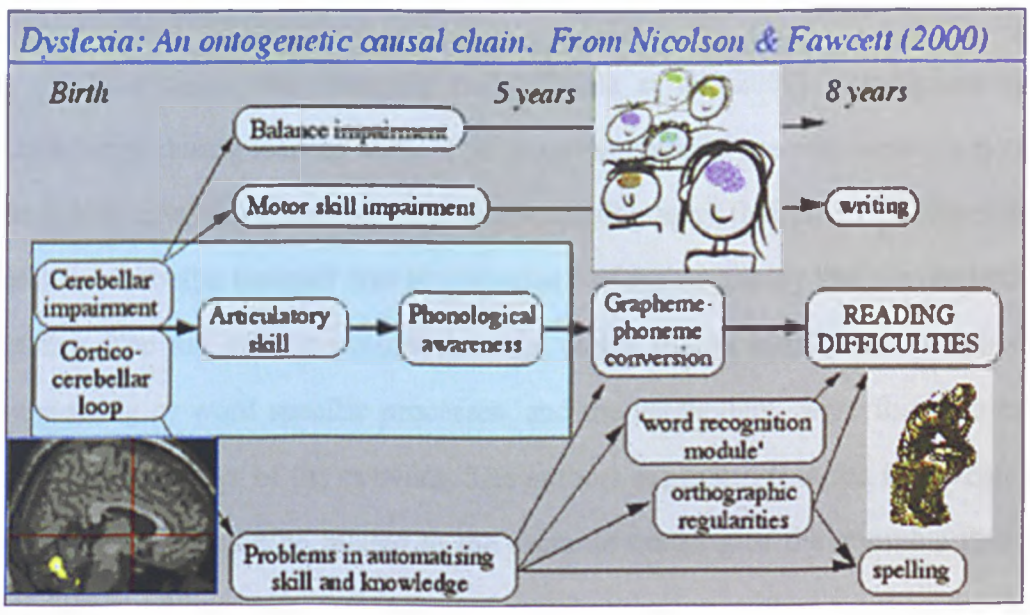


**Figure 1.3. Cerebellar deficit hypothesis**
Diagram representing the causal chain and development of impairment of different skills in dyslexia according to cerebellar deficit hypothesis by Nicolson and Fawcett (2000).

Thus, the cerebellum has emerged as one of the most consistent anatomical locations for differences between dyslexics and controls. There is now little doubt that cerebellar function is mildly disturbed in substantial proportion of dyslexics, and that this deficit is correlated with reading difficulties. The cerebellar problems could be linked to reading via direct and indirect routes. Since the cerebellum plays a role in motor control and speech articulation a dysfunction in articulation could lead to deficient phonological processing. The importance of the cerebellum as an 'inner speech' mediator is also relevant to reading, as difficulty in 'sounding out' the letters in a word would also affect phonological processing. Inefficient articulation could affect reading also indirectly, via taking up more of the conscious resources and leaving fewer resources for the perceptual processing during reading. Another indirect influence of the reduced articulation in reading is that the reduced speed of articulation could lead to inefficient working memory and defective phonological loop, which in turn could lead to impaired language acquisition. The causal chain and development of behavioural deficits in dyslexia according to the cerebellar deficit hypothesis is represented in Fig. 1.3 on a diagram adapted from Nicolson and Fawcett (2000).

In a recent neuroimaging study Kujala et al. (2007) investigated neural connectivity during reading without prior assumptions of specific areas' or network structures' involvement using magnetoencephalography (MEG). A left-hemisphere cerebro-cerebellar network was identified at 8-13Hz frequency that was sensitive to reading. The left inferior occipitotemporal cortex that is usually involved in early letter-string or word specific processes, and the cerebellum, were found to be the main driving nodes of the network. The authors suggested that the involvement of the cerebellum could be related to the accurate tracking of the stimulus timing in this silent reading task. An increased synchronisation within a subset of nodes, including left occipitotemporal, left superior temporal and orbitofrontal cortices was observed with participants' efforts to comprehend the text. The authors concluded that, according to their data, the cerebellum is intimately involved in complex cognitive tasks as part of a cognitive network. In another recent neuroimaging study

(Kronbichler et al., 2008) the grey matter volume was studied in 13 dyslexic and 15 nonimpaired reading adolescents. It was reduced for dyslexic readers in the left and right fusiform gyrus, the bilateral anterior cerebellum and in the right supramarginal gyrus. The authors suggested that the extended areas of reduced gray matter volume in dyslexic readers' cerebellum indicate structural abnormalities strongly associated with dyslexia and warrant further investigation.

Thus, as suggested in many recent neuroimaging studies, the cerebellum is an integral part of the cognitive network involved in reading, and changes in function or anatomical structure in any part of this network would result in behavioural deficits displayed by dyslexic readers. For example, it was suggested by Eckert (2004) that anatomical abnormalities in frontal-temporal-parietal and cerebellar networks may be related to deficits in processing speech sounds (phonology) and abnormalities in occipital-temporal-frontal-cerebellar networks may account for deficits in processing word forms (orthography).

While it is widely accepted that speech articulation is important for the development of the phonological processing, there is evidence that some dyslexics have language problems that are not easily explained by such impairments. For example, there have been cases of a normal development of phonological skills despite severe dysarthria or apraxia of speech (Ramus et al., 2003b). The opponents of this theory therefore consider it unlikely that such deficits alone could account for the wide range of problems dyslexics have.

The cerebellar deficit hypothesis was criticised, similarly to the phonological deficits hypothesis, on the grounds of its inability to explain sensory deficits (Ramus et al., 2003a), although Fawcett and Nicolson (2001) suggested the existence of separate cerebellar and magnocellular subtypes in dyslexia. It is also criticised on accounts of what proportion of dyslexics is affected by motor skills compared to a considerably higher proportion of individuals with phonological deficits. For example, some studies could not find motor difficulties (Wimmer et al., 1998; Kronbichler et al., 2002) or found only in a subgroup of dyslexic participants they tested (Yap and van der Leij, 1994; Wimmer et al., 1998; Ramus et al., 2003b).

It has also been suggested that abnormalities in cerebellum and motor dysfunction were found in children with other developmental disorders, such as SLI (e.g., Bishop, 2001) and ADHD (Denckla et al., 1985; Wimmer et al., 1999).

### 1.2.3. The magnocellular deficit hypothesis

Besides the influential theories of cognitive and neurobiological basis of dyslexia described above, there is another major theory that is based on the evidence of sensory deficits, both visual and auditory. These deficits were found in some dyslexic individuals and were linked to the abnormalities in magnocellular pathways of the brain (Stein and Walsh, 1997). According to the magnocellular deficit hypothesis, literacy difficulties may be a consequence of impaired development of large neurones in the brain (magnocells) that are responsible for timing sensory and motor events (Stein, 2001).

Before discussing the research studies that report sensory deficits and magnocellular pathway impairment in dyslexia it is necessary to provide a description of the visual system and central visual pathways. The visual system has the complex task of (re)constructing the three dimensional world from a two dimensional projection of that world on the retina. I will examine the flow of visual information from retina to midbrain and thalamus, and then from the thalamus to the visual cortex.

The eye is a complex biological device and its working is often compared to the functioning of a camera. Light entering the cornea is projected onto the back of the eye where it is converted into an electrical signal by specialised retinal neurones called photoreceptors. Unlike other sensory structures such as the cochlea or the somatic receptors in the skin, the retina is not a peripheral organ but part of the central nervous system (Kandel et al., 1995). It contains two types of photoreceptors: rods and cones. Rods are found primarily in the periphery of the

retina and are used to see at low levels of light. Cones are found primarily in the centre of the retina, the fovea, and are used to distinguish colour and other features of the visual world at normal levels of light (e.g., Kaplan et al., 1990). In the retina the photoreceptors synapse directly onto bipolar cells, which in turn synapse onto ganglion cells. Unlike photoreceptors, which respond to light with graded changes in membrane potential, ganglion cells transmit information as trains of action potentials. The bipolar cells together with horizontal and amacrine cells are interneurones between the photoreceptors and the ganglion cells that can also combine signals from several photoreceptors (Tessier-Lavigne, 1995). Each ganglion cell has a receptive field, which is a specific area of the retina where stimulation of photoreceptors by light causes either an increase or decrease in the firing rate of the ganglion cell. The receptive field of most ganglion cells is not homogeneous and is divided into two parts: a circular zone at the centre, and a surround. A recent insight is that this centre-surround organisation of the receptive fields in retinal ganglion cells is well-suited for efficient representation of the natural images and visual signals sent to the brain (Lennie, 2003).

In primates generally and in humans and macaques specifically, there are two populations of ganglion cells that send visual information to the brain (Hendry and Reid, 2000). These are the M cells with large centre-surround receptive fields that are sensitive to motion and depth, indifferent to colour and rapidly adapt to the stimulus, and P cells with smaller centre-surround receptive fields that are sensitive to colour and shape (Lennie, 1998). These are different from the X and Y type cells in cat that were first studied by Enroth-Cugell and Robson (1966). According to Lennie (1980), the important characteristic of Y-cells is the non-linear summation of their response to incoming stimulus, whereas the X-cells show a linear summation of the response. However, this distinction may not be exhaustive in monkey's retina where a linear summation is sometimes found in ganglion cells that need not be X-cells (for a detailed review, see Lennie, 1980). It was also found that the receptive fields of Y cells are about 2.5 times larger compared to X cells (Lennie, 1980), the axons of Y ganglion cells in cat may conduct the action

potentials 2-3 ms faster than X ganglion cells (for a review, see Troy and Lennie, 1987). These different time-courses of the response led Cleland et al. (1971) to introduce the terms 'transient' and 'sustained' which corresponded to Y and X cells of cat respectively. Lennie (1980) discusses some important differences in the properties of cells in the cat and monkey, and existence of ganglion cells in macaque similar to X and Y cells of cat.

In particular, the larger M cells are known to respond to the gross features of the object and its movement, and the smaller P cells are mostly wavelength-selective and thought to be responsible for the analysis of fine detail of the image, although some M cells may also be involved in this function. According to Callaway (1998), P cells in the macaque have more sustained visual responses than M cells, and their finer calibre axons provide slower conduction velocities compared with M cells, making them useless for the detection of rapid movement. On the other hand, M cells with large receptive fields respond transiently to visual stimuli, prefer low spatial frequencies and are sensitive to luminance contrast (e.g., Shapley and Lennie, 1985). This makes them poorly suited for the analysis of shape and colour but excellent for detecting subtle luminance changes or rapidly moving stimuli (Callaway, 1998). There is also a third population of ganglion cells in primates, the K cells, with very large centre-only receptive fields that are sensitive to colour and indifferent to shape or depth (Hendry and Reid, 2000).

The axons of all ganglion cells stream towards the optic nerve, where they become myelinated and together form the optic nerve. The optic nerves from each eye join at the optic chiasm. Each optic nerve carries a complete representation of one half of the binocular zone in the visual field. Fibres from the nasal hemiretina of each eye cross to the opposite side of optic chiasm, whereas fibres from the temporal hemiretina do not cross (Lennie, 1980; Mason and Kandel, 1995). The right and left halves of the field of view are sent to the right and left brain hemispheres respectively to be processed. That is, the right side of primary visual cortex deals with the left half of the field of view from both eyes, and similarly for the left side of the visual cortex (Nolte, 2002). Thus, information from the right

visual field travels in the left optic tract, and information from the left visual field travels in the right optic tract (see Fig. 1-4).

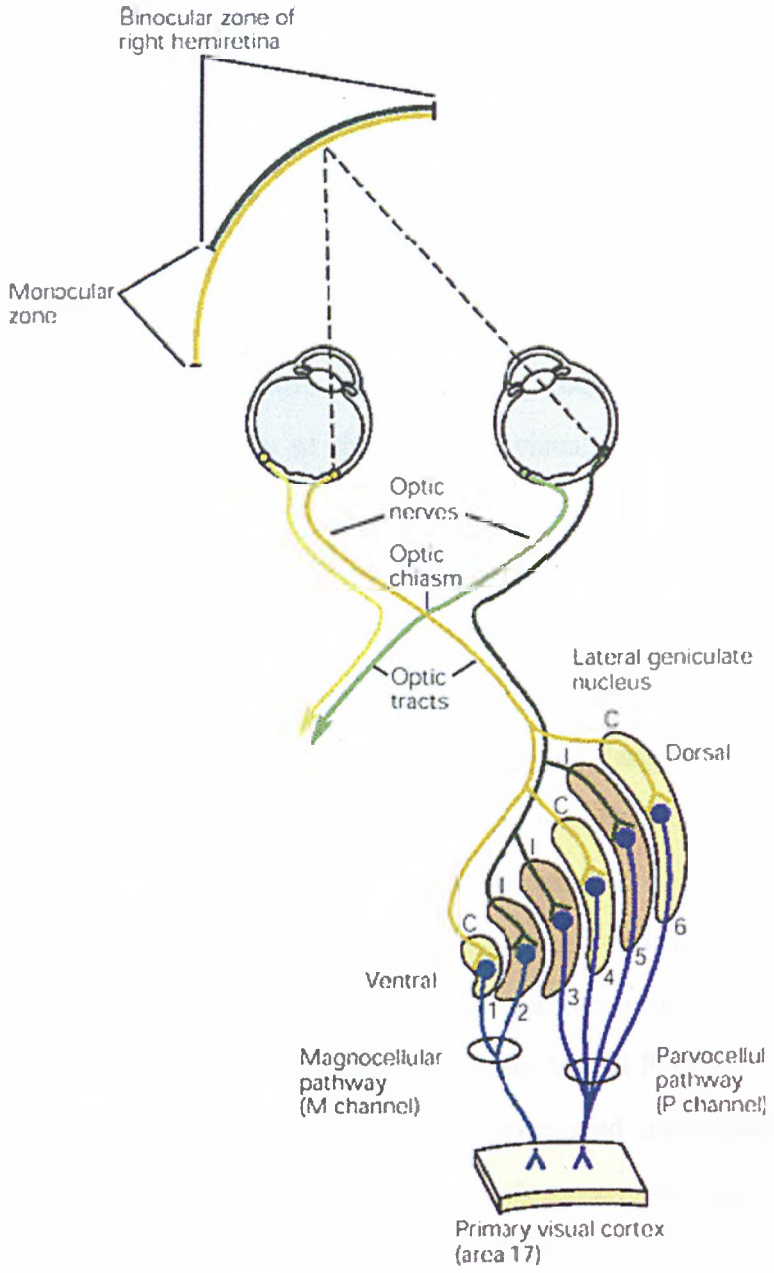


**Figure 1.4.** Projections of retinal ganglion cells to layers in LGN

Retinal fibres from both eyes that enter each optic tract project to three subcortical regions. About 90% of these fibres go to the lateral geniculate nucleus (LGN) in the thalamus. These axons originate from the M, P and K ganglion cells in the retina. Only LGN processes the visual information that ultimately results in visual perception. Another population of axons sends inputs to the pretectal area of

the midbrain to produce papillary reflexes, whereas the superior colliculus uses its input to control saccadic eye movements (Nolte, 2002).

Ganglion cells in the retina project in an orderly manner to points in the LGN, so that there is a visuotopic representation of the contralateral half of the visual field in each LGN. The LGN of primates contains six layers of cell bodies separated by intervening layers of axons and dendrites (e.g., Lennie et al., 1990; Merigan and Maunsell, 1993). The layers are numbered from 1 to 6, ventral to dorsal. Layers 1, 4 and 6 correspond to information from the contralateral (crossed) nasal visual field, whereas layers 2, 3 and 5 correspond to information from the ipsilateral (uncrossed) fibres of the temporal visual field. The two most ventral layers of the nucleus contain large M cells and are known as magnocellular layers (after the layers in which they terminate). Their main retinal input is from corresponding M ganglion cells of the retina. The four dorsal layers 3-6 are known as parvocellular layers and receive input from P ganglion cells in the retina (see Fig. 1.4). These two types of cells, '*magno*' (meaning large in Latin) and '*parvo*' (meaning small in Latin) form the magnocellular and parvocellular pathways to the visual cortex. Since the layers of the nucleus are stacked on top of one another, the six maps of contralateral hemifield are in precise vertical register. Hubel and Wiesel (1968) found receptive fields of LGN neurones have the same concentric fields as those in the retina. However, unlike the M and P cells in the retina the M and P pathways or channels of the LGN are segregated anatomically into different cellular layers. The existence of these two pathways is an example of a parallel processing which is important for reconstructing the visual world, where each type of information will go through a different route to perception (Lennie, 1998).

The optic radiations carry information from the thalamic LGN to layers 4 of the primary visual cortex or visual area 1 (V1). The human visual cortex is highly complex and consists of 6 layers of cells. I will not go into detail of the cortical structure here, however, some details are provided in the next chapter when describing EEG sources. Cortical layer 4, which is the principal layer of inputs from LGN, has 4 sublayers: 4A, 4B, 4Cα and 4Cβ. As found by Lund (1988), the M cells

of the LGN relay to V1 layer 4Cα, the P cells of the LGN relay to V1 layer 4Cβ, and the K cells.

Thus, the magnocells are said to be determinants of 'where' in the brain, and the parvocells the determinants of 'what' in the brain. In the primary visual cortex, V1, their paths separate. The magnocells project to the dorsal stream of parietal cortex and medial-temporal (MT) area or V5, whereas parvocells follow the ventral pathway to the area V4 in the inferior-temporal cortex (Lennie, 1998) A schematic representation of magnocellular and parvocellular systems is shown in Fig. 1.5. As can be seen in the diagram, the magnocellular pathway projects to V2, then to V3 and MT (V5), the area found by Dubner and Zeki (1971) and Zeki (1973) to be concerned with depth and motion. The pathway then continues to MST and other areas in the parietal cortex concerned with visuospatial function. Neurons throughout this system respond rapidly but transiently, they are relatively insensitive to colour and respond poorly to contours or borders defined by colour contrast. The parvocellular system projects from layers in V1 to V2, V4 and finally to inferior-temporal cortex. Neurons in this system are sensitive to orientation of edges and perception of shape, slowly adapting and capable of the high resolution important for seeing stationary objects in detail.

The theoretical framework of the magnocellular deficit hypothesis of dyslexia builds upon the existence of these two separate and parallel visual pathways – magnocellular and parvocellular. The fast magnocellular system deals with high temporal and low spatial frequency stimuli, whereas the parvocellular pathway processes high spatial and low temporal frequency stimuli (e.g., Merigan and Maunsell, 1993). Visual perception is proposed to be affected in dyslexia by an impaired magnocellular system in several ways. According to some studies, it is necessary for saccadic suppression (suppression of the flow of visual information during saccadic eye movements) and for the control of binocular vergence to occur during fixating a word (Stein and Walsh, 1999). Some earlier accounts were directed at a possible role of M inputs in eye movements or in keeping the packet of information processed by P system during each fixation separately from the next

packet of information by the saccade-driven (possibly, M-cell) inhibition on sustained (possibly, P-cell) channels (Pavlidis, 1981). I will discuss some of these issues and related recent literature further below.

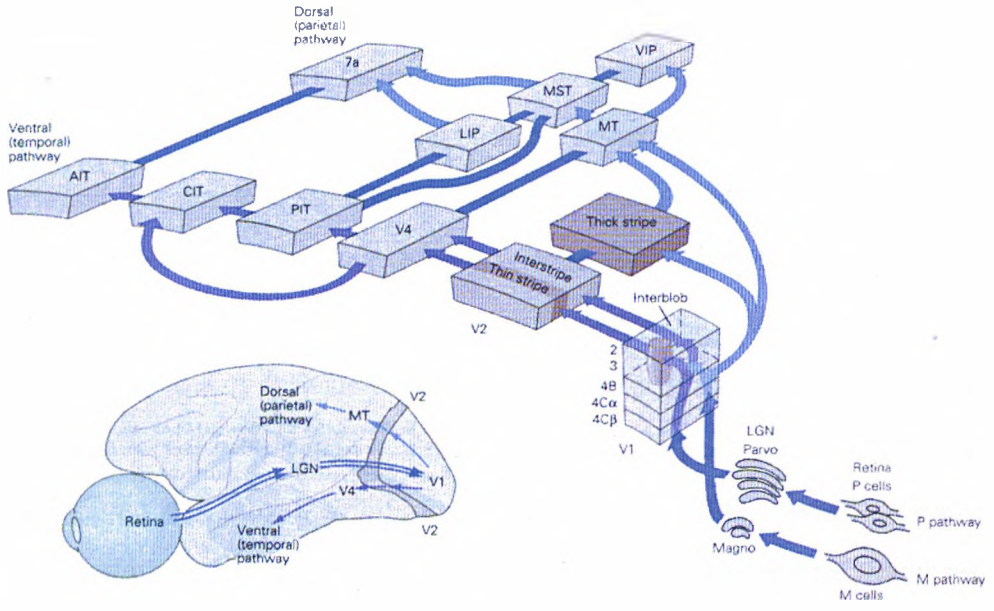


**Figure 1.5. Magnocellular and parvocellular pathways**
Diagram representing the pathways of magnocellular and parvocellular systems from retina to higher cortical areas.

The early anatomical evidence of abnormalities and pathological development of the magnocellular system among dyslexics was reported by Livingstone and colleagues who compared the magnocells in the deeper levels of LGN from the post-mortem brains of 5 dyslexics and 5 controls (Livingstone et al., 1991). They discovered that the magnocells were more disorganised and up to 27% smaller in dyslexics. There were no such group differences for the parvocells. They suggested, that this anatomical evidence may be consistent with psychophysical and physiological findings, since smaller cell bodies are likely to have thinner axons and, consequently, slower transmission speed. An early demonstration of low level visual impairment was reported in dyslexics in a psychophysical study by Lovegrove and co-authors (1980; 1982). They reported that spatial contrast and temporal flicker sensitivity were impaired in dyslexics compared with controls, particularly at lower spatial frequencies and lower level luminance of the stimuli

(favoured by magnocellular system), as well as at high temporal frequencies of the flicker. At higher spatial frequencies served by the parvocellular system, their contrast sensitivity was the same as in controls. It was suggested by these authors that dyslexics had deficit in the inhibitory function of the M system producing a visual trace from one fixation that causes masking effects during next fixation. However, as suggested by Hulme (1988), this would predict an impairment in dyslexia during reading connected text and not when reading printed words one at a time under fixation. Yet, according to Vellutino et al. (2004), poor readers find it as difficult to identify printed words one at a time under fixation as to identify them while reading connected text. It has been also suggested that the divergent eye movement patterns of dyslexic children during reading can be explained in terms of magnocellular deficits, e.g., a statement like "letters seem to move around and merge" (Stein and Talcott, 1999) implies that dyslexic readers would have to make a greater effort to perceive an unknown letter string and therefore would need to make more and longer fixations during reading. Thus, a deficient magnocellular system could lead to errors in visual perception due to deficits in binocular vergence during the fixation of the word (Stein and Walsh, 1999). Furthermore, a failure in correct guidance of eye movements by the magnocellular system during targeting the location of next fixation could result in larger number of corrective saccades during fixation, which, in turn, could lead to longer fixations on one word among dyslexics (Stein, 2001). As suggested earlier by Cornelissen et al. (1994), the balance between central and peripheral fixations may be disturbed in dyslexic children due to deficits in magnocellular pathway, which in turn, could cause reduced efficiency in letter detection. It was shown in the subsequent studies (Cornelissen and Hansen, 1998; Cornelissen et al., 1998a; Cornelissen et al., 1998b) that impaired magnocellular function may be the cause of degraded information about positions of letters with respect to each other, which could lead to errors when reading words.

The earlier reports by Martin and Lovegrove (1987) of lower flicker sensitivity among dyslexics were hotly debated on the basis of the fact that it is a

slight impairment that is found only in small numbers of dyslexics (for a discussion, see Stein, 2001). It was suggested that much larger numbers are needed to confirm this peripheral deficit of magnocellular system and that a more consistent way of showing a magnocellular deficit in dyslexics would be testing their sensitivity to visual motion (Stein, 2001). This is so because motion engages not only peripheral magnocells but also central processing stages up to at least area V5 (MT). In order to explain these issues more clearly I will consider the earlier relevant research. Thus, in a psychophysical study by Cornelissen et al. (1995) contrast sensitivity and coherent motion thresholds were measured in dyslexics and controls at photopic levels, i.e., the luminance levels usually experienced during reading. One of the aims of the study was to show that if 'contrast detection deficit' could affect children's reading in mesopic (low) levels of luminance, then it would also persist at photopic (bright light) luminance levels that are more usual during reading. In the earlier work by Martin and Lovegrove (1984) it was reported that dyslexics and controls were better distinguished on flicker sensitivity than on static contrast sensitivity at mesopic levels of luminance. The authors also reported a negligible (possibly not significant) difference between dyslexics and controls on static contrast sensitivity at photopic luminance levels. Therefore, Cornelissen et al. (1995) suggested that if these measures are found deficient in dyslexic readers at mesopic levels, they should also cause problems in bright light (photopic) levels of luminance that are more usual during reading. They decided to replicated the earlier work by Martin and Lovegrove (1984) and measure static contrast sensitivity and flicker sensitivity in dyslexic and control participants at photopic levels of luminance. The other aim of the study was to test M pathway deficit in dyslexics more directly and compare their ability to detect coherent motion perception with that of controls by using random-dot kinematograms (RDK). As already shown earlier (Cornelissen et al., 1994), around two-thirds of dyslexic children and adults show 3-4% higher coherence thresholds compared to non-dyslexic controls. The results of the study by Cornelissen et al. (1995) did not show any significant differences between dyslexics and controls in static contrast sensitivity or flicker

sensitivity in photopic conditions. The authors concluded that based on the absence of differences between the groups, defective luminance contrast detection could not contribute directly to children's reading problems. On the other hand, coherent motion thresholds of dyslexics were about 3-4% higher than in controls. Thus, unlike flicker sensitivity, coherent motion sensitivity in dyslexics is worse than in controls both in mesopic and photopic, more usual for reading, conditions. According to the results of this study, poor motion sensitivity among dyslexics could be related to their reading difficulties and it is a more reliable measure of the M pathway deficit than flicker sensitivity. Subsequent psychometric and neuroimaging research (briefly described below) also suggested that the primary role of the visual magnocellular pathway is not so much in detection of fast moving stimuli, as in flicker sensitivity experiments, but in detection of low contrast and slowly moving stimuli. Thus, the electrophysiological recordings in monkeys have shown that the most effective way of measuring the sensitivity of the magnocellular system, including the V5/MT area in parietal cortex, is to measure the detection of visual motion using random dot kinematograms (for discussion, see Cornelissen et al., 1998b; Stein, 2001). In these experiments, some proportion of randomly moving dots is set to move coherently in one direction. The proportion of dots that is necessary for the coherent motion to be perceived by the observer is called 'motion coherence threshold'. It can only be perceived if the motion signals are integrated over a wide area and not only in local areas around the point of fixation. Thus, this measure of 'global coherent motion' is currently considered to be a more reliable measure of the function of the magnocellular system as compared to the flicker fusion thresholds. Further evidence was collected showing impaired performance of dyslexics in motion perception tasks (Cornelissen et al., 1995; Eden et al., 1996; Cornelissen and Hansen, 1998).

As mentioned earlier, it was suggested that this impairment of M pathway, i.e., coherent motion deficit, directly contributes to an impaired letter position encoding, which in turn, contributes to reading disability (e.g., Cornelissen and Hansen, 1998). According to Stein (2003), whenever unstable fixation and

unwanted eye movements occur, the images slip over retina and generate powerful motion signals that, in turn, are fed back by the M-system to ocular motor centres in order to bring the fixation back on target. It was suggested that this unstable eye control leads to errors in letter position encoding and therefore, to a failure in acquiring adequate orthographic skills for reading. Cornelissen et al. (e.g., 1996; 1998a) also suggested that it is possible this could occur via either 'bottom-up' or 'top-down' mechanisms. According to the former, deficits in motion detection task could directly reflect abnormal magnocellular function, whereas, according to the latter, these deficits could be caused by deficient attentional processing via magnocellular system. Vidyasagar (1999; 2001) proposed a neural model of how early attentional selection could provide a neurological mechanism for early spatial selection in visual word recognition and reading. According to this model, the dorsal pathway could identify and select relevant positions in space, and this information could be passed on to the ventral system for more detailed analysis. This explanation of how M deficit could affect reading disability in dyslexia is described by Vidyasagar (2005). According to this '*visuo-spatial attention deficit*' explanation of dyslexia, the large receptive fields of the ventral stream involved in object recognition do not code well for location, and the feedback from the dorsal stream could feed the letters of each word in a temporal sequence to the ventral stream. In a recent MEG study by Pammer et al. (2006) spatial processing in word recognition was studied by presenting words with normal spatial letter-configuration and with constituent letter spatially shifted in relation to each other. The results of the study showed posterior parietal activation consistent with dorsal pathway involvement occurring between 100-300ms and then again at 200-400ms after stimulus onset. Similar results were reported in a recent study by Kevan and Pammer (Kevan and Pammer, 2008). They used a paradigm combining frequency doubled stimuli with endogenous cueing in order to study M deficits in dyslexic readers both at (lower) retinal level and at higher-order level that required attention shifts locate the target. The results of this study showed deficits at both levels. The authors suggested that lower level M deficits in sensitivity probably relate to

reading accuracy and irregular word reading, whereas the higher order deficits relate to reading speed and nonword reading in addition to reading accuracy and irregular word reading.

According to Valdois et al. (1995), attentional deficits in one dyslexic person were mirrored by those seen in a patient with acquired dyslexia after parietal cortex damage. It has been reported that dyslexics with deficits in motion coherence perception also showed impairment on visual search tasks, while dyslexics with normal motion perception are unimpaired, suggesting that dyslexics with visual problems related to magnocellular functions also have problems related to the function of posterior parietal area (Iles et al., 2000). Some studies have also shown that dyslexics' performance is impaired on spatial cuing tasks using a 'covert-orienting' paradigm, where attention is shifted from one place to the other without any eye movements (Posner, 1980). The time interval required to identify one target presented in close temporal succession (400-600ms) after recognising another target, so called 'attentional blink', has been reported to be delayed by 30% in dyslexics when compared to non-dyslexic readers (Hari et al., 1999). Another marker of parietal dysfunction, known as 'left neglect', i.e., a right-sided bias in selecting and processing the visual information, was also reported to be present among dyslexics (Hari et al., 1999). For example, dyslexic participants showed an asymmetry in their attentional focus: greater resources were available in the right visual hemifield rather than their left visual hemifield (Facoetti and Turatto, 2000). Various studies have reported attention deficits in dyslexia, in both visual (for a review, see Vidyasagar, 2004) and auditory (Petkov et al., 2005) modalities whether with or without accompanying ADHD (Kupietz, 1990; Richards et al., 1990). Fast attention shifts, both across space (for a review, see Jaskowski and Rusiak, 2005) and over time (e.g., Visser et al., 2004) are also affected in part of this population. Recently Facoetti et al. (2005) reported focused multimodal attention problems in dyslexic children when visual and auditory stimuli were used in the same sample of participants. Whether the attentional deficiencies in dyslexia are associated with magnocellular deficits was recently questioned by Skottun and Skoyles (2006).

They argue that the reduction in attention of dyslexic readers may occur independently of magnocellular deficits.

Many researchers have also reported auditory deficits in dyslexic population. An early study by Tallal and Piercy (1973) demonstrated that children with SLI are poorer in an auditory task of processing stimuli that incorporate brief, rapidly changing components, especially when these changes occur in tens of the milliseconds time range that characterises the acoustics of ongoing speech. They found that children with SLI were impaired in discriminating syllables 'ba' versus 'da' that naturally incorporate 40 ms time intervals (Tallal and Piercy, 1974) but not when the duration of time intervals was increased to 85 ms (Tallal and Piercy, 1975). Tallal and colleagues (Tallal et al., 1993) suggested that dyslexic children require longer to process rapidly changing auditory stimuli. They argued that phonological and reading-related difficulties shown by dyslexic children may be caused by this deficit in rapid auditory processing. According to Galaburda et al. (Galaburda et al., 1994) neuroanatomical abnormalities were discovered also in the auditory magnocellular pathway to the thalamus. There is evidence that dyslexics indeed may have poorer categorical perception of certain contrasting phonemes and non-speech sounds (Mody et al., 1997; Serniclaes et al., 2001) as well as deficits in backward masking (Rosen and Manganari, 2001; Ramus et al., 2003a).

The magnocellular theory unified the visual and auditory deficit theories and suggested that both sensory systems are affected in dyslexia (Stein and Walsh, 1997). The proponents of this theory suggest that phonological problems are caused by a basic deficiency in hearing sounds and that a visual deficit might independently contribute to reading problems. Ramus (2003) estimated that substantial minority of dyslexic children (29%) show visual and auditory processing problems. The neuroanatomical works by Livingstone et al. (1993) and Galaburda et al. (1994) showed problems among dyslexic children both in auditory and visual paths of the magnocellular systems. The post-mortem examination of five dyslexic brains showed that magnocells of the visual magnocellular pathway were smaller and fewer than normal in the lateral geniculate nucleus, whereas abnormalities were

also shown in the auditory magnocellular pathway to the thalamus. In his formulation of magnocellular theory, Stein (2001) unified sensory and motor control deficits under fundamental sensorimotor cause of reading problems in dyslexia. He further claimed that 'since the cerebellum receives a heavy magnocellular input and itself can be considered the 'head' ganglion of the magnocellular systems, this is further evidence for the hypothesis that impaired magnocellular development underlies dyslexics' problems'. The cerebellar deficit hypothesis authors, however, encompass the role of the cerebellum in central processing mechanisms, such as development of the automaticity of skills, rather than in sensory processing ones (Nicolson et al., 2001). They aknowledge that a minority of dyslexic individuals may also (or alternatively) suffer from weakness in the sensory processing cortico-cerebellar circuitry. The generalised version of the magnocellular hypothesis with causal connections at neurological and behavioural levels was proposed by Ramus (2003) in a diagram that is shown in Fig. 1.5. It displays schematically how, according to Ramus, the auditory and visual sensory and motor deficits may cause impairments in reading.

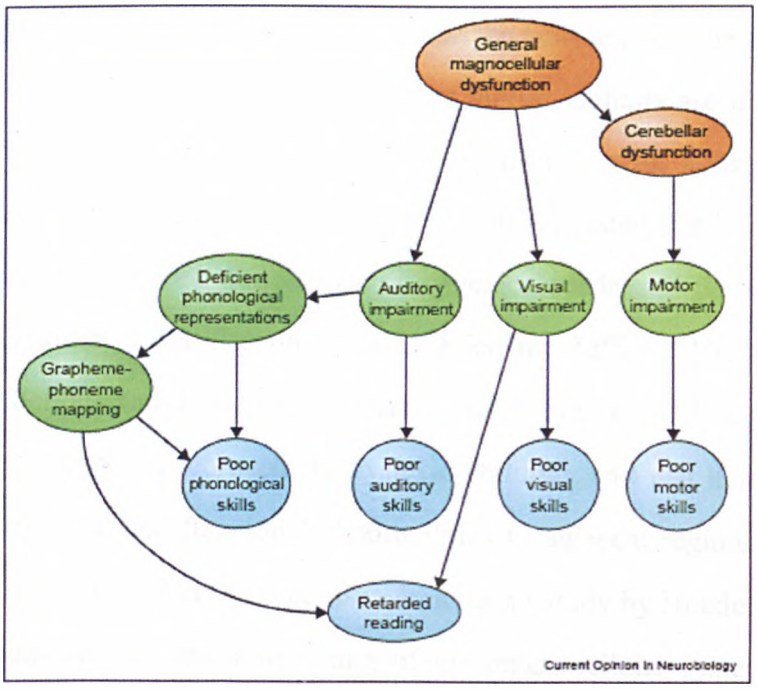


**Figure 1.6. Magnocellular deficit hypothesis by Ramus (2003)**
A diagram showing the generalised version of the magnocellular hypothesis of dyslexia adapted from Ramus (2003). The causal links are represented at neurological (upper), cognitive (middle) and behavioural (lower) levels.

However, as already discussed above, the magnocellular and visual attentional deficits in dyslexia may cause deficits in orthographic processing independently of phonological skills. As shown in some recent studies (e.g., Cornelissen and Stein, 1995; Talcott et al., 1998a), good readers had higher motion sensitivity, so that coherent motion thresholds could account for 25% of the variance in reading ability. The motion sensitivity measured in such way could account for variance in indices of visual/orthographic reading skills independently of any correlation with phonological ability (Talcott et al., 2000; Stein, 2003).

Numerous studies have reported differences between dyslexic and control readers in the functionality of the magnocellular system. However, the question of whether the magnocellular deficits found in dyslexia are a neurological marker (or epiphenomenon) of the dyslexic brain or have a causal relationship to reading difficulties is still hotly debated (e.g., Skottun and Skoyles, 2007, 2008). Skottun and Skoyles (2008) have criticised the studies on M pathway deficit in dyslexia suggesting that cortical area MT receives not only magnocellular but also parvocellular and koniocellular inputs, so that coherent motion may be also obtained with isoluminant colour stimuli that do not activate the magnocellular system. They have also argued that coherent motion deficits are not specifically linked to dyslexia but are also reported in connection with autism, Williams's syndrome and schizophrenia. Frith and Frith (1996) suggested that it is unlikely that magnocellular deficits are a direct cause of dyslexics' reading difficulties but rather a biological marker. It was also suggested by Eden and Zeffiro (1998) that although the sensory deficits and difficulties in learning to read may not be causally related but they may sometimes co-occur in dyslexic children, and that dyslexic persons may have structural and functional abnormalities in adjacent regions of the brain supporting linguistic and visual processes. In a recent study by Hutzler et al. (2006) no relationship between the functioning of the magnocellular system and visual perception and oculomotor control during the string-processing task was found in dyslexic readers. The authors argued that although numerous studies have found a deficit in the magnocellular system of dyslexics, the coexistence of sensory deficits

and reading difficulties may have correlational rather than a causal relationship. According to a recent model put forward by Ramus (2003; 2004) the phonological deficit is the core deficit of dyslexia, whereas the magnocellular and cerebellar deficits are comorbid markers without a causal relationship to dyslexics' reading difficulties. However, Reid et al. (2006) argued that this model may be problematic as in their study some of the dyslexic participants showed literacy difficulties without the phonological deficit, whereas the deficits in naming found in other participants could be due to deficits in precise timing mechanism. In addition, the authors also suggested that if a dyslexic person has both phonological deficit and difficulties with swapping the order of letters in the word (like one of their participants), it could be difficult to claim that only the phonological deficits are the cause of reading problems in this case. The authors concluded that the wide variety of dyslexic profiles and relatively low frequency of some types of deficits in dyslexia make it difficult to establish the causal links between their reading problems and less frequently occurring deficits. They also suggest that many longitudinal studies of individuals with familial risk of dyslexia from birth to adulthood, based on large and representative samples, are necessary in order to decide whether the magnocellular and cerebellar deficits have causal or correlational links with different sub-types of dyslexia.

## 1.3. Background to electroencephalography and event related potentials (ERPs)

### 1.3.1. Electrophysiological basis of the EEG signal

In the late 19th century Richard Caton (1875) discovered that brain electrical signals could be recorded directly from the surface of the exposed cortex using a reflecting galvanometer. Some years later Hans Berger (1929) was able to detect these brain waves with electrodes placed on scalp. Since these early discoveries of the 'feeble currents of the mind' the electroencephalogram (EEG) has become a powerful physiological tool, which is now being investigated by many laboratories around the world. Our understanding of the basic mechanisms underlying its expression and their significance to normal and abnormal brain functions is therefore expanding rapidly.

The EEG records the activity of many hundreds of thousands of neurons through electrodes placed on the scalp. It is a record of the fluctuations of the electrical activity of large ensembles of neurons in the brain. Specifically, it is a measure of the extracellular current flow associated with the summed activity of many individual neurons. It is usually assumed, that surface recorded potentials reflect predominantly the activity of cortical neurons within (at least) $6cm^2$ of the cortical area underlying the EEG electrode (Näätänen, 1992). Furthermore, the EEG recordings reflect postsynaptic potentials rather than action potentials for two reasons. First, the postsynaptic potentials extend over a larger portion of the cell membrane and generate a field that corresponds rather to a dipole perpendicular to the membrane surface. Secondly, action potentials have very short duration (1-2ms) and tend to overlap much less than the postsynaptic potentials, which last much longer (10-250ms) (Lopes da Silva and Van Rotterdam, 1999). To appreciate the physiological mechanisms underlying the EEG signal we need to briefly review the cortical morphology.

The cerebral cortex contains two major classes of nerve cells: pyramidal and nonpyramidal. Pyramidal cells are excitatory neurones that project their axons to other areas of the brain and to the spinal cord. They are the major projection neurons of the cerebral cortex. In addition, they can project locally, i.e., have

recurrent axon collaterals in a plane parallel to the cortical layer. These local connections play an important role in the collective electrical activity of cortical neuron ensembles. The dendrites of pyramidal cells often project across several layers, and they are usually oriented perpendicular to the surface of the brain. In addition, dendrites also contain local regions capable of generating action potentials that amplify synaptic currents (Martin, 1995; Silberberg et al., 2002). Nonpyramidal cells have oval-shaped bodies. Their axons typically do not leave the cortex and terminate on nearby neurons. Stellate cells form the main group of nonpyramidal cells. These cells have axons that are oriented vertically in the plane of the cortical columns. They usually receive information directly from thalamic neurones, which they convey to interneurones or pyramidal cells in the same column. Other nonpyramidal cells, such as basket cells, have their axons oriented horizontally in the plane of the cortical layers. They form dense synaptic connections that envelope the soma of the postsynaptic neuron, hence the name basket. The basket cell is thought to produce surround or pericolumnar inhibition, which enables neurons in a given cortical column to function in relative isolation from neighbouring columns (Douglas and Martin, 2004).

The summed activity of pyramidal cells (in the order of thousands of millions) that fire in synchrony while processing information is the principal source of EEG potentials (Peterson et al., 1995). Far field potentials can also be recorded, which reflect activity generated in subcortical structures such as the brain stem nuclei (Hari et al., 1982; Stern, 1982; Musiek, 2004). The EEG is an extracellular recording obtained by using macroelectrodes. This type of recording is similar to electrocardiography. Recordings are made at sites distant from the source of electrical activity. Both the EEG and electrocardiogram (ECG) are based on the theory of volume conduction, which describes the flow of ionic current generated by nerve cells or cardiac muscle through the extracellular space (Lopes da Silva and Van Rotterdam, 1999).

Thus, potential changes recorded from the scalp are generated by the summed ionic currents of many thousands of neurons located under the recording electrode. The net ionic current is recorded as a voltage across resistance of the extracellular space. If we consider an individual neuron, the flow of current is produced by an excitatory synaptic potential on the apical dendrite of the cortical pyramidal cell. The excitatory postsynaptic potential (EPSP) is produced by a

current flowing inward through the synaptic membrane and outward along the large expanse of the extrasynaptic membrane (Buzsaki and Traub, 1997). The site of inward current is called the sink because this is where the current flows into the cell. The site of outward current is called the source. The sink is on the negative side of the extracellular potential, and the source is on the positive side. At the site of the generation of EPSP the extracellular recording has a negative sign if the tip of the electrode is closer to the sink, and the potential has a positive sign if the tip of the electrode is closer to the source (Pedley and Traub, 1990; Holmes and Khazipov, 2007). The activity of a single neuron cannot be recorded from the scalp because the amplitude of its potential is too small and the macroelectrodes are insufficiently selective to distinguish this activity from that of its neighbours. Fortunately, the scalp recording is a summed activity of large numbers of neurones. Thalamic input activates thousands of cortical neurones synchronously. The initial cortical response to thalamic input is a formulation of a sink in deeper layers (where the excitatory synapses are located) and a source in superficial layers (Steriade et al., 1993; Nunez, 1995). A recording electrode on the surface of the scalp is therefore closer to the source than to the sink. The sign of the electrical signal will depend on where in the cortex the excitatory synapses are located, i.e., in superficial or deeper layers. As shown on a schematic diagram in Fig.1.7, if the source is closer to the recording site then the recording will have a downward deflection. If the sink is closer to the recording electrode then the recording will have an upward deflection. Thus, additional information about the distribution of cortical synapses is necessary to determine the direction of deflection of recorded potentials (Martin, 1995).

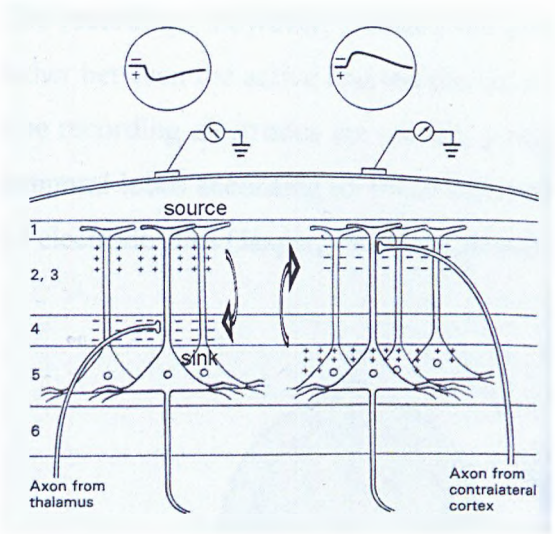


**Figure 1.7. ERP sources**
Schematic representation of the orientation of the recorded potential depending on the location of the synaptic potential according to Kandel et al. (1995).

As mentioned earlier, the reason why pyramidal cell activity contributes more to the EEG signal than nonpyramidal cell activity is that pyramidal cells are oriented perpendicular to the surface of the cortex (Karl, 1993). Because of the latter the sources and sinks are also oriented perpendicular to the surface of the cortex and synaptic potentials generated on their dendrites are recorded with little attenuation at the surface of the scalp. The nonpyramidal cells are not oriented in any particular fashion relative to one another or to pyramidal cells, thus, their contribution to the EEG is probably insignificant. The synaptic potentials contribute more to the EEG because they are slower than action potentials, and therefore can summate (Näätänen, 1992).

## 1.3.2. Recording EEG

As described above, the EEG is a result of summed activity of hundreds of thousands neurons in the area underlying the recording electrode, and postsynaptic potentials rather than action potentials. To record the EEG at least two electrodes should be used. An active electrode is placed over a site of neuronal activity, and an indifferent electrode is placed at some distance from this site. Usually in EEG recordings numerous active electrodes are placed over different parts of the head.

The recordings, however, measure the potential difference between two electrodes, either between the active and indifferent electrode or between two active electrodes. The recording electrodes are usually placed over the frontal, parietal, occipital and temporal lobes according to 10-20 International system of electrode placement with 19 electrode sites (Jasper, 1958), as shown in Fig. 1.8.

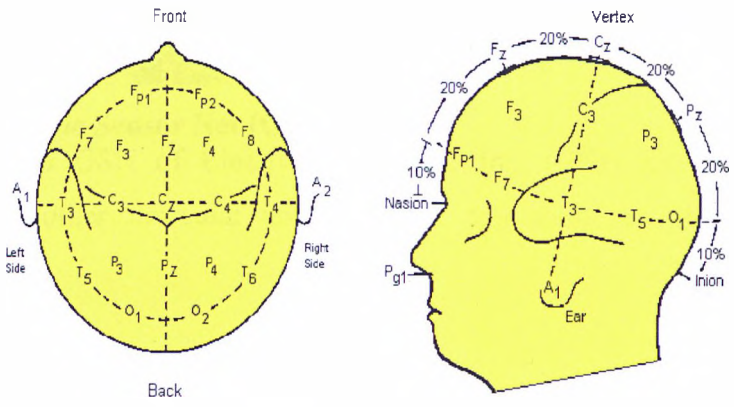


**Figure 1.8. 10-20 International System**
The standard placement of EEG recording electrodes according to 10-20 International system at the top and sides of the head. Abbreviations to multiple electrode placements are: A, auricle; C, central; Cz, vertex; F, frontal; FP, frontal pole; O, occipital; P, parietal; T, temporal. The multiple electrodes placements overlying a given area (e.g., frontal) are indicated by numerical subscripts.

More advanced recording techniques are used recently with a high density recording electrode nets that may have up to 256 or more channels. An example of such high density net that is used in the current work and provided by Electrical Geogesic Inc. (EGI) is displayed in Fig. 1.8. These modern high density electrode nets allow recording not only EEG data but also eye movement related activation. For example, in the Geodesic Sensor Net (GSN) shown in Fig. 1.8, three pairs of electrodes are used for recording the eyes movements. Thus, two pairs of vertically arranged electrodes above and below the eyes record the horizontal eye movements, whereas one pair of electrodes, i.e., one electrode at the side of each eye, records the vertical eye movements. In the current work the central electrode at the vertex, Cz, was used as a reference (see Fig. 1-8 for location of Cz on the scalp).

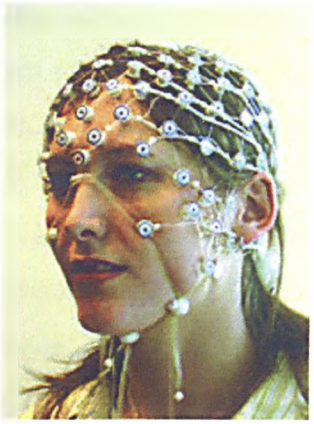

**Figure 1.9. Geodesic Sensor Net (GSN)**
The 256 channels GSN of Electrical Geodesic Inc. (EGI) for the EEG, eye movements and other muscular and electrical activation recording in human participants.

### 1.3.3. Deriving ERPs from EEG

The EEG is usually recorded either when the participant is awake or asleep. It is also recorded during specific sensory stimulation such as presentation of a flash of light or a tone. The component of the EEG that is specifically related to a significant stimulus is called sensory evoked potential or event related potential (ERP) (Picton and Hillyard, 1988). The sensory evoked potential, e.g., visual evoked potential (VEP), is a specific change in the ongoing EEG resulting from stimulation of a sensory pathway. Sensory evoked potentials are distinguished from the ERP. Thus, sensory evoked potentials reflect the processing of the physical characteristics of a stimulus and are often useful in clinical assessment of the sensory system's function or in evaluating demyelinating diseases. They consist of multiple components that are described below and displayed in Fig. 1.10. Event-related potentials, on the other hand, are dependent on the context in which the stimulus is presented and whether the stimulus is expected or is a surprise. According to Picton et al. (2000), recently the term 'event-related potentials' is used for endogenous potentials in order to differentiate them from the (exogenous) evoked potentials. Components whose characteristics (amplitude, latency, scalp distribution) seem to depend on physical attributes of the stimulus, such as their modality and intensity, are called 'exogenous' or 'sensory' potentials, sometimes also referred to as 'evoked

potentials' (EP). The event related potentials are components whose characteristics are relatively independent of the physical properties of the stimulus and are more dependant on mental set. These potentials are called 'endogenous' or 'cognitive' (Rugg and Coles, 1995). Usually, the 'exogenous' components or sensory EPs occur within the first 100 ms after the stimulus presentation, whereas the 'endogenous' ERP components occur after the first 100 ms. The EPs can be both endogenous and exogenous, however, the ERPs are always endogenous and can only be recorded when a cognitive process occurs independently of any specific evoking event such as a decision making or a response initiation (Picton et al., 2000).

Both sensory evoked potentials and ERPs are extracted from the EEG using computer averaging techniques. The EEG is recorded during repetitive stimulation, such as visual or auditory stimuli, that activate the sensory receptors and evoke brain electrical activation. The computer samples EEG for a brief period before and after the stimulus and the sampled data are averaged to enhance the signal-to-noise ratio. This is performed because the small ERP signal (~ 5-10 μV) recorded in one individual trial is obscured by the larger EEG signal (~ 50 μV) that is a result of many ongoing neural processes. The averaged ERPs reflect the relevant, repetitive and time-locked neural activity, while the non-repetitive signals that reflect random activity fail to contribute systematically to these specific portions of the ERP average. In order to improve further the signal-to-noise ratio additional processing is used such as filtering that helps to remove the artefactual electrical activity from sources other than brain. Usually the amplifiers that are used to record ERP include filter settings that eliminate any activity above and below selected frequencies. This allows the attenuation of high frequency electrical activity, such as the activity that is attributable to eye movements and muscles, as well as the activity at the electrical mains (50-60 Hz).

Evoked potentials consist of multiple components related to various aspects of subcortical and cortical processing. Although the recordings made from scalp electrodes reflect mostly cortical processing in the immediate environment of the electrode, earlier components reflecting subcortical processing also can be distinguished. The early components of evoked potentials reflect the processing of the physical properties of the stimulus, whereas the later components are more related to higher brain functions. An example of evoked potential's component

latencies recorded to an auditory stimulus is displayed in Fig. 1.9. The first set of deflections (within 10 ms from stimulus onset) represents brain stem potentials that are termed far-field potentials because they originate from distant sites. The second set of deflections (within 100 ms from stimulus onset) has longer latencies and is believed to be generated from the thalamic auditory relay nucleus and neurons in the auditory cortex. The ERPs (after 100 ms of stimulus onset) are generated in higher-order cortical areas and have longer latencies than sensory evoked potentials. The amplitude of the ERPs changes depending on the context in which the stimulus is presented, and may or may not be invoked by the external event. Because the temporal resolution of these measurements is in the order of milliseconds, ERPs can accurately measure the timing of the cognitive processes that take place in the brain. According to Picton and co-authors (2000), the spatial resolution of ERP measurements is limited both by theory and by our present technology, but multichannel recordings can allow us to estimate the intracerebral locations of these cerebral processes. Both temporal and spatial information provided by the ERP data can be used in different research studies and help to understand how brain implements various psychological tasks as well as establish the deviations in the impaired brain from the function of the healthy brain in order to make specific diagnoses in medicine or psychology.

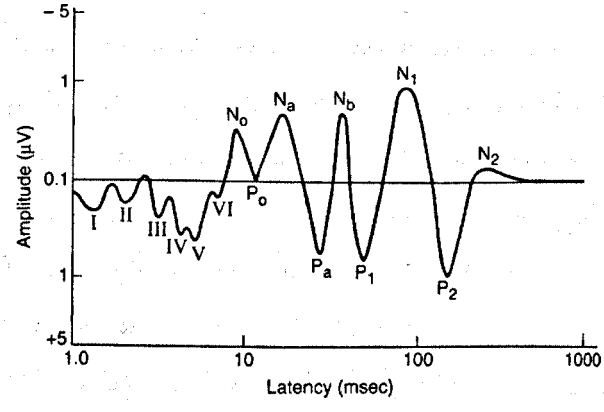


**Figure 1.10. Auditory evoked potential**
The components of the waveform according to Picton et al. (1974). Components I-VI are generated in the auditory pathway, from cochlea to the medial geniculate nucleus. Sources for the later negative ($N_0$-$N_2$) and positive (Po-P2) components are thalamic nuclei, auditory cortex and association cortices.

### 1.3.4. ERP components definition and measurement

We would like now to concentrate in more detail on the definition and possible generators of the ERP components. For simplicity, hereafter, I will refer to the EP and ERP components as early and late ERP peaks respectively. A commonly used procedure for measurement of ERP waveforms is to identify prominent peaks and troughs and label them according to their amplitude, latency and polarity. ERP waveforms can be plotted with upward deflections indicating positive or negative potentials at the active electrode relative to the reference. Both conventions are used in the literature and there is no consensus as to which is preferable. This is often indicated with a sign '+' or '-' at the upper end of the voltage calibration axis. In the current project the positive sign is used for the upper deflections of the ERP waves. There is no a priori reason to believe that interesting aspects of cerebral processing would be reflected in these positive and negative peaks. However, this traditional approach worked surprisingly well for many research purposes. The goal is to understand the ERP waveforms both in terms of intracerebral sources and experimental manipulations. A component of ERP would be a temporal pattern of activity in a particular region of the brain that relates in a specific way to how the brain processes information. Through systematic examination of the amplitude and latency of numerous deflections in the electrical potentials that comprise the ERP, it has been possible to link particular components of a response to specific psychological processes. The examination of these components can provide information regarding the sequence of perceptual and cognitive operations involved in processing a stimulus or generating a response (Luck and Hillyard, 1994).

Currently, there are two hypotheses regarding the neural origins of ERP components generation: evoked model and phase-resetting model (Makeig, 2002). According to the former and more traditional view, the stimulus evokes a time-locked, neural-population induced response in each trial, and this response is enhanced and clarified by signal averaging to produce an ERP peak (e.g., Hillyard and Picton, 1987). An alternative view for explaining the generation of the ERP peaks was proposed by Sayers et al. (1974) and currently is supported by other researchers (e.g., Basar et al., 1997; Polich, 1997). According to this model, the ERP components result from reorganisation of already existing ongoing EEG-activity. In other words, every component may contain oscillatory responses in

various frequency ranges of the EEG, depending on information processing demands. For example, it was reported that most of the large amplitude components in human sensory EP lie in the theta and/or alpha frequency range (Basar, 1998). According to another study (Basar-Eroglu et al., 1992) the P300 response may be predominantly within the theta and delta frequency range of the EEG.

Thus, according to a traditional view, the ERP peaks emerge as summation of response from neuronal populations triggered by stimulus properties or psychological processes. These responses recorded in individual EEG trials emerge from the noise when many trials are averaged. Therefore, the ERP peaks reflect some important electrical responses that can be exogenous or endogenous (discussed earlier) and reflect various brain activation processes. Often the ERP peaks are studied in order to investigate the normal and abnormal processes in the brain, in healthy and clinical population. The amplitude and latency of these peaks may vary between control and clinical populations, even when the participants are not able to or have difficulties producing overt responses (Connolly, 2000; D'Arcy, 2003). The ERP components are an important tool to study the neural correlates of sensory, attentional and cognitive processes. Their examination can provide information regarding the sequence of perceptual and cognitive operations involved in processing a stimulus or generating a response. For example, in processing an auditory event, early components of the ERP (e.g., N1) represent activity in the first cortical areas to receive sensory input (e.g., auditory cortex) and subsequent deflections such as P2 reflect early stimulus evaluation and feature detection (Luck and Hillyard, 1994) in temporal cortex. The later components of the ERP (e.g., P300 or P3) are thought to process information at more advanced cognitive levels, e.g., during shifting attention or updating mental representations in working memory (Donchin et al., 1986). The P300 is thought to be generated by a distributed network with frontal and parietal contributions, possibly also involving hippocampus (Bashore and van der Molen, 1991; Polich and Criado, 2006). Still later components can reflect responses to violations of semantic (N400) or syntactic (P600) expectancy (Osterhout et al., 1994).

The early components usually consist of sharp positive and negative peaks that form the P1-N1 complex and demonstrate that neural synchrony occurs in narrow time windows probably alternating between inhibitory and excitory processes (reflected by the P1 and N1 components respectively; Hillyard et al.,

1994). During visual stimulation the P1 can be recorded with a latency of 90-120 ms, and the N1 can be recorded at the latency of 150-190 ms, which shows that the interpeak latency between these early components can be as little as 60 ms (Hillyard et al., 1994). Numerous studies indicate that these early components reflect mostly sensory and early attentional processes (e.g., Eason, 1981; Hillyard et al., 1994). It was also reported that they may have a frequency characteristic that corresponds to an oscillation in the alpha frequency range, i.e., somewhere between 6 and 12 Hz (Basar et al., 1997). According to Mangun et al. (1993), briefly flashed visual stimuli evoke positive and negative components over parietal regions that begin as early as 35-40ms after stimulus onset, however, only the larger, more prominent peaks (P1, N1, P2) can be readily observed. Early VEPs are usually the larger over the hemisphere contralateral to the visual field of the unilaterally presented stimulus (Mangun et al., 1993). It is reported that the P1 is generated in the vetro-lateral extrastriate cortex (Broadman's area 18 and/or 19), whereas the N1 may be of maximal amplitude over parietal scalp locations (Mangun et al., 1993). In the current studies I have planned to record these early components of evoked potentials as they may reflect the early processes in brain activation of dyslexic readers that may be different from that of controls. The reports of attention and visual sensory deficits among dyslexics may well be possible to investigate through use of these early detectors of sensory deficits (if present) in the dyslexic brain. There are some previous reports that suggested these early components may be deviant in dyslexics when compared to controls. For example, recently Maurer et al. (2007) reported an impaired tuning of a fast occipito-temporal response for print in dyslexic children learning to read, reflected in atypically symmetrical and delayed N1. Deviant early brain activation in dyslexic children was also found in response to unexpected words (Brandeis et al., 1995) and during spoken word recognition (Bonte and Blomert, 2004). The ERP studies related to each individual task presented in this thesis are discussed further in the corresponding chapters below.

As already mentioned, the later brain potentials such as ERP component P300 (or P3), tend to be regarded a 'cognitive' neuroelectric phenomenon since it is generated in psychological tasks that require the subject to attend to and discriminate the stimuli that differ from one another on some dimension (Polich and Kok, 1995). These discrimination processes trigger a large positive going peak with a latency of about 300-600ms. This component was first reported more than 40

years ago by Sutton et al. (1965) and it was related to 'basic information processing mechanisms of attention allocation and immediate memory'. According to Polich and Kok (1995) the studies of P300 have expanded dramatically since, due to its significance as a means to assess cognitive function in many research and applied areas (for a review, see Polich and Kok, 1995). According to Donchin and Coles (1988), the most significant interpretation of P300 is that it reflects updated mental representations of the stimulus environment. After initial sensory processing, the current stimulus in compared with the previous one in the working memory. If no stimulus attribute is changed, the old 'schema' is maintained. Some researchers consider the P300 latency as a measure of stimulus classification speed, which is not related to response initiation (e.g., Kutas et al., 1977; Polich and Criado, 2006). The latency of P300 is usually correlated with cognitive efficiency, and it can increase with healthy ageing (e.g., Polich, 1996; Taroyan et al., 2004) as well as with compromised mental capability (e.g., O'Donnell et al., 1992). This late ERP component has been also reported to be linked with word frequency effect, for example, in a lexical decision task its latency was shorter for common compared to uncommon words (Polich and Donchin, 1988). The authors suggested that the uncommon words may require more processing capacity for their evaluation compared to more common words. Thus, the P300 component is known for its relation to cognitive function of the brain and evaluation of the incoming information. For the reasons mentioned above I was interested to investigate this part of the ERP response in the studies described here, in addition to more early sensory evoked potential components. Some previous studies reported a smaller and delayed P300 in children with developmental dyslexia (e.g., Taylor and Keenan, 1990). My goal was to see whether there will be differences in brain potentials of dyslexics from controls in the attentional and decision making performance, visual magnocellular function and lexical decision task. Some previous ERP studies in relation to these tasks among dyslexic population will be discussed in more detail below when describing each study individually.

Another component within this late time window (300-600 ms) of ERP peaks that is often reported in literature is the N400 – a negative deflection in the ERP response about 400 ms after stimulus onset that was originally observed in the subjects reading sentences ending with sematically incongruous words (Kutas and Hillyard, 1984). An anomalous N400 has been reported in children with language

disorders (e.g., Neville and Mills, 1997) where the amplitude of this component was enhanced, whereas other studies reported reduced N400 amplitude among dyslexic children (e.g., Stelmack et al., 1988). In the current work I was also interested to find similar brain activation in these later time windows beyond P300 and after 400ms from the stimulus onset, e.g., P600 reported in recent studies and mentioned earlier in this section. In these similar time windows I found positive peaks with latency of about 400 ms and 500 ms, that were labelled P4 and P5 (or P400 an P500) that were only found in language related Study 3, i.e., the lexical decision task. These findings confirmed that the deflections in time windows of 400-600 ms may be related to reading and language processing. Similar 'lexicality' effects were found in recent study by Hauk et al. (2006), where the amplitude of the ERP was larger to pseudowords than to words. Some relevant details are discussed further within the description of Study 3.

As already briefly reflected on earlier in this section, there are different ERP labelling systems that are currently in use, each has advantages and drawbacks. The two most common approaches are to designate the observed peaks and troughs in the waveform in terms of polarity and order of occurrence in the waveform (N1, P2, etc.), as in the studies described in this thesis, or in terms of polarity and typical peak latency (e.g., N125, P200, etc.). The latter version can be used to describe a mean deflection over specific time window, e.g., N20-50, N300-500. Negative latencies can be used to label movement-related potentials that precede the response onset. For example, N-90 indicates a negative deflection that peaks 90 ms prior to the response. There are inherent problems with both the latency and ordinal systems, because a waveform feature that represents a particular psychological process may vary in its timing or order of appearance depending on experimental circumstances, age or clinical status. For these reasons, when describing the methods of peak definition, authors must provide the information about the latency range and mean value for each peak, as well as variations as a function of scalp site and experimental condition. For example, to emphasize variations among components at different scalp sites, the recording site could be incorporated in the label (N175/Oz).

An important distinction needs to be made between the terminology that uses the waveform features measured in a given data set and theoretical terminology that represents particular psychological processes. For example, for some ERP

components theoretical labels have been assigned that indicate the assumed functional role of the components. These include 'readiness potential', 'mismatch negativity', 'processing negativity'. In other cases, polarity-latency labels such as P300 or N400 are used in a theoretical sense, referring not to waveform feature but to a psychological entity with specific functional properties. The growing use of the ERP research methods has resulted in numerous component definitions, which makes it difficult to understand whether the theoretical entities used in one study are equivalent to those used in another study. This could be helped by keeping the observational and theoretical terminology separate.

Peak amplitude measurements are usually made relative to the prestimulus baseline (baseline to peak) or with respect to adjacent peak (or trough) in the waveform (peak-to-peak). Baseline-to-peak measurements are preferable to peak-to-peak measurements given the successive peaks might well reflect different psychological processes. Although peaks are usually picked at the point of maximum amplitude (or minimum) voltage, this selection may be problematic if the data are noisy or if the waveform is not symmetrical about the peak, or if the peak is broad, or if there are two peaks. There are alternative ways of determining the amplitude and latency of ERP components. For example the latency of a maximal peak, recorded at an electrode from a group of electrodes in the area, could be used for defining the amplitude and latency of the same peak recorded at other channels in the group. Or both the amplitude and latencies values of the peak in all channels in the group could be averaged. The latter method was used in the current study, which also helped to reduce further the signal-to-noise ratio in the ERP signal. Usually the peaks in the individual subject data are measured in time windows of peaks defined by group averaged data, especially for the clinical populations who may have more noisy and variable data. The amplitude of the ERP peaks can also be measured as a mean in a window centred on the peak, with a fixed latency measured at the peak from the stimulus onset, i.e., from the onset of the ERP till the maximum point voltage of the peak.

## 1.4. The aims of the project

My objectives were to develop combined neurophysiological and behavioural tests of the magnocellular and phonological deficit hypotheses, as well as of the attention deficits in dyslexic children with no overlapping symptoms of ADHD, using the new high-density ERP methodology. The cognitive tests (outlined briefly in the next section) were intended to be performed in the same samples of dyslexic and non-dyslexic participants, with simultaneous recording of the ERP and behavioural measures, such as reaction times and error rate. I intended to find out whether these sensory, phonological and attention deficits would be present in the same group of dyslexic participants, in what proportions, and how this would be correlated with the brain electrical activity.

### 1.4.1. Study 1: Investigation of the Continuous Performance Test

The cued continuous performance test (CPT) is primarily a test for attention deficit. Single letters are presented sequentially every 2 s. The observer has to respond only to the stimulus after an O, and only if the stimulus is X. ADHD children perform poorly on this test. A recent German ERP study (Zillessen et al., 2001) established robust differences between ADHD and drug-treated ADHD groups. My aim was to use the same design and paradigm as in this and in previous CPT studies (Fallgatter et al., 1997; Fallgatter and Strick, 1999) in dyslexic children without comorbid ADHD symptoms and establish whether the attentional deficits are present in 'pure' dyslexic adolescents as compared to their age and IQ matched nondyslexic controls. As in my first study outlined above, the aim was to record simultaneously the electrophysiological and behavioural indicators of the performance in the same sample of participants.

### 1.4.2. Study 2: Investigation of magnocellular system performance

As discussed earlier in section 1.2.3, detection of coherent motion in random dot kinematograms has been shown to be a reliable test of visual magnocellular function (Cornelissen et al., 1995; Cornelissen et al., 1998a; Slaghuis and Ryan, 1999). In the behavioural studies threshold judgment tasks have been used, and they are notoriously difficult for the observer. This method would not be possible to use with the ERP paradigm. Therefore, I replicated the paradigm used in previous ERP studies (e.g., Scheuerpflug et al., 2004; Schulte-Korne et al., 2004) and used different low levels of coherent motion in stimuli. As suggested earlier, for the correct judgement of this event (e.g., Slaghuis and Ryan, 1999) a minimum extent of coherence is needed which might be higher for dyslexics compared to controls. The lowest level of coherence in the current study was selected at 10%, as previously the VEPs could not be reliably elicited below the value of 7% coherence of the moving dots (Niedeggen and Wist, 1999). I have also decided to use low contrast of the stimulus (between the moving dots and the background, Michelson 5%) in order to avoid the activation of parvocellular system (details are discussed later in Study 2). I planned to replicate previous ERP studies (Scheuerpflug et al., 2004; Schulte-Korne et al., 2004) in English speaking dyslexic and non-dyslexic adolescents with concurrent recording of the ERP and behavioural measures of the performance.

### 1.4.3. Study 3: Investigation of ERPs to words and pseudowords

It is well known that dyslexic children are particularly impaired on reading pseudowords, an effect usually attributed to phonological deficits. Recent Austrian and Hungarian ERP studies (Klimesch et al., 2001; Wimmer et al., 2002; Csepe et al., 2003) used three conditions - reading numbers, words and pseudowords. Analysis of the ERPs identified a number of important differences between dyslexic and control children, which the authors attributed variously to parietal lobe dysfunction, abnormality in Broca's area and the angular gyrus, and abnormality of visual working memory. My aim was to replicate these studies and their paradigm

in English speaking adolescents with simultaneous recording of electrophysiological and behavioural correlates of word recognition in this lexical decision task (decide whether the stimulus is a word or a pseudoword). I was interested to study different stages of word/pseudoword processing, from the early, i.e., pre-lexical, visual word form recognition to the later stages of decision making and behavioural response choice.

### 1.4.4. The expected theoretical and practical outcomes of the project

The studies outlined above were undertaken in dyslexic and non-dyslexic English-speaking adolescents. To the best of my knowledge there have not been equivalent studies with English-speaking adolescents that investigated combined neurophysiological and behavioural measures of various deficits suggested by the major theories of dyslexia. Conducting these tests in the same group of participants would allow us to compare the brain and behavioural mechanisms as well as proportion of these deficits in this age group of English speaking dyslexic individuals. These studies would provide an overview of brain-based processing in dyslexia and further insights into suggestions of some of the major theories of dyslexia that the individual studies could not. The results of the first study described in this thesis have been already published in Clinical Neurophysiology (Taroyan et al., 2007), whereas the other two studies are also submitted for publication in other peer-reviewed journals. The papers were derived from the lengthier descriptions presented in this thesis. It is necessary to mention that ideally I had to have an extra control group of younger children matched for reading abilities with my group of dyslexic participants, i.e., at the same reading age. It was argued by Bryant and Bradley (1985) that it is necessary to question whether the differences between the groups are not simply due to their different reading experiences. However, there is an additional issue as the adolescence is known to be a very active period in terms of brain maturation processes, both in its structure and function (Whitford et al., 2007). Therefore, it may be difficult to compare our participants and younger children because of different stages in overall brain maturation they may be at, which could also be reflected in the ERP activation and between-group differences.

I think this is an interesting issue and its consideration would be an aim in my future research.

In terms of applied outcomes this project would also provide useful results. There is a pressing need for non-invasive 'brain-based' diagnostic methods. The ERP tests developed here may be helpful in various research applications, both in developmental disorders and ageing studies. Additionally, these objective electrophysiological correlates of deviation in brain activation of dyslexics that could possibly be found in the current studies could also add to the knowledge of theoretical issues of dyslexia. These electrophysiological indicators could be used to provide brain-based 'benchmarking' of different interventions, as well as to facilitate the development of interventions that are optimal for each individual child.

# 2. STUDY 1. BEHAVIOURAL AND NEUROPHYSIOLOGICAL CORRELATES OF DYSLEXIA IN THE CONTINUOUS PERFORMANCE TASK

## 2.1. Introduction

The multi-symptomatic and heterogeneous nature of dyslexia has led to a number of competing theories attempting to explain its cognitive and neurobiological mechanisms. As already mentioned in the Introduction, among currently influential theories are the phonological deficit hypothesis, the magnocellular deficit hypothesis, and the cerebellar deficit hypothesis. To remind the reader, I would like to briefly outline their statements below. Thus, according to the magnocellular deficit hypothesis the processing of fast incoming information is impaired in dyslexia and is caused by abnormalities in magnocellular sensory pathways (Lovegrove et al., 1980; Stein and Walsh, 1997). According to the phonological deficit hypothesis (Bradley and Bryant, 1978; Vellutino, 1979) a difficulty in identifying, sequencing and reproducing sounds or syllables (phonemes) within a word is at the core of dyslexia. This cognitive theory has been recently supported by biological findings of disconnections between language areas through the Sylvian fissure (Paulesu et al., 1996; Horwitz et al., 1998). The automaticity deficit hypothesis (Nicolson and Fawcett, 1990) suggests reading problems in dyslexia arise from general lack of ability to automatise any skills, including reading and phonology. The cerebellar deficit hypothesis (Nicolson et al., 1995) proposes that the automaticity problems and a range of other problems in dyslexia (e.g., Nicolson and Fawcett, 1994b; Fawcett and Nicolson, 1999; Nicolson et al., 2001) are caused by abnormalities in the cerebellum. Additionally, it has also been suggested that development of interhemispheric functional asymmetry may be disregulated in dyslexics (Galaburda et al., 1985) and the transfer of motor and sensory information between hemispheres degraded due to changes in the corpus callosum of dyslexic brains (Gladstone and Best, 1983; Gross-Glenn and Rothenberg, 1984; Robichon and Habib, 1998; von Plessen et al., 2002). All these findings show that subtle developmental changes in a network of many brain

structures may be at the basis of sensory and cognitive problems in dyslexia (Galaburda, 1999; Eckert, 2004).

Dyslexia is frequently accompanied by other, non-linguistic problems, such as visuo-motor coordination, attention, and early sensory processing. There is a high rate of comorbidity with other developmental syndromes including ADHD, Specific Language Impairment, and Developmental Coordination Disorder (Fletcher et al., 1999; Bishop, 2002). Kaplan et al. (2001) established that among 179 children in Calgary receiving special support, the incidence of ADHD was 69%, the incidence of dyslexia was 64%, the incidence of developmental coordination disorder was 17%.

Many studies of perception in children with dyslexia do not take into account the potential presence of ADHD in a systematic fashion (Breier et al., 2003). The estimates of comorbidity of dyslexia with ADHD vary widely, ranging from 10% to 45% (Purvis and Tannock, 2000). This means that only (slightly more than) half of children diagnosed with dyslexia have 'pure' dyslexia, i.e., impairment related only to the reading process. Thus, it is still not clear whether the attentional deficits in dyslexia are specifically related to this developmental disorder or are a result of co-occurring ADHD symptoms.

The Continuous Performance Test (CPT) is a well-recognised and reliable measure of sustained attention (Rosvold et al., 1956; Cornblatt et al., 1988; Halperin et al., 1991) that consistently discriminates ADHD from control groups by conventional performance indices such as reaction time (RT), number of correct hits, misses and false alarms (e.g., Barkley et al., 1991; Losier et al., 1996; van Leeuwen et al., 1998). Interestingly, children with dyslexia were reported to perform poorly on CPT (Tarnowski et al., 1986; Eliason and Richman, 1987). But it still remains a question whether children with dyslexia show attentional deficits in CPT in absence of ADHD symptoms. A major issue addressed by the current study was therefore whether participants with 'pure' dyslexia (that is, without comorbid ADHD) would show an abnormal CPT performance.

It is likely that, even if behavioural differences are not marked in children with developmental disorders, there still may be underlying neurophysiological differences – reflecting their atypical brain organisation (e.g., Baving et al., 2006). Indeed, the automaticity deficit theory claims that under conditions of low cognitive load dyslexic participants may well perform at normal levels, by 'consciously

compensating' for their incomplete automatisation of the underlying skills. It is only when the cognitive load is made heavier, for instance via a dual task, that the underlying differences are revealed. I addressed this issue by the use of event related brain potentials (ERP). This electrophysiological technique is non-invasive and it provides an insight into rapid changes of brain electrical activity with high time resolution. The subtle nature of developmental dyslexia makes this method more informative because it can provide objective markers in evaluation, say, of the different stages of cognitive processing required for reading.

ERPs have been used to study attention in dyslexia and were frequently reported to be attenuated and sometimes delayed in dyslexic children (Lovrich and Stamm, 1983; Taylor and Keenan, 1990; Fawcett et al., 1993; Schulte-Korne et al., 1999a), which may be associated with poor attention and insufficient processing of task-relevant stimuli (Habib, 2000). Several ERP studies in dyslexia have found not only attenuated P300 amplitudes in the dyslexic group but also reversed or absent hemispheric lateralisation compared to controls on a low level vision task (Schulte-Korne et al., 1999b), with auditory stimuli (Pinkerton et al., 1989) and on a spatial attention shifting task (Wijers et al., 2005). These results show once more that developmental dyslexia is not just a language-related difficulty but it also concerns other cognitive domains involved in learning to read.

ERPs have been used to study brain activity in CPT in normals and clinical groups (e.g., Frank et al., 1998; Brandeis et al., 2002; Fallgatter et al., 2003; Herrmann et al., 2003). In the extended version of the CPT, OX-CPT, participants are presented with a rapid succession of letters and have to respond to the target letter X only if it was preceded by the letter O (e.g., Fallgatter et al., 1997; Fallgatter and Strick, 1999). This paradigm was used to record ERPs to task relevant stimuli and irrelevant distractors, in response activation (Go) and response inhibition (NoGo) conditions of the CPT. Whether this association with response inhibition is valid is still under debate in the current literature (see Dien et al., 2004; Salisbury et al., 2004). I briefly return to this issue in the Discussion. It has frequently been reported that hyperactive children had abnormally small P3 amplitudes of ERPs (as well as abnormal RTs and error rates) compared to healthy controls both in Go and NoGo conditions, (e.g., Jonkman et al., 1997; Seifert et al., 2003; Banaschewski et al., 2004).

I applied this paradigm to our dyslexic and control groups. An assessment of dyslexic participants was carried out by a diagnosing psychologist to make sure that none of them had ADHD symptoms. The key issue addressed in this study was whether dyslexics would show a decrease in behavioural performance of CPT in the absence of ADHD symptoms. A further key issue was whether the underlying brain electrical activity would show systematic differences between dyslexic and control groups.

## 2.2. Methods

### 2.2.1. Participants

I studied 10 adolescents with developmental dyslexia (3 females) and 10 control participants (3 females) with no reading or writing impairment. All participants were right-handed, the handedness was tested on Edinburgh Handedness Inventory (Oldfield, 1971). All participants had normal or corrected to normal vision, and no history of brain injuries or neurological problems. They were not under any medical treatment. The participants with dyslexia were diagnosed previously by qualified psychologists. Mean data of age, full scale IQ (Wechsler, 1991), reading age (RA) and spelling age (SA) (Wechsler, 1993) for both groups are displayed in Table 2.1. Criteria for inclusion in the dyslexic group were a discrepancy of at least 18 months between their age and RA/SA and an IQ > 90[1]. The main criterion was the RA, however, we have also used the SA as an additional criterion for inclusion in the dyslexic group, as it is typically more resistant to remediation. One factor ANOVAs did not show significant differences between the dyslexic and control groups on IQ scores [$F(1,18) = 3.7$, $p>.07$], however, as expected the dyslexics had significantly lower RA [$F(1,18) = 39.4$, $p<.0001$] and SA [$F(1,18) = 37.6$, $p<.0001$] scores compared to controls. None of the participants showed any evidence of ADHD as

[1] One dyslexic subject improved his RA and SA scores since the time of diagnosis, one dyslexic participant's IQ decreased to 87, and one control subject dropped his SA score. However, both behavioural and ERP data of each of these subjects were very characteristic for their respective group averages. The statistical analysis performed without these subjects did not change the significance values of neither ERP, nor behavioural results or the Group effect size.

measured on the DSM-IIIR scales (American Psychiatric Association, 1987) by the school teachers and the diagnosing psychologist. We do not have the individual scores from teachers, however, none of the participants scored higher than 1 (the cut-off for ADHD is usually 7). All participants were paid for their participation. The study was approved by the local ethics committee (Psychology Department, Sheffield University). The information about the EEG recording was provided in advance and the written research consent forms were obtained. These forms are attached in the Appendices 7.1 and 7.2 respectively.

**Table 2.1 Psychometric data of participants**
Mean values for each group of participants (ranges in parentheses)

| | Controls (N=10) | Dyslexic (N=10) |
|---|---|---|
| Age (years) | 16.1 (14.4 -18.3) | 16.3 (15.5 – 17.4) |
| IQ (standardised IQ score) | 117.6 (99 - 135) | 105.8 (87 - 124) |
| Reading age (years) | 17.1 | 12.1 (9.3 – 17.1) |
| Spelling age (years) | 16.4 (12.6 – 17.1) | 10.6 (7.6 – 17.1) |

## 2.2.2. Design/Paradigm

A modified version (Strik et al., 1998) of the classical CPT (Rosvold et al., 1956) was used in this experiment. It was designed and run on a Dell DIMENSION 8300 microcomputer (version 2002) PC using E-prime V1.0 (Psychological Software Tools, 2002). A sequence of 440 letters programmed in quasi random order from 12 different letters (A-H, J, L, O & X) were displayed one at a time, i.e., one letter within each trial (440 in total) on the computer screen. Each trial started with a fixation period of 1350 ms, prompting the subject to fixate two thin vertical lines in the centre of the screen. Then one of the 440 letters appeared in between fixation lines and was displayed for 500ms. The fixation period in the beginning of the next and all consecutive trials served also as an inter-stimulus interval (ISI) between the letter presentations. Thus, in the beginning of each trial the observer saw two fixation lines on a blank screen for 1350 ms, next a letter was displayed within the fixation lines for 500 ms. Thus, each trial lasted for 1850 ms. The letters

on the screen were 12 mm high and 11 mm wide obtaining a visual angle of 1.15° vertically and 1.05° horizontally at a viewing distance of 60 cm.

Participants were instructed to press the response button with the index finger of their right hand as quickly as possible each time the letter 'O' was followed directly by letter 'X' (Go condition). Thus, if one trial (consisting of fixation period and letter presentation) had letter 'O' in it, and the next trial (also having a fixation period followed by a letter presentation) had letter 'X' in it, then participant had to press the response button. The other 10 letters (A-H, J & L) or trials with these letters required response inhibition if they immediately followed the trials with letter 'O' (NoGo condition) and served as meaningless distractors when presented next to any other letter than 'O'. Thus, there was always an interstimulous interval between the letters, i.e., a fixation period of 1350 ms without letters that was followed by the stimulus displayed for 500 ms, so that each trial lasted for 1850 ms. We had 440 trials (and 440 letters within them) lasting 1850 ms each.

A session lasted about 14 min and included 80 presentations of the letter O, [40 times followed by an X (Go condition) and 40 times followed by another letter except O or X (NoGo condition)]. There were also 40 letters X without preceding O and 240 other distractor-letters (A- H, J & L).

Participants were seated in a comfortable chair in an acoustically shielded, dimly lit room. They were asked to fixate two thin vertical lines in the centre of the monitor at eye level, and to refrain from eye movements, head or other body movements during stimulus presentation. Each participant had a short training session in order to familiarise them with the task. Both speed and accuracy were equally emphasized during explanation of the test. The written instructions were provided as well (see attached in Appendix 7.3). The recording was monitored and controlled by the experimenter in the adjacent room.

### 2.2.3. Data acquisition

The EEG was recorded from 128 electrode sites plus a Cz reference at the vertex using the Geodesic Sensor Net (GSN) (Tucker, 1993) of Electrical Geodesics, Inc. (EGI). The GSN is a network of elastic bands holding an array of

small plastic tubes that contain sponges with Ag/AgCl sensors. In order to monitor eye movements, the horizontal and vertical electrooculogram (EOG) was recorded by 6 most anterior electrodes in the Net. The GSN was connected to the EGI high-input impedance amplifier (200 MOhm, Net Amps). The bandpass-filter of the recording system was set at 0.1 to 100 Hz. Individual sensors were adjusted until impedances were below 50 KOhm. All channel signals were amplified by a factor of x1000 and digitised with a 12-bit A/D converter at a sampling frequency of 250 Hz. The data were collected by a Power Macintosh OS X (10.2.8) and stored for off-line analysis. Simultaneously with the EEG, trial specific information, such as condition type (Go, NoGo, other distractor), accuracy of response and mean reaction times (RTs) of correct responses were collected through E-prime on the PC and stored on the Macintosh for further analysis.

### 2.2.4. Data analysis

Further processing and analysis was performed off-line using Eprime for the RTs and using NetStation 4.0 EGI software for the EEG data. Mean RTs from the whole experiment, the number of omission errors (misses) and commission errors (false alarms) were determined for each participant. Mean RTs for the first and second halves of the experiment were calculated as well in order to test and compare dyslexic and control groups for the ability to sustain attention towards the end of the test.

The EEG data were digitally bandpass filtered in the range of 1- 40 Hz. The highpass-filter was set at 1Hz in order to exclude the slow direct current shift from trials, and a lowpass-filter was chosen at 40 Hz to remove any mains interference. Segmentation of the continuous EEG into epochs starting 200ms before stimulus onset and lasting 1000ms after was performed next for each category (experimental condition), recording site, and participant. Artefacts were removed first automatically, based on an average (200 $\mu$V) and transit (100 $\mu$V) amplitude thresholds, as well as the EOG (70 $\mu$V) threshold. Additionally all segments were inspected visually for remaining muscle or other artefacts not reaching the threshold values. Individual bad channels were replaced with a spherical spline algorithm (Srinivasan et al., 1996). Trials with more than 20 bad channels were discarded

from further analysis. On average, 90% of the trials (epochs) were retained. The ERPs were computed by averaging all remaining trials, time-locked to stimuli, lasting 1200ms including 200 ms prestimulus baseline. The onset of ERPs in Go condition was locked to the onset of target letter 'X' (presented after O), and the onset of ERPs in NoGo condition was locked to the onset of nontarget letters (any letter from A-J, H & L without preceding O). The Go ERPs were obtained only from EEG epochs accompanied with the correct response, and the NoGo ERPs were obtained only from trials with correct inhibition (no button press) of the response. The Go and NoGo ERPs were analysed further and are reported in this study. A baseline-correction of all potentials was performed by subtracting the averaged 200 ms of prestimulus recording from the entire wave. These individual participant ERPs were re-referenced to an averaged value across all electrodes, and corrected for polar average reference effect (Junghöfer et al., 1999).

The group average ERPs were computed separately for the dyslexic and control participants in the Go and NoGo conditions. The main ERP component of interest in this study was P300. It was identified by visual inspection of group average and individual data in a time window of 300-400 ms. This late ERP peak was most distinct and of largest amplitude in parietal region but it was not clearly observed in occipital areas (see Figs. 2.1 & 2.2). I also identified early ERP components, P1 (~100 ms from stimulus onset) and N1 (~150 ms), that were best defined and with a maximal amplitude in occipital areas but they were not well defined in parietal regions (see Figs. 2.1 & 2.2). P1 and N1 from occipital areas and P3 from parietal regions were submitted to further analysis. A P2/N2 (~200-250 ms) complex was not analysed further because although present in some individual ERPs it was smeared with the large P3 in most of the individual data and in group average ERPs.

### 2.2.5. Statistical analysis

The mean RTs to correct hits for each participant across the whole experiment were submitted to statistical analysis as one factor (Group) ANOVAs. The mean RTs for the first and second halves of the experiment separately were also analysed in a 1 within ($1^{st}$ half/$2^{nd}$ half) x 1 between (Group) factors ANOVA

in order to assess the level of sustained attention or vigilance in each group and between the groups at the beginning and towards the end of the experiment.

The amplitude and latency of the early (P1 and N1) and late (P3) ERP components from the occipital and parietal regions respectively were submitted for statistical analysis separately for the left, right and central areas. In order to improve the signal to noise ratio and give more statistical power to the data (Oken and Chiappa, 1986) a group of channels in selected regions was averaged. Similar channel grouping has been used elsewhere (e.g., O'Connor et al., 2007). Thus, the upper three channel groups (circled as shown in Fig. 2.3) correspond to the left, central and right parietal regions (P3, Pz, P4), the lower three groups correspond to the left, central and right occipital areas (O1, O2, Oz). The amplitude of the peaks in individual subject ERPs were found in the time windows defined by the peaks in group average ERPs and automatically measured relative to the pre-stimulus baseline. The latency of the peaks was computed relative to the stimulus onset. The peak amplitude and latency values from all electrodes in a group were averaged. Although the number of channels in lateral and central groups was not the same, I wished to include the midline channels in the analysis. However, this difference in number of channels used for averaging between the lateral and central sites did not affect differently the variance within each participant group. As can be seen in Tables 2.2 and 2.3, the standard deviations within each group of participants were very similar between these areas both for the amplitude and latency of ERP peaks and both in Control and Dyslexic groups. Usually the latency was locked to the peak with a maximal amplitude found in parietal channels P3 and P4 (shown in Fig. 2.3) for the P3 component, and in occipital channels O1 and O2 for P1 and N1 components. If there were two large peaks in the search window, the one that had the same latency as the majority of channels was taken as a guideline. A similar approach has been used elsewhere (e.g., Wimmer et al., 2002; Rossion et al., 2003), and averaging a set of neighbouring channels is a standard ERP analysis (Picton et al., 2000). It is known to improve further the signal-to-noise ratio and provide more reliable ERPs (Curran et al., 2001).

The average amplitude and the latency values of ERP components from each group of electrodes and for each participant were subjected to repeated measures analysis of variance (ANOVA) with 1 between-subjects factor Group (dyslexics

versus controls) and 2 within-subjects factors Condition (Go versus NoGo) and Area (left, central and right).

The criterion for statistical significance was $p < 0.05$. The statistical analysis was performed using StatView (SAS Institute, 1998).

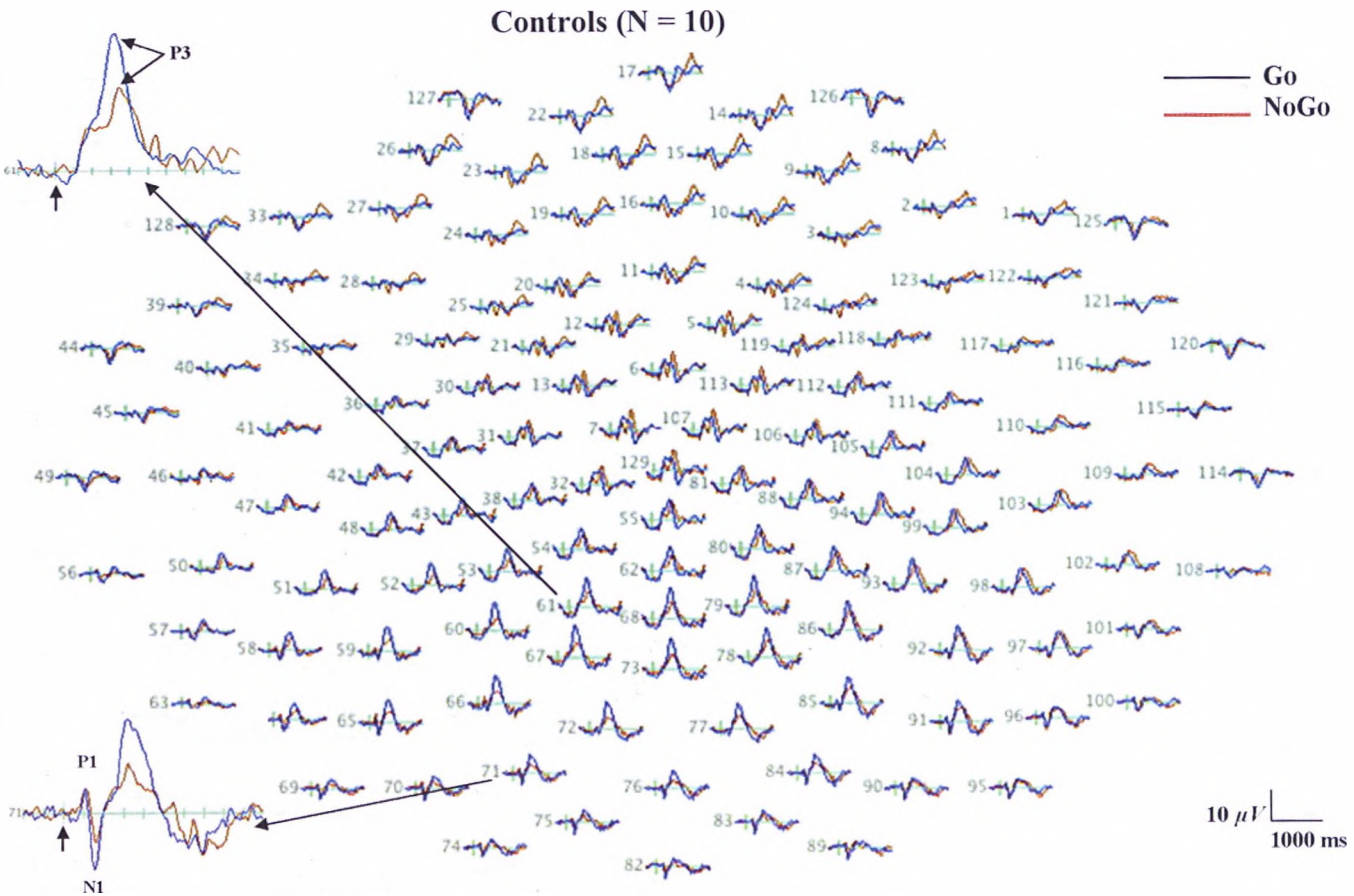


**Figure 2.1. Control group average ERPs in CPT**
The waveforms are shown for the Go (—— ) and NoGo (—— ) conditions at all electrode sites. The larger scale waveforms in the left top and bottom corners of Figs. 2.1 & 2.2 show the representative ERPs and characteristic peaks from parietal and occipital sites. The vertical lines on the waveforms (arrows on larger scale ERPs) indicate the stimulus onset at 0 ms.

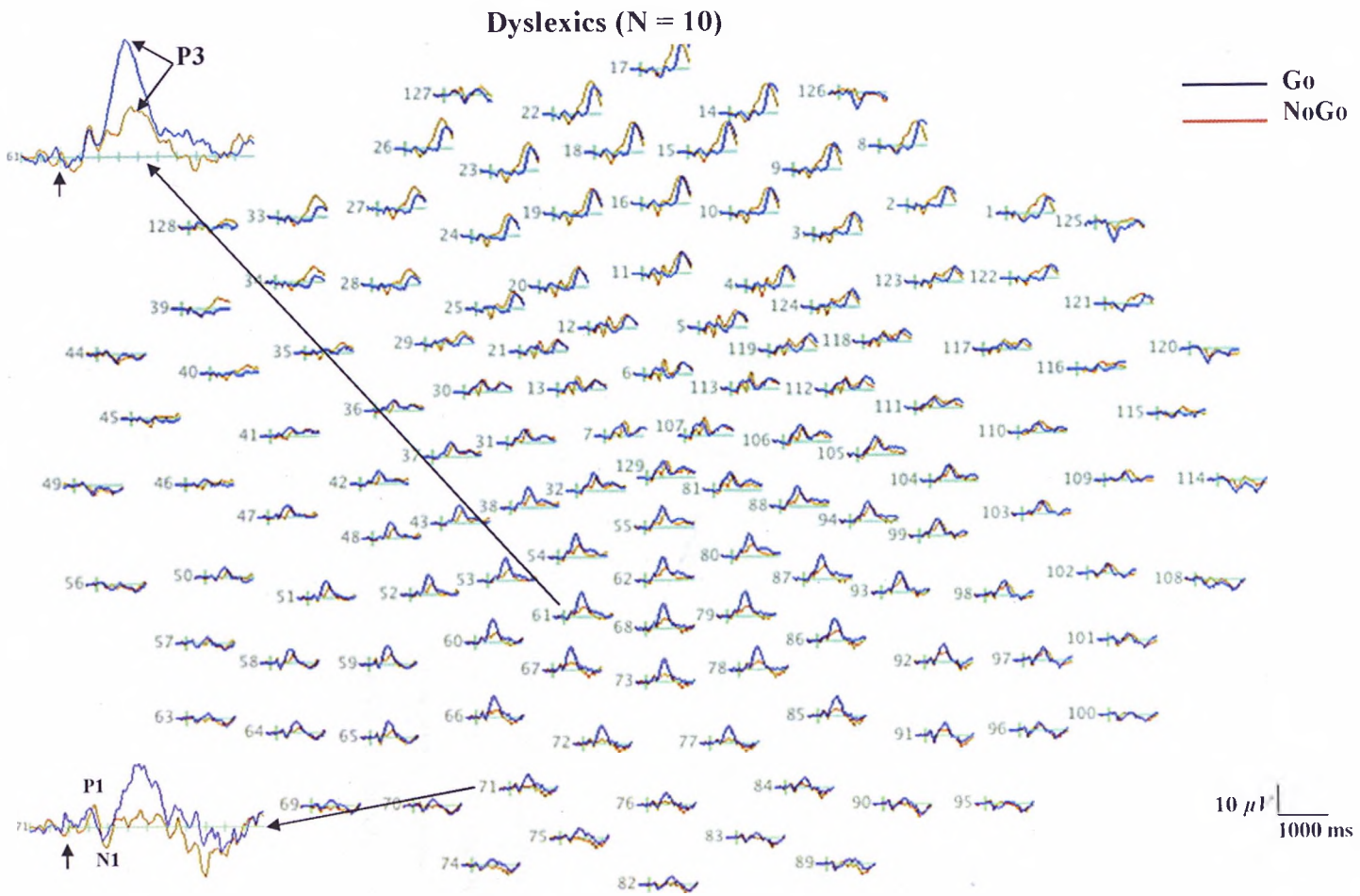


**Figure 2.2. Dyslexic group average ERPs in CPT**
The waveforms are shown in Go (——) and NoGo (——) conditions at all electrode sites. Graphical format same as in Fig. 2.1.

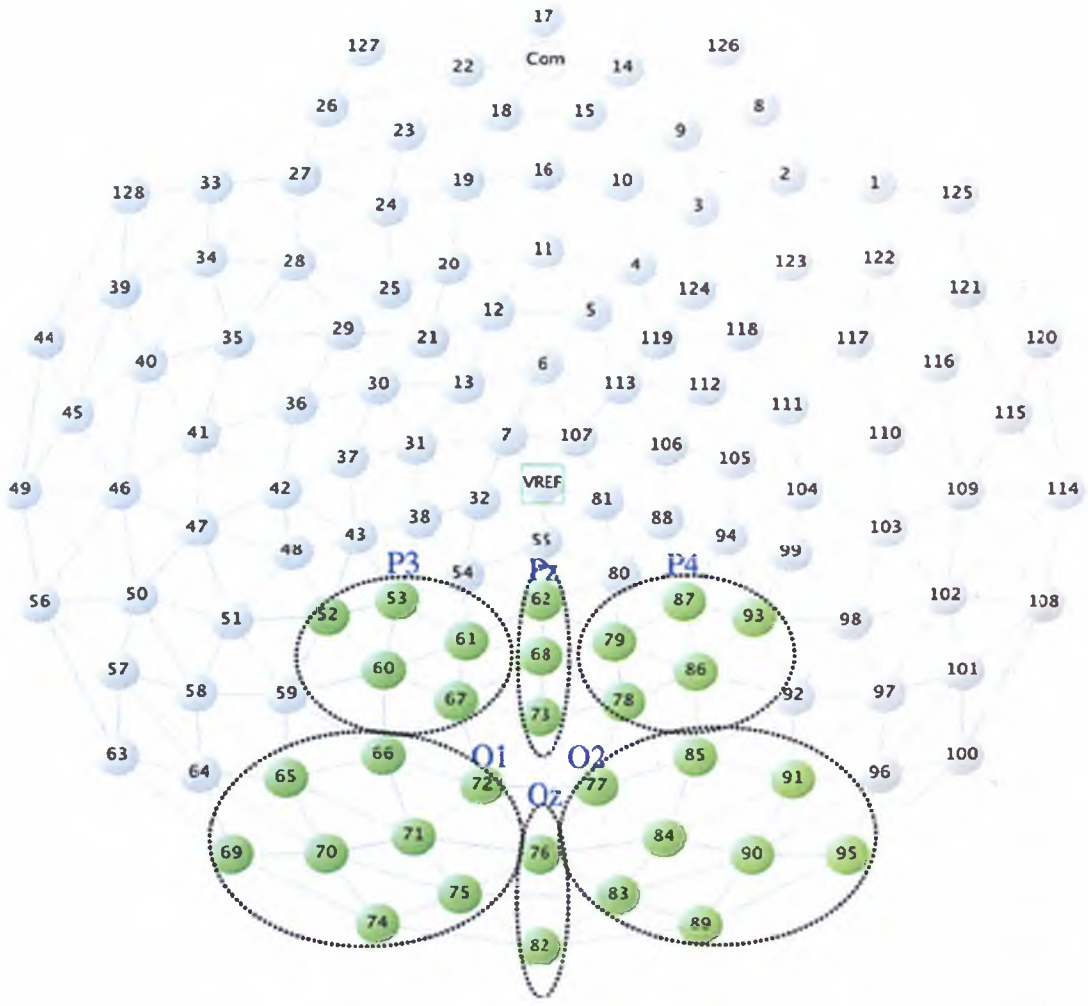


**Figure 2.3. Channel groups selected for averaging ERPs**

A representation of electrode sites in the left, right and central parietal (upper circled channel groups) and occipital (lower circled channel groups) regions. The approximate sites corresponding to International 10-20 System (Jasper, 1958) (mapped on 128 channel EGI Net) are shown directly above the electrodes, e.g., electrode 62 corresponds to Pz, etc.

## 2.3. Results

### 2.3.1. Behavioural data

The error rate was low in both groups. On average, dyslexics made 1.0 (0-3) (mean, range in parentheses) omission (misses) and 0.2 (0-1) commission (false alarms) errors, whereas controls made 0.2 (0-1) omission and 0.1 (0-1) commission errors. Reaction times to correct responses (mean ± SD) were 421.8 ± 89.5 ms in the dyslexic group and 418.2 ± 38.2 ms in the control group. This difference was not significant [$F(1,18) = 0.01$]. The next issue was whether the dyslexic participants had difficulty sustaining their performance across the whole of the experiment. The very few errors in both groups (see above) were made randomly throughout the duration of the experiment. The RTs calculated separately for the first and second halves of the experiment were 418.4 ± 95.9 ms and 425.2 ± 89.6 ms in the dyslexic group, and 438.4 ± 62.1 ms and 398.1 ± 37.8 ms in the control group. As the behavioural data show, sustained attention was at similar levels throughout the experiment in both groups, although the mean RT values slightly improved in the controls towards the end. The variability (SD) was generally larger and decreased less in the second half of the experiment in dyslexics compared to controls. However, the two factors (Group, $1^{st}$ half/$2^{nd}$ half) ANOVA did not reveal any significant differences [largest $F(1,18) = 2.9$]. Thus, there were no significant differences or any consistent differences between two groups in behavioural indices of the performance.

**Table 2.2. The amplitude values of the main ERP peaks in CPT study**

The values shown in μV (mean +/- SD)

| Group | Go | | | NoGo | | |
|---|---|---|---|---|---|---|
| ERP peak | Left | Central | Right | Left | Central | Right |
| Controls | | | | | | |
| P1 | 2.7 ± 1.5 | 1.7 ± 1.2 | 2.4 ± 1.3 | 3.4 ± 1.6 | 2.6 ± 1.1 | 3.0 ± 1.1 |
| N1 | -5.6 ± 2.5 | -6.1 ± 2.6 | -6.4 ± 2.8 | -4.7 ± 2.4 | -4.4 ± 2.4 | -5.0 ± 2.8 |
| P3 | 14.9 ± 4.7 | 15.7 ± 5.3 | 14.7 ± 4.7 | 9.6 ± 2.9 | 11.1 ± 3.7 | 12.0 ± 4.1 |
| Dyslexics | | | | | | |
| P1 | 3.4 ± 2.1 | 3.5 ± 2.5 | 4.5 ± 2.3 | 3.0 ± 2.1 | 3.3 ± 2.0 | 3.8 ± 1.7 |
| N1 | -3.3 ± 2.3 | -4.0 ± 3.4 | -4.1 ± 3.4 | -3.7 ± 2.9 | -3.7 ± 3.6 | -4.0 ± 3.3 |
| P3 | 10.9 ± 2.8 | 11.4 ± 3.2 | 11.1 ± 2.8 | 5.8 ± 2.9 | 6.3 ± 2.3 | 6.6 ± 1.4 |

**Table 2.3. The latency values of the main ERP peaks in CPT study**
The values shown in ms (mean +/- SD)

| Group | | Go | | | NoGo | |
|---|---|---|---|---|---|---|
| ERP peak | Left | Central | Right | Left | Central | Right |
| Controls | | | | | | |
| P1 | 106 ± 8.7 | 102 ± 5.2 | 106 ± 8.5 | 113 ± 7.9 | 115 ± 14.0 | 110 ± 7.7 |
| N1 | 163 ± 23.4 | 161 ± 26.4 | 165 ± 22.1 | 172 ± 24.5 | 169 ± 20.1 | 174 ± 16.5 |
| P3 | 333 ± 18.8 | 321 ± 18.7 | 329 ± 15.6 | 360 ± 35.9 | 348 ± 39.1 | 375 ± 33.9 |
| Dyslexics | | | | | | |
| P1 | 115 ± 19.0 | 109 ± 16.7 | 113 ± 16.9 | 116 ± 19.2 | 116 ± 19.7 | 117 ± 15.8 |
| N1 | 171 ± 19.3 | 165 ± 22.0 | 169 ± 25.6 | 175 ± 20.8 | 176 ± 26.6 | 176 ± 26.8 |
| P3 | 350 ± 38.7 | 347 ± 25.7 | 348 ± 25.3 | 370 ± 27.7 | 366 ± 41.5 | 373 ± 44.9 |

### 2.3.2. ERP data

The group average ERP waveforms in the Go and NoGo conditions at all recording sites for the control and the dyslexic participants are shown in Figs. 2.1 & 2.2 respectively. The larger scale waveforms in the left top and bottom corners of Figs. 2.1 & 2.2 show representative ERPs with characteristic peaks in parietal and occipital areas. The mean values of ERP peaks in each group are displayed separately for the amplitude (Table 2.2) and the latency (Table 2.3) measured in both conditions at the locations selected for the statistical analysis. These data are also displayed in graph in Appendix 7.6.

#### 2.3.2.1. P3

The amplitude and latency of the main ERP component of interest in this study, P3, were selected for statistical analysis as described earlier (see Methods). The repeated measures ANOVA with 3 factors (Group, Condition, Area) revealed a range of significant differences in all main factors. For the P3 amplitude, there were significant main effects of Group and Condition but not Area [$F(1,18) = 11.0$, $p<.01$; $F(1,18) = 40.1$, $p<.0001$; $F(2,36) = 2.1$, NS respectively]. As can be observed in topographic maps of Fig. 2.4 as well as in Table 2.3 the P3 amplitude was larger in Controls compared to Dyslexics, and it was larger in Go than NoGo condition across both groups. The only significant interaction was between Condition and Area [$F(2,36) = 7.6$, $p<.01$].

For the P3 latency there was no significant main effect of Group, but there were significant main effects for Condition (shorter in the Go than the NoGo condition) and Area [$F(1,18) = 2.2$, NS; $F(1,18) = 11.8$, $p<.01$; $F(2,36) = 4.7$, $p<.05$ respectively]. The P3 amplitude was larger and its latency longer in the right area (see Tables 2.2 & 2.3). A detailed description of hemispheric differences is provided in subsequent analyses reported below. No interaction approached significance.

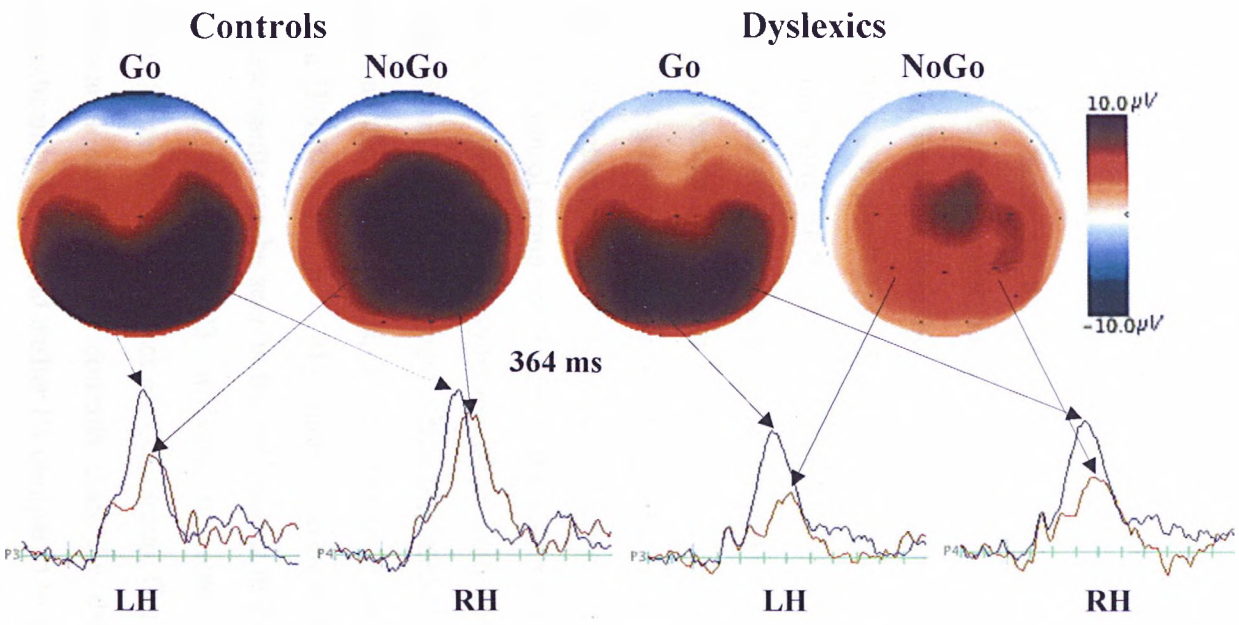


**Figure 2.4. Topographic ERP maps for P3 peak in CPT**
Activation recorded at the time point of maximum P3 amplitude for both groups in Go and NoGo conditions. The black spots indicate the channels nearest to 10-20 system locations. The accompanying ERP waveforms below show the representative channels with maximal P3 amplitude selected from parietal area of left (LH) and right (RH) hemispheres according to 10-20 system.

In view of the marked differences – in terms both of possible interpretation and P3 latency and amplitude - between the Go and NoGo conditions, two factor analyses were conducted for each condition separately. In terms of P3 amplitude, in the NoGo condition there were significant main effects of both group (larger in the Controls compared to the Dyslexics) and area (larger in the right hemisphere) [$F(1,18) = 14.3$, $p<.01$; $F(2,36) = 5.8$, $p<.01$ respectively] whereas in the Go condition group was significant (larger in the Controls compared to the Dyslexics) but area was not [$F(1,18) = 5.5$, $p<.05$; $F(2,36) = 0.9$, NS respectively]. In terms of P3 latency, in the NoGo condition the main effect of group was not significant, and that of area was (longer in the right hemisphere) [$F(1,18) = 0.3$, NS; $F(2,36) = 3.8$, $p<.05$ respectively], whereas in the Go condition group was significant (shorter in the Controls compared to the Dyslexics) but area was not [$F(1,18)=4.4$, $p=.05$; $F(2,36)=1.5$, NS respectively]. No interactions approached significance in any of the above two factor analyses.

In terms of the significant Condition x Area interaction effect for P3 amplitude, subsequent analysis showed that the P3 amplitude was significantly larger in the Right than the Left parietal area in the NoGo condition for the Controls [$F(1,9) = 8.9$, $p = 0.015$]. This effect can be observed in the topographic maps and accompanying ERP waveforms shown in the Fig. 2.4. The interpolated voltage maps taken over the scalp surface are captured at a time point of P3 peak in the group average data. It can be seen that the peak amplitude was located maximally over occipito-parietal sites in both groups. However, it can also be seen on the maps and accompanying ERP waveforms that the amplitude of P3 in the NoGo condition in the Control group was larger in the right parietal area than the left, whereas in the Dyslexic group it was symmetrical in both conditions. Additional analysis of the significant Area effect revealed that the latency of this component was significantly asymmetrical in Controls, it was shorter in the left compared to the right parietal area [$F(1,9) = 6.5$, $p < .01$]. Such differences were absent in the Dyslexic group. These results can be seen in the waveforms in Fig. 2.4 and Table 2.3.

In summary, P3 analyses revealed distinct differences in the brain waveforms for all main factors, i.e., Group, Condition, Area. The P3 was larger and appeared earlier in the controls than the dyslexics. The Go condition led to significantly larger and earlier P3 compared to the NoGo condition. A lateralisation

effect in amplitude and latency of P3 was found in the Control group but not the Dyslexic group.

#### 2.3.2.2. P1/N1

Similar statistical analysis of the early ERP components, P1 and N1, did not reveal significant amplitude differences for any of the main factors: Group, Condition, Area. However, there were group differences at a tendency level (See Tables 2.2 & 2.3). ANOVA revealed significant differences in the latency of the early ERP components for Condition effect. It was shorter in the Go than NoGo condition as a main effect both for P1 [$F(1,18) = 8.1, p = 0.01$] and N1 [$F(1,18) = 5.4, p < .05$], i.e., in both participant groups.

## 2.4. Discussion

To summarise the findings: a) there were neither significant differences nor even any consistent between-group trends in the behavioural indices of CPT performance between the control and dyslexic groups; b) ERPs were larger and with shorter latencies in the controls, which was highly significant for the late ERP component P3; c) across both groups the early and late ERP components were significantly larger and with shorter latencies in the target Go compared to the NoGo condition; d) I did not find any hemispheric differences for the early ERP components but the late P3 peak was significantly lateralised in the controls, whereas in the dyslexics it was symmetrical.

The absence of consistent differences between the control and dyslexic groups on the behavioural measures is partly in agreement with some previous psychophysical studies already mentioned (e.g., Schulte-Korne et al., 1991; e.g., Moores et al., 2003), in that, I too did not find sustained attention differences between the two groups. The performance level did not deteriorate throughout the duration of the session. The RTs to correct hits were similar in both groups with only a few more omission and commission errors among the dyslexics, whereas in some other studies these behavioural indices were found to be significantly worse in dyslexics (e.g., Richards et al., 1990; Visser et al., 2004). Such discrepancy in the

results may be due to the fact that group differences on the behavioural level become more apparent with the increasing level of task difficulty when, for instance, multiple objects must be attended (Richards et al., 1990; Visser et al., 2004) or in multimodal attention tasks (Facoetti et al., 2005). Nicolson and Fawcett (1994b) established that dyslexic children had normal simple RTs but not so when two simple reactions (foot and hand) were blended into choice reaction to two stimuli (tone and flash). Thus, the increased task complexity could account for the differences in performance between their control and dyslexic subjects. In my task the level of difficulty was intermediate between simple reaction and choice, omission reaction, where either execution or inhibition of the response was required, with a Go response unnecessary unless an O had just been presented. Although the RT variability was slightly larger for the dyslexics, the mean values were similar in both groups and no significant differences were found for either of the main factors. The task demands in the present study were probably not as intensive on attentional resources and processing speed than in the other studies, which may be why the dyslexic group performed as well as the controls. It may also be that the dyslexics showed attentional problems in other studies owing to inclusion of dyslexic participants with overlapping ADHD symptoms.

The differences between the groups became manifest at the brain level, in my ERP findings. Although only as a trend in the early ERP components, the larger amplitude and earlier latency in controls group were highly significant for the later P3 peak. My results show once more that these correlates of the brain electrical activity are highly sensitive, they reveal subtle between-group differences in cognitive function that are not always distinguishable at the behavioural level. Such dissociation between behavioural and ERP correlates was found and interpreted similarly in other studies (Baving et al., 2006; Fallgatter et al., 2006). There were no significant group effects in the early ERP peaks in my study. However, a number of studies have shown significant differences between control and dyslexic groups in early components of brain activity, e.g., for auditory evoked potentials (Pinkerton et al., 1989), visual word and pseudoword ERPs (Wimmer et al., 2002), and in MEG studies of speech and non-speech sounds processing (Heim et al., 2003; Parviainen et al., 2005). The CPT task used in this study involved attention processes and response choice, either execution or inhibition. It was well suited to evoke the late P3 ERP component that is known to be related to stimulus conscious processing and

evaluation (Duncan-Johnson, 1981). In the recent ERP studies that used this paradigm the P3 component recorded to target and nontarget stimuli was variously attributed to attentional, response preparation and response selection processes (e.g., Reinvang, 1998; Banaschewski et al., 2004; Shucard et al., 2004; e.g., Jonkman, 2006). The attenuated P3 amplitude in the dyslexic group replicates similar findings in other modalities and different tasks (e.g., Erez and Pratt, 1992), and indicates a deviant activation for the CPT related brain processing as well in this group. The delayed latencies of the ERP peaks for the dyslexics are possibly associated with an increased cognitive processing time (Silva-Pereyra et al., 2001).

The larger and earlier ERP peaks in the Go than the NoGo condition were present in both groups and highly significant for both P3 amplitude and latency and the latency of the early P1 and N1 components. In my experiment the Go condition was the target, task relevant stimulus that possibly required more attentional resources compared to the NoGo stimuli regardless of whether or not a motor response is required (e.g., Shucard et al., 2004). The shorter latency of the ERP peaks in the target Go condition indicates faster processing of this stimulus (Kutas et al., 1977) characteristic to both groups. However, the NoGo P3 has been frequently reported to be larger and its latency longer compared to Go P3 in frontal areas, especially in the right hemisphere (e.g., Fallgatter and Strick, 1999). The authors suggested that this 'NoGo-anteriorization' could possibly be explained by inhibition processes being more demanding compared to executive ones – though see Verleger et al. (2006) and Salisbury et al. (2004) for counter views. It has also been suggested that while the NoGo P3 has a frontocentral distribution, the Go P3 may be maximal in the parietal region (Jonkman et al., 2006, Bokura et al., 2001).

The Go/NoGo condition effects were lateralised in controls both for amplitude and latency values. NoGo P3 was larger and its latency longer in the right hemisphere. Thus, the amplitude and latency hemispheric effects in the control group indicate a lateralisation of the NoGo ERPs to the right hemisphere. No hemispheric effects were observed in the dyslexic group. The fact that dyslexics did not show such lateralisation, but they had symmetrical Go and NoGo P3 shows an altered functional and, possibly, structural organisation of the dyslexic brain. It supports the idea that the development of interhemispheric asymmetry and integration and collaboration of information between the two hemispheres may be disregulated in dyslexia.

Thus, the main group differences in electrophysiological correlates of the CPT performance were expressed in attenuated, delayed and atypically symmetrical ERPs in the dyslexic group. The findings of attenuated and delayed ERPs in dyslexics confirm earlier studies performed on different tasks, e.g., visual attention function in response to words or pseudowords (Wimmer et al., 2002) or auditory selective attention (Lovrich and Stamm, 1983). Several authors, including Facoetti et al. (2005), attribute the reduced amplitude of the P3 responses in the dyslexic group to impaired attentional processes caused by abnormalities in the posterior parietal cortex. It may also be applicable to this CPT task. The absence of a hemispheric effect in dyslexics, i.e., atypically (compared to controls) symmetrical P3, supports the findings from the previous studies that used different tasks, such as spatial attention-shifting (Wijers et al., 2005), visual and auditory linguistic tasks (e.g., Wimmer et al., 2002; e.g., Heim et al., 2003).

One significant contribution of this work is that it established a reliable and highly sensitive behavioural and neurophysiological measure of CPT performance in 'pure' dyslexia, that was indexed by high level of behavioural performance, but involved an attenuated, delayed and atypically symmetrical P3 ERP component. It also showed that the subtle nature of dyslexia, even if indistinguishable on behavioural level, can be revealed by use of electrophysiological techniques.

In conclusion, these ERP results are consistent with the findings of processing abnormalities in right parietal cortex and disregulated interhemispheric function in dyslexia. By contrast, there appeared to be no differences in the attentional processing parameters, as indexed by the behavioural measures of reaction times and performance accuracy, either early or late in the task. This set of results suggests strongly that although there are clear processing deviations that may lead to problems under conditions of high attentional load, impaired attentional performance is not a core deficit in dyslexia. The ERP differences between the dyslexic and control groups are not in themselves conclusive evidence in favour of any specific theory of dyslexia. These results confirm the previous knowledge that the functional reorganisation in the dyslexic brain is not restricted to one function or one skill, such as reading, but affects a broad range of modalities, areas and tasks.

# 3. STUDY 2. NEUROPHYSIOLOGICAL AND BEHAVIOURAL CORRELATES OF COHERENT MOTION PERCEPTION IN DYSLEXIA

## 3.1. Introduction

Early evidence for magnocellular abnormalities in dyslexia derived from neuroanatomical analysis (Livingstone et al., 1991) that indicated the magnocellular layers in the lateral geniculate nucleus (LGN) contained fewer and smaller cells than normal. While early work by Martin and Lovegrove (1987) had identified problems in detection of visual flicker, reconceptualisation of the role of the magnocellular pathway indicated that detection of low contrast coherent motion provided the most sensitive index (Cornelissen et al., 1995; Eden et al., 1996; Cornelissen and Hansen, 1998; Cornelissen et al., 1998a; Cornelissen et al., 1998b; Talcott et al., 1998b; Talcott et al., 2003). These issues, including how magnocellular impairment can affect reading abilities in dyslexia, are discussed in more detail in Section 1.2.3 of the Introduction. A meta-analysis of the results from a number of visual studies (Ramus, 2003) suggested that only about 29% of individuals with dyslexia have visual sensory problems.

In addition to the evidence of magnocellular deficits in dyslexia from many psychophysical studies described earlier, a recent fMRI study by Eden et al. (1996) also demonstrated coherent motion detection problems among dyslexics. According to this work, no activation in V5/MT of dyslexics was recorded to low contrast 100% coherent random dot kinematograms (RDK). Subsequent studies led to ambivalent findings. For instance, Vanni et al (1997) presented counterevidence showing V5 activation in dyslexics. Global coherent motion can be detected from local motion cues when RDK stimuli are 100% coherent, i.e., the motion of the whole pattern can be perceived from the motion of a small group of dots within the pattern when all dots move in the same direction. It is possible that V5 activation found by Vanni et al. (1997) was a response to coherent (global) motion perceived from local motion which is possibly not impaired in dyslexia. When dot lifetime is limited (e.g., 100 ms was used in the current study) integration over space, as well as over time, is required even for the 100% coherent stimuli in order to perceive global

coherent motion (Talcott et al., 2000). However, the stimuli used by Eden et al. (1996) and in experiment 3 (where V5 activation in dyslexics was also reported) in the study by Vanni et al. (1997) used continuously moving dots.

ERPs have been previously used in investigations of dyslexia with paradigms ranging from low vision stimulation to complex visual selective attention tasks (Livingstone et al., 1991; Facoetti et al., 2005). The evidence of coherent motion perception deficits in dyslexia has been also contradictory in recent electrophysiological studies. Thus, Schulte-Korne et al. (2004) reported that visual evoked potentials to high contrast and low coherence level (only 10%, 20%, or 40% of the dots moving coherently) RDK stimuli were significantly attenuated in dyslexics, whereas Scheuerpflug et al. (2004) did not find any significant group differences in a similar study. The low coherence and limited dot lifetime of the RDK stimuli used in Scheuerpflug et al. (2004) and Schulte-Korne et al. (2004) ensured that the global motion could not be perceived from local motion cues, as only some percentage of dots in the pattern moved coherently. However, the high contrast stimuli, known to activate the parvocellular system, could improve coherent motion perception with additional contrast cues and increase the brain activation among dyslexics to levels comparable with controls in the Scheuerpflug et al.'s (2004) study. As it is already known, the magnocellular pathway is relatively more activated than the parvocellular pathway at low luminance levels (Purpura et al., 1988; Tootell et al., 1995), it has higher luminance contrast sensitivity (Eden et al., 1996). It responds better to low spatial frequency, low contrast and moving stimuli (Merigan and Maunsell, 1993). Although it is already known that differences in luminance contrast sensitivity are negligible between dyslexics and controls in photopic conditions, however, at mesopic levels of luminance the deficits are still present among dyslexics (Martin and Lovegrove, 1987; Cornelissen et al., 1995). I decided to use low contrast stimuli as in fMRI study by Eden et al. (1996) displayed at mesopic luminance levels.

Thus, the continuous motion stimuli used in the neuroimaging studies were 100% coherent, which could lead to global coherent motion being perceived from local motion cues. On the other hand, the ERP studies described above used lower coherence levels of the motion stimuli and a limited dot lifetime but high levels of contrast (Michelson 97%). In the current study I decided to combine these features, i.e., to use low contrast of the stimuli with different low coherence levels. My aim

was to test the magnocellular function, i.e., coherent (global) motion perception, in dyslexia by means of recording ERPs to RDK stimuli that combined low contrast and low coherence levels of the stimuli with mesopic luminance levels.

From psychophysical studies described earlier in the Introduction (e.g., Cornelissen et al., 1995) it is known that dyslexics have higher threshold levels in perception of the coherent motion. However, the psychophysical methods of coherent motion direction detection (e.g., Hansen et al., 2001) would not be easy to combine with the ERP paradigm. I have replicated the paradigm used in previous ERP studies described above. By means of using different low levels of coherence in motion stimuli, I hoped to detect differences between dyslexic and control groups in one of these perceptually difficult conditions. The lowest degree of correlation or coherence in motion of dots in the stimuli was chosen to be 10% because it was established earlier that VEPs cannot be reliably recorded below 7% of coherence (Niedeggen and Wist, 1991). I also have used large size of the stimuli as in Eden et al. study (1996), as it has been shown before that larger size motion stimuli can evoke more reliable ERPs with larger amplitude (e.g., Muller et al., 1990).

I aimed to use the behavioural data to distinguish possible 'magnocellular' dyslexics from the remainder. Therefore, simultaneously with the ERPs, the participants' behavioural responses - the response latencies to correct responses and number of errors - were collected. To the best of my knowledge, no combined behavioural and electrophysiological results of coherent motion processing in dyslexia have been reported before in one study with the same sample of participants.

By recording behavioural and ERP data I hoped to be able to identify for the behavioural data two subgroups of dyslexic participants: those with and without coherent motion detection problems, and then to evaluate whether two subgroups did or did not have different ERP pattern from normal.

## 3.2. Methods

### 3.2.1. Participants

Nine dyslexic adolescents (3 females) and ten control adolescents (3 females) took part in this study. It was carried out one year after the first study. The participant set was almost the same with exception of 1-2 people being replaced in each group due to the previous participants' unavailability. All participants were right-handed, with normal or corrected to normal vision and no history of brain injuries or neurological problems. The study was approved by the local ethics committee (Psychology Department, Sheffield University) and all participants gave their written informed consent. The participants were assessed for dyslexia by qualified psychologists, and none showed any evidence of ADHD on the DSM-IIIR scales (American Psychiatric Association, 1987). Mean values of age, full scale IQ (Wechsler, 1991), reading age (RA) and spelling age (SA) (Wechsler, 1993) for both groups are shown in Table 3.1. Criteria for inclusion in the dyslexic group were a discrepancy of at least 18 months between their reading and spelling age and their chronological age together with an IQ > 90[2], which are standard UK criteria. One factor ANOVAs did not show significant differences between the dyslexic and control groups on IQ scores [$F(1,17) = 2.5$, $p>.1$], but as expected dyslexics had significantly lower RA [$F(1,17) = 22.2$, $p<.0002$], and SA [$F(1,17) = 35.4$, $p<.0001$] scores compared to controls.

**Table 3.1. Psychometric data in motion study**
The group mean data (ranges in parentheses)

| | Controls (N=10) | Dyslexic (N=9) |
|---|---|---|
| Age (years) | 16.6 (15.4 -19.3) | 17.1 (15.6 – 17.8) |
| IQ (standardises IQ score) | 119.7 (103-132) | 111.5 (99 - 124) |
| Reading age (years) | 17.1 | 13.0 (9.3 – 17.1) |
| Spelling age (years) | 17.1 | 11.5 (8.6 – 17.1) |

[2] One dyslexic participant had improved his RA and SA scores since the time of diagnosis, however, his behavioural and ERP data were characteristic of dyslexic group averages. The statistical analysis performed without this subject did not change the significance values of neither ERP, nor behavioural results or the Group effect size.

### 3.2.2. Stimuli

Random dot stimuli were designed in Matlab using Psychophysics Toolbox (Brainard, 1997; Pelli, 1997) and displayed on 20 inch LCD PC monitor (1028 x 768 pixel resolution, 75 Hz refresh rate). The low contrast (Michelson 5%) stimuli consisted of black dots displayed with an average density of 4 dots/deg$^2$ on a light grey background, and subtended 30deg x 20deg angular size at a viewing distance of 60 cm. The luminance of the moving dots measured by Seconic L-778 light meter was 8 cd/m$^2$, whereas the luminance of the grey background was 12 cd/m$^2$. The mean luminance of the stimulus on screen was at mesopic levels and about 10 cd/m$^2$, and the room illumination was dimmed to about 30 lux (measured with Light Meter RS 180-7133). The Michelson mean contrast of the stimulus was calculated according to the equation: (Lmax – Lmin) / (Lmax + Lmin). By using the luminance of the dots (Lmin) and the background (Lmax) specified above we derived at Michelson contrast of 0.2 or 5%. Each 2x2 pixel dot subtended 0.06 deg$^2$ size, moving at a speed of 5 deg/s, with a lifetime of 100ms. The matrix consisted of 500x380 dots. The latter ensured no smooth tracking eye movements occurred (Hansen et al., 2001).

### 3.2.3. Design/Paradigm

There were three coherent conditions with 10%, 25%, or 40% of the dots moving upwards with the remaining dots appearing at pseudo-random locations with each frame. There was also one incoherent (control) stimulus where all dots appeared at pseudo-random locations with each frame. For all stimuli techniques were used in generation to ensure a random but homogeneous texture with no clumping of dots. Equal numbers of coherent trials (40 for each of the three conditions) and incoherent trials (120) were presented in quasi random order. We have chosen this number of trials in order for the recording not to be too onerous, especially for our young participants, and to be no more than about 15 min. The EGI recording nets are comfortable to be used in different age groups, however, we wanted to make sure our participants did not get too tired or less engaged in their performance. It is known from the previous ERP literature that 30 trials is a good working number when deriving averaged ERPs (e.g., Boller and Grafman, 2000).

We decided to have slightly more, i.e., 40 trials per each condition, in order to obtain reliable ERPs that would also not affect the duration of the experiment. Each trial started with a small fixation cross displayed in the centre of the screen for 1000 ms, followed by the stimulus (either coherent or incoherent motion, 500ms) also containing the fixation cross, followed by a blank screen for 1500ms that provided a rest from fixation and extra time for making the response. The participants pressed one button on the response box when they saw coherent motion and the other button when they perceived random motion. Short training sessions were provided and the written instructions were provided as well (see Appendix 7.4 attached).

### 3.2.4. Data acquisition

The responses and mean response latencies of correct responses were collected (simultaneously with the EEG data) by a Power Macintosh OS X (10.2.8) and stored for off-line analysis.

The EEG was recorded using the same system as in the first study (see section 2.2.3).

### 3.2.5. Data analysis

Mean response latencies of correct responses and the number of correct and incorrect responses were determined for each participant. Since the number of trials in the incoherent condition was about 3 times larger than in each coherent condition, the percentage of incorrect responses for each condition and each subject was calculated and submitted to further analysis.

The EEG data (analysed using NetStation 4.0 EGI software) were digitally processed as described in the previous study (see section 2.2.4).

The group average ERPs were computed separately for the dyslexic and control participants in each condition. I identified P1 (~140 ms from stimulus onset), N1 (~190 ms), and P2 (~ 270 ms) ERP components in occipital channels (in lower circles in Fig. 3.1), and P3 (~560 ms) at parietal sites (in upper circles in Fig. 3.1) by visual inspection of group average and individual data. ERPs from these selected occipital and parietal areas are reported in this study.

### 3.2.6. Statistical analysis

The mean response latencies to correct hits and the percentage of incorrect responses for each participant were submitted to repeated measures analysis of variance (ANOVA) with 1 between-subjects factor Group (dyslexic versus control) and 1 within-subjects factor Condition (3 coherent and 1 incoherent).

The amplitudes of the peaks in individual subject ERPs were found in the time windows defined by the peaks in group average ERPs and automatically measured relative to the pre-stimulus baseline. The latency of the peaks was computed relative to the stimulus onset. The values from all electrodes in each group (see Fig. 3.1) were averaged and the means were obtained for P1, N1 and P2 separately in the left and in the right occipital (two lower circles) and for the P3 separately in the left and in the right parietal (two upper circles) channel groups. The average amplitude and latency values of ERP components for each participant were submitted to statistical analysis as 1-between (Group) and 2-within, Condition and Area (left and right), factor ANOVAs.

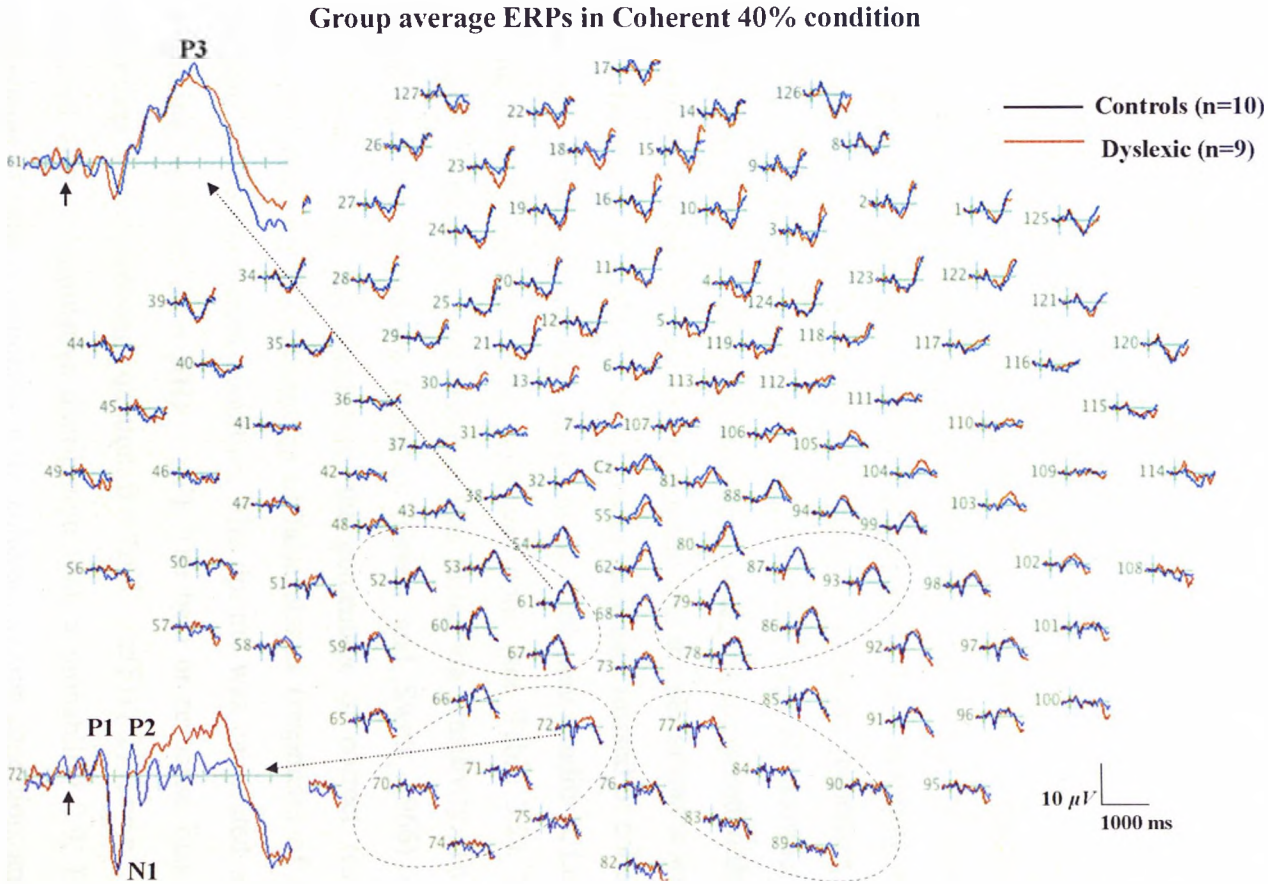


**Figure 3.1. Group average ERPs in Coherent 40% condition**
The waveforms are shown for control (——) and dyslexic (——) participants at all electrode sites. The larger scale waveforms in the left top and bottom corners show the representative ERPs and characteristic peaks from parietal (upper circled channels) and occipital (lower circled channels) regions. The vertical lines on the waveforms (arrows on larger scale ERPs) indicate the stimulus onset at 0 ms.

## 3.3. Results

### 3.3.1. Behavioural data

The mean response latencies to correct responses and the percentage of incorrect responses from all trials for each condition are displayed for both dyslexics and controls in Table 3.2. According to the results of ANOVA there were no significant between-group differences in the response latencies to correct responses [$F(1,17) = 0.9$] or in percentage of incorrect responses [$F(1,17) = 1.6$]. The Condition effect was significant as a main factor for response latencies [$F(3,51) = 17.7$, $p<.0001$]. As can be seen in Table 3.2, the response latencies were longer in the Incoherent and Coherent 10 % conditions compared to the Coherent 40% and Coherent 25% conditions across both groups. The Condition effect was also significant as a main factor for the number of incorrect responses [$F(3,51) = 7.1$, $p<.001$]. As can be seen in Table 3.2, the percentage of incorrect responses was larger in the Coherent 10% and Incoherent conditions compared to the 40% and 25% coherent conditions. It should be mentioned that the performance within the groups was different, with dyslexics having more responses missed in coherent conditions, and controls having more false alarms in the incoherent condition, i.e., responding as seeing coherent motion when there was none (see Table 3.2). Therefore, it is necessary to allow for any response bias factor via sensitivity. The response bias (beta) and the sensitivity (dprime) (Green and Swets 1966) of participants' performance were calculated from the percentage of correct responses in each coherent condition and percentage of false alarms (responses of seeing coherent motion) in the Incoherent condition. The dprime was calculated according to the following equation: $d' = z(H) - z(F)$. The beta or response bias was calculated according to the following equation: $\beta = (z(H) + z(F))/(-2)$. The z is an inverse of a standard normal cumulative distribution with a probability 0.9, H (hit rate) is a percentage of correct responses in the coherent motion condition, and F (false alarm rate) is a probability of incorrect responses in the incoherent motion condition.

The beta and separately the dprime values were submitted to 1-between (Group) and 1-within (Condition) factor ANOVAs. The dprime values were larger in the controls compared to dyslexics but this effect did not reach significance

[F(1,17) = 2.9]. There were also no significant between-group differences for the beta values [F(1,17) = 0.3]. The group mean dprime and beta values are displayed in Table 2.

However, the inspection of the individual data revealed that one dyslexic participant had markedly lower dprime and beta values than the other participants in all coherent conditions. For example, in the coherent 10% condition dprime for this participant was 0.8 compared to the dyslexic group average value of 2.1, and in the coherent 25% condition his beta value was -0.8 compared to the group average value of -0.2. Further analysis showed that these values were more than 3 standard deviations below the mean of the rest of the dyslexic participants. Omission of this participant from the statistical analysis reduced further the F values in the between-group comparison of the performance sensitivity [F(1,16) = 1.97]. The Condition effect was significant [F(2,34) = 10.6, p<.001] with dprime values smaller in the Coherent 10% compared to the Coherent 40% and 25% conditions in both groups. It was also highly significant for the response bias data [F(2,34) = 14.4, p<.0001].

### 3.3.2. ERP data

The group average ERP waveforms in the Coherent 40% condition at all recording sites are shown in Fig. 3.1 for the control and the dyslexic participants. The larger scale waveforms in the left top and bottom corners of Fig. 3.1 show representative ERPs with characteristic peak P3 in parietal and earlier peaks P1, N1 and P2 in occipital channels. The mean values of ERP peaks in each group are displayed separately for the amplitude (Table 3.3) and the latency (Table 3.4).

A mixed measures ANOVA with 3 factors (Group, Condition, Area) did not reveal any significant differences between dyslexic and control groups for the early (P1, N1 and P2) and for the late (P3) ERP components[3]. It can be seen in the Tables 3.23 and 3.4 that the N1 amplitude was larger and N1 and P2 latencies were longer in controls compared to dyslexics, whereas the P3 latency was slightly longer in dyslexics, but these differences did not approach significance. We have also

[3] We have obtained the ERPs by averaging the EEG trials accompanied with a correct response. However, the ERPs obtained from all available EEG trials did not differ in their shape or the amplitude and latency values of the peaks, and the statistical analysis also did not show any change in the results.

performed a linear trend analysis of the ERP components amplitude and latency with the coherence level, and then obtaining their interaction with the between-group factor. One would expect such linear trends in the later ERP components, which reflect coherent motion processing, but not in earlier components, e.g., P1, which mainly reflects the initial response to the stimulus onset, i.e., the appearance of the random dot pattern in our case. We have performed this analysis in SPSS. As expected, the results of the statistical analysis showed a significant trend for the later ERP peak, P3. The P3 amplitude increased significantly with the increasing coherence level [$F(1,17) = 18.3$, $p<.001$]. However, no significant results were found for the Condition x Group interaction factor [largest $F(1,17) = 1.6$].

There were other significant effects that are reported below. The Condition effect was significant for the P1 and P2 amplitudes [$F(3,51) = 2.9$, $p<.05$; $F(3,51) = 3.5$, $p<.05$ respectively]. As can be seen in Table 3.3 the amplitude of P1 and P2 was larger in the Coherent 10% condition compared to the other conditions for the controls but not for the dyslexics. For the P3 amplitude, there were significant effects for the Condition and Area main factors. It can be observed in Table 3.3 and topographic maps of Fig. 3.2 that the P3 amplitude was larger in the Coherent 40% condition compared to the other conditions [$F(3,51) = 5.6$, $p<.01$], as also found in the linear trend analysis, and it was also larger in the right compared to the left hemisphere across both groups [$F(1,17) = 7.5$, $p<.05$].

As can be seen in Table 3.3 and Fig. 3.2., the amplitude of the P3 is slightly larger for the controls' than for the dyslexics' group in coherent 10% condition. In order to check for possible between-group differences that may have been overlooked in the main analysis, i.e., via averaging across channel groups in each area (specified by circles in Fig. 3.1), I have performed an additional, single channel analysis. The amplitude of P3 ERP component in 10% coherent condition was compared between dyslexics and controls at P3 channel (53) in the left parietal area and P4 channel (87) in the right parietal area. The data were very similar to the results of the main analysis and no significant or any approaching significance differences were found. The group average data for the single channel analysis are shown in brackets (in Italic) above the main data in the Table 3.3.

**Table 3.2. Behavioural data in motion study**
The data are shown for both participant groups (means ± SD)

| | Response latency (ms) | | Incorrect responses (%) | | Sensitivity (dprime) | | Response bias (beta) | |
|---|---|---|---|---|---|---|---|---|
| | Controls | Dyslexics | Controls | Dyslexics | Controls | Dyslexics | Controls | Dyslexics |
| Coherent 40% | 570.2 ± 75.7 | 580.7 ± 79.7 | 2.6 ± 2.6 | 8.5 ± 5.5 | 4.2 ± 1.7 | 3.3 ± 1.9 | -0.5 ± 1.2 | -0.4 ± 0.7 |
| Coherent 25% | 584.0 ± 75.1 | 580.2 ± 64.2 | 2.8 ± 3.8 | 6.5 ± 5.7 | 4.5 ± 1.7 | 2.9 ± 0.8 | -0.8 ± 1.5 | -0.2 ± 0.3 |
| Coherent 10% | 630.4 ± 76.5 | 632.3± 84.4 | 10.6 ± 7.8 | 21.3 ±10.9 | 2.7 ± 1.3 | 2.1 ± 0.7 | 0.2 ± 1.1 | 0.2 ± 0.4 |
| Incoherent | 664.6 ± 113.4 | 641.3 ± 65.3 | 19.7 ± 18.0 | 13.8 ± 12.9 | | | | |

**Table 3.3. The amplitude of the ERP peaks in all motion conditions**
The values are shown in μV (mean ± SD)

| Group | Coherent 40 | | Coherent 25 | | Coherent 10 | | Incoherent | |
|---|---|---|---|---|---|---|---|---|
| ERP peak | Left | Right | Left | Right | Left | Right | Left | Right |
| Controls | | | | | | | | |
| P1 | 1.9±1.4 | 2.3±1.8 | 1.6±0.9 | 1.5±1.2 | 3.0±2.4 | 3.1±2.1 | 1.1±0.5 | 1.4±0.7 |
| N1 | -5.0±2.4 | -5.0±2.7 | -6.0±2.4 | -5.9±2.5 | -4.9±2.2 | -4.5±2.3 | -5.2±1.7 | -5.0±1.5 |
| P2 | 1.2±2.4 | 1.6±3.1 | 0.0±3.2 | -0.1±3.0 | 2.2±3.5 *(6.0±4.1)* | 2.1±3.4 *(7.0±3.8)* | 0.5±2.2 | 0.5±2.6 |
| P3 | 6.7±4.2 | 7.3±4.0 | 5.4±2.5 | 6.0±2.7 | 6.0±3.6 | 6.6±4.2 | 5.7±2.1 | 6.1±2.6 |
| Dyslexics | | | | | | | | |
| P1 | 2.1±1.3 | 2.2 ±1.3 | 2.1 ±1.8 | 2.0±2.1 | 1.6±1.1 | 1.7±1.1 | 1.2±0.7 | 1.2 ±0.5 |
| N1 | -4.1±3.2 | -4.2±3.2 | -3.8±2.8 | -4.0 ±3.2 | -4.5±3.9 | -4.4±3.2 | -3.1±2.4 | -3.3±2.3 |
| P2 | 1.2±2.5 | 1.3±3.0 | 1.3±2.4 | 1.1±3.2 | 0.8±2.8 *(5.0±2.3)* | 0.8±3.2 *(5.7±2.0)* | 0.7±1.9 | 0.4±2.3 |
| P3 | 6.8±1.4 | 7.6±1.3 | 5.6±1.5 | 7.1±1.9 | 5.1±1.8 | 6.1±1.7 | 5.2±1.7 | 6.3±1.3 |

**Table 3.4. The latency of the ERP peaks in all motion conditions**
The values are shown in ms (mean ± SD)

| Group | Coherent 40 | | Coherent 25 | | Coherent 10 | | Incoherent | |
|---|---|---|---|---|---|---|---|---|
| ERP peak | Left | Right | Left | Right | Left | Right | Left | Right |
| Controls | | | | | | | | |
| P1 | 138.2±14.7 | 141.3±14.4 | 144.5±25.9 | 143.7±28.2 | 141.5±22.9 | 148.1±19.0 | 133.5±14.5 | 133.0±16.5 |
| N1 | 228.6±27.7 | 222.0±24.8 | 226.4±22.4 | 222.6±18.7 | 226.3±14.3 | 225.9±17.0 | 224.6±17.9 | 224.6±18.0 |
| P2 | 280.9±20.6 | 278.2±19.3 | 285.0±14.9 | 288.6±16.6 | 286.5±19.7 | 289.8±19.7 | 289.1±16.5 | 289.6±19.3 |
| P3 | 567.4±64.9 | 566.4±88.6 | 560.1±38.8 | 565.2±66.5 | 555.5±82.2 | 563.0±53.2 | 557.9±81.4 | 568.2±82.0 |
| Dyslexics | | | | | | | | |
| P1 | 148.5±16.7 | 146.1±17.0 | 150.2±27.8 | 154.7±26.9 | 143.6±18.5 | 144.5±14.9 | 143.3±23.6 | 146.3±27.2 |
| N1 | 210.7±25.8 | 211.2±23.5 | 216.7±26.2 | 217.5±24.1 | 214.3±24.4 | 211.6±20.8 | 217.8±23.8 | 217.0±22.0 |
| P2 | 272.4±36.1 | 276.0±35.9 | 276.9±34.0 | 274.5±34.7 | 274.5±32.6 | 276.3±28.8 | 284.7±29.0 | 280.6±31.4 |
| P3 | 539.6±76.2 | 585.2±86.7 | 570.9±80.5 | 585.2±75.0 | 600.8±88.1 | 588.7±81.1 | 582.1±60.6 | 586.3±80.5 |

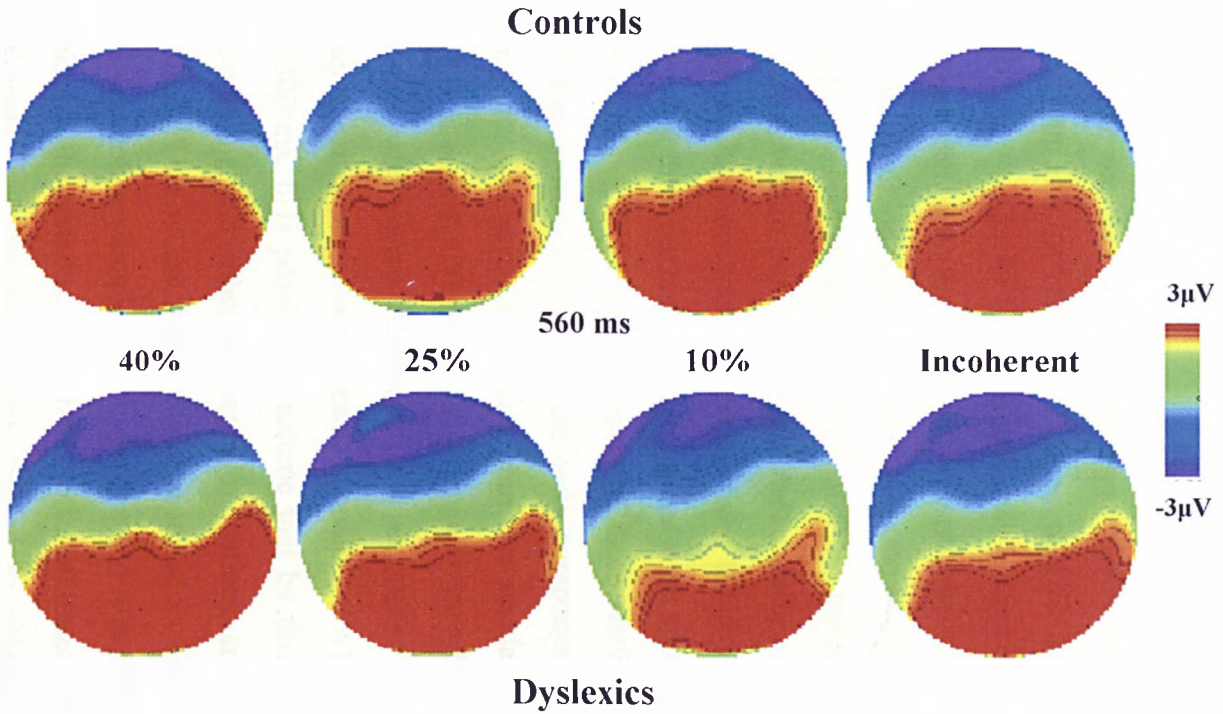


**Figure 3.2. Topographic ERP maps for P3 peak in all motion conditions**
Activation maps captured at 560 ms in all coherent and incoherent conditions for Control and Dyslexic groups. The black spots represent 128 channels as in Fig. 3.1.

### 3.3.3. Behavioural and ERP results of the 'magnocellular' dyslexic participant

As reported earlier, one dyslexic participant showed much lower dprime values than the other dyslexics in all conditions, especially in the coherent 10% condition (see section 3.3.1). Therefore, I decided to see whether the deviations in behavioural data of this participant would be reflected in or related to changes in his brain activation. If the sensitivity of his performance was worse than that of other dyslexic participants in the group, it could be the case that the ERP amplitude and latency could be affected as well. Especially it was interesting to find out whether ERP abnormalities, if found, would be reflected in the early or late, or both, components. The inspection of his ERP data revealed that the latency of the N1 ERP component was delayed by 20-50 ms, and the latency of the P2 by 70 ms, compared to the group average values. Consequent analysis showed that the latencies of the N1 and P2 ERP peaks for this participant were more than 3 standard deviations longer than the mean value for the rest of the group, with the largest differences in the 10% coherent condition. However, there were no such differences in the latency of the early peak P1 and the late peak P3 of this participant, with values being within 1 standard deviation from the mean of the reminder of the group.

These results show that one person from the dyslexic group has showed distinct differences from the rest of his group that were apparent both in his behavioural and ERP results. The interesting aspect of these results is in the latency of his ERP components deviations. Thus, the early component, P1, was not affected and its' latency for this participant was within one standard deviation of the group mean value, i.e., around 160 ms. The differences were reflected in N1 and P2 components latencies, which were delayed for this participant for about 50 to 70 ms from the group mean latency. As the mean latencies of N1 and P2 components are within 200-300 ms, it is possible to assume that by this time the networks involved in processing global coherent motion in parietal areas of the cortex were already involved. This is the usual timing reported in ERP literature for processing of coherent motion stimuli (e.g., Niedeggen and Wist, 1999; Kuba et al., 2001). Thus, I think, that the response in the brain to initial onset of the stimulus is intact for this participant, but the later stages, related to coherent motion processing in the associative areas of the visual cortex, i.e., possibly in the posterior parietal area, are

affected. I conclude this based on his largely delayed behavioural responses and ERP components, N1 and P2, much delayed from the group mean latency. Therefore, this participant could be described as 'magnocellular' dyslexic. It is known, that only a subgroup of dyslexic readers is reported to have magnocellular deficits. Provided we could find more age and IQ matched control and dyslexic participants, the number of 'magnocellular' dyslexic participants could have been larger. But with the current size of our group, there was only one participant from a dyslexic group who exhibited magnocellular deficits. With regard to his later ERP component, the P3, it should be noted that its latency for this participant was very similar to the rest of the group. Thus, if the range in the group latency for this component was around 450-650 ms, the P3 latency for the 'magnocellular' participant was about 500-630 ms depending on the motion condition. We do not find any differences in his P3 latency from the rest of the group. It could be explained by the fact that by this time (around 500-600ms) most of the processes related to coherent motion integration in the brain would have been completed. At this time latency, I think, later, cognitive related processes of decision making and response choice would be engaged. And it seems that these are intact for the 'magnocellular' dyslexic, i.e., similar to his group results. At a group level, the latency of P3 was slightly longer in dyslexics compared to controls, especially in a difficult condition of very low, 10% coherent motion stimuli (see Table 3.4). That effect did not approach significance level but this type of delay in ERPs of dyslexic participants was similar to our two other studies reported in this thesis (e.g., Taroyan et al., 2007), where the later ERP components were found to be significantly delayed among dyslexics in comparison with controls.

In summary, one dyslexic participant from the group showed magnocellular deficits reflected both in his behavioural and ERP responses. His sensitivity of performance was marginally worse than the group average, whereas the N1 and P2 components were much delayed compared to the whole group data. Such combined ERP and behavioural performance deviations show problems with global coherent motion processing for this dyslexic participant.

## 3.4. Discussion

Our behavioural data are partly in disagreement with previous reports of coherent motion perception deficits in dyslexia (e.g., Cornelissen et al., 1995; Eden et al., 1996) in that there were no significant between-group differences in our study in terms of performance accuracy and response latencies to correct responses. Overall the behavioural performance was good in both groups with only 10-20% of errors made in perceptually difficult coherent 10% and incoherent conditions. This suggests much lower thresholds than in the studies with more common coherent motion threshold measurements, such as direction judgement tasks (e.g., Cornelissen et al., 1995; Cornelissen and Hansen, 1998). Relatively good performance of our participants may reflect the fact that we used coherent/incoherent judgement task as opposed to motion direction detection. The stimuli used in many psychophysical studies (e.g., Cornelissen et al., 1995; Hansen et al., 2001) consisted of two patches of RDK, where coherent motion appeared in a random order in one or the other patch (also see Solan et al., 2007). The observers in these studies were required to *detect* and *locate* a motion contrast rather than only to detect motion, and both these functions may have contributed to performance differences between their dyslexic and control participants. In another psychophysical study no between-group differences were reported when only unidirectional motion was used, however, an impairment in the dyslexic group was detected when more difficult bi-directional transparent stimuli were employed (Hill and Raymond, 2002). It was suggested by Cornelissen et al. (1998a) that difficulties in attention switching between the patches in addition to low level disruption of motion processing may have caused the deficient performance among dyslexics. The authors argued that the 'poor' motion detectors could have deficits either in pre-attentive (low level, pre-striate input) or attentive (higher order, extrastriate input) processes but this distinction may not be so clear as attentional modulation of processes may occur throughout the system (Cornelissen et al., 1998a). It was shown in another recent study that when the results on attention and coherent motion detection tests were combined, 91.3% of poor readers were correctly classified (Solan et al., 2007). Thus, the absence of these additional demands on the attention system may have been the cause of better coherent motion discrimination

by our dyslexic participants. Other methodological differences, including limited dot lifetime and larger size of the stimuli (as suggested the latter may cause more unstable fixation and deficient eye movements), may also have caused the absence of between-group differences in our and some previous psychophysical as well as ERP (e.g., Scheuerpflug et al., 2004) studies.

No between-group differences were found for early P1, N1 and P2, and late P3, ERP components either. The absence of any group differences in electrophysiological correlates between dyslexics and controls in our study is in agreement with some (e.g., Scheuerpflug et al., 2004) but not with other (e.g., Schulte-Korne et al. 2004) previous reports. In a recent study by Kuba et al. (2001) abnormal delay in the latency of motion VEPs was found in 48% of the dyslexics to expansion stimulation, and only in 20% of dyslexics to linear motion stimuli. This discrepancy in the results supports the idea that visual perceptual deficits in dyslexia may be highly dependent on the sample of participants tested as only a subset of the dyslexic population were reported to have magnocellular deficits (Ramus 2003). Although our task required motor response and executive decision making, the magnocellular deficits, if present at a group level, would be revealed in the ERP components, similar to the condition related effects described below.

As already reported, for one dyslexic participant the sensitivity of the behavioural performance was much lower compared to the rest of dyslexic group. Furthermore, individual participant ERP analysis revealed an abnormal activation in this participant's data that was different from the group average, i.e., there was a large delay in the latency of his N1 and P2 ERP components. There were no such differences for the early P1, and the later, P3, ERP components of this participant. These findings suggest that the early processing, i.e., P1 response to the stimulus onset and appearance of the dots, is probably intact for this participant, but the later, coherence-dependent processing reflected in the N1 and P2 (200-270 ms) components is affected. Thus, magnocellular problems in this dyslexic participant that were manifested in abnormal (delayed) activation of the N1 and P2 ERP components probably indicate an impaired coherent-motion processing. These sensory visual problems indexed by delayed ERPs may have caused a poorer sensitivity of his behavioural performance. The absence of deviations in P3 latency of his ERPs from the group data suggests that at later, cognitive stages of processing and response choice (~ 600 ms) his brain activation was not different

from the rest of the group. Thus, magnocellular deficits in coherent motion perception were found for one dyslexic participant in our study. Additionally, the differences between our and some previous ERP studies may support the idea that visual sensory deficits in dyslexia are specific to stimulus characteristics, experimental design and analysis (Vanni et al. 1997; Scheuerpflug et al. 2004). For instance, our study was different from previous works in that ERPs were recorded in response to global coherent motion RDK without local motion or high contrast (parvocellular) cues.

The absence of any significant between-group differences in the ERP results and individual participant analysis indicated no impairment of global coherent motion perception among the other 8 dyslexic participants and showed similar brain processing in the two groups. The larger P3 amplitude in the higher (40%) coherent motion condition and the larger P3 amplitude in the right compared to the left hemisphere were characteristic of both groups. These findings replicate the results from previous studies that showed increased brain activation with higher coherence levels of motion (Patzwahl and Zanker 2000; Schulte-Korne et al. 2004) as well as higher sensitivity of the right hemisphere in coherent motion processing (Niedeggen and Wist, 1999). The increased P1 and P2 amplitude and longer response latencies in the 10% compared to 40% and 25% coherent conditions may be a result of increased attentional efforts and more brain activation required for processing of this perceptually difficult stimulus.

In conclusion, we were able to dissociate the dyslexic participants on the basis of their behavioural data. Most of the group showed essentially normal behavioural and ERP performance, whereas one participant showed abnormal behavioural and ERP performance. These findings support the idea that between-study differences may reflect different incidence of magnocellular deficits in the dyslexic population. However, as already mentioned, our findings, i.e., the absence of between-group differences, may have also been caused by the type of motion stimuli that we used. In the current study we did not employ attention switching in the stimuli similar to psychophysical studies (discussed earlier in this section) that could identify higher order magno or attention deficits among dyslexics.

It has been suggested earlier that there are two syb-types in developmental dyslexia - phonological and surface types (Castles and Coltheart, 1993). It was suggested by these authors that the phonological dyslexics in their sample were

below normal range in pseudoword reading, whereas the surface dyslexics had problems with exception word reading but were not impaired on pseudoword reading. However, this study was criticised by Stanovich et al. (1997) on the basis of the argument that when interpreting these sub-types it is important to provide comparisons with reading age matched controls (e.g., Manis et al., 1996). When chronological age (CA) defined sub-types were compared to reading-level (RL) controls by Stanovich et al. (1997), the phonological dyslexics displayed good exception word reading but profound deficits in pseudoword naming, phonological sensitivity, working memory and syntactic sensitivity, whereas the surface dyslexics showed a profile very similar to that of the RL controls. The authors argued that phonological dyslexia is characterised with true developmental deviancy, whereas surface dyslexia is characterised with developmental lag or delay in the development of the reading ability. It was also suggested recently that children who display similar patterns may not have the same underlying deficits (Joanisse et al., 2000). For example, phonological dyslexia may be caused by deficits in either speech perception or other aspects of phonology, whereas the surface or delay pattern may be caused by both endogenous (e.g., lack of computational resources) and exogenous (e.g., lack of experience) factors. The authors suggested that additional measures that assess other aspects of language and experience are needed in order to identify different potential causes of the same behavioural pattern. In a recent review of studies on phonological awareness in reading acquisition Castles and Coltheart (2004) proposed a set of requirements that is needed to fulfil in order for an empirical work to be capable of providing support for such a hypothesis. In this re-assessment of evidence that phonological awareness directly influences the process of reading acquisition the authors examined in detail the longitudinal and experimental training studies in this area. It was concluded that while it is possible to design and carry out a study that would provide unequivocal evidence of such a causal link, no such a study exists in the literature.

Thus, there is still no clear agreement in dyslexia literature as to what are the causes of the range of perceptual and cognitive problems among dyslexics. In the current study we were able to identify one dyslexic participant with coherent motion detection problems. It is possible that provided we employed stimuli with higher attentional demands similar to those used in earlier psychophysical studies, we may have found deficits at a group level among our dyslexic participants.

# 4. STUDY 3. READING WORDS AND PSEUDOWORDS IN DYSLEXIA: ERP AND BEHAVIOURAL TESTS IN ENGLISH SPEAKING ADOLESCENTS

## 4.1. Introduction

Reading acquisition is a complex and multi-stage process that requires many years of training. It involves identification of letters and letter combinations (graphemes), their subsequent conversion to sounds (phonemes), which are then combined to give the whole word pronunciation (phonology) and, eventually, its meaning (semantics). In transparent languages, such as German or Italian, the mapping between graphemes and phonemes is straightforward, and it allows the young readers to reach proficiency in reading considerably quickly (Frith et al., 1998). This is not the case in languages with deep and irregular orthography, such as English. Current cognitive models of reading suggest there are different types of strategies in languages with complex orthography. According to the dual-mechanisms model (Coltheart et al., 1993; 2001) orthography-to-phonology translation can be accomplished through lexical or sublexical procedures. The processing of frequently used words, especially those with irregular grapheme-to-phoneme relationship, is thought to be accomplished through a direct route from the word's visual form to its phonology and meaning. When processing novel words and pseudowords, however, individual letters are mapped onto phonological units before these are assembled into a phonological word form (Price and Mechelli, 2005), as in beginning readers. The pseudowords are word-like letter strings that do not have a stored representation in the mental lexicon, but are phonologically and orthographically regular.

Numerous functional imaging studies have concentrated recently on the research of different stages in reading. In a recent review of neuroimaging research Price and Mechelli (2005) argued that reading activates widely distributed brain regions from occipitotemporal to posterior temporal, precentral and frontal cortical areas. Pugh and colleagues suggested that posterior reading circuits including both dorsal (temporo-parietal) and ventral (occipito-temporal) components are disrupted

in people with reading disability, which is compensated by heightened reliance on both inferior frontal and right hemisphere parietal regions (Pugh et al., 2001). In an earlier MEG study by Salmelin et al. (1996) distinct time courses in activation during passive reading of words were found for dyslexic and control participants. Controls showed activation at about 180 ms after stimulus onset in the left temporo-occipital area, whereas dyslexics either did not show any activation in this area or showed a slowly increasing late response. In a more recent study Helenius et al. (1999) showed an earlier activation at about 150 ms in the left inferior occiptio-parietal area among fluent readers to the letter-string stimuli, whereas no such activation was found among dyslexic readers. The results of this study were interpreted according to the recent magnocellular visual deficit explanation of dyslexia (e.g., Cornelissen et al., 1998b). In a MEG study by Wilson et al. (2007) with English speaking normally achieving readers the words and pseudowords activated the same anatomical areas but in a different sequence after the first 100 ms of word onset. Thus, the activation to both words and pseudowords was recorded initially in the left posterior fusiform gyrus with no differences between conditions. Then, activation to words proceeded to inferior temporal (110-150 ms) and to superior temporal area eventually, whereas for pseudowords it was recorded in the superior temporal (95-215 ms) first, and then in the inferior temporal area. The authors suggested that the neural processes in the left posterior region, where the activation for words and pseudowords was similar, had already discerned the word types, and engaged one pathway for lexical items, i.e., words, that proceeded to semantic inferior temporal area first, and another parallel pathway for the pseudowords that proceeded to the phonological superior temporal area first. The non-familiar pseudowords would need an initial phonological decoding first before the semantic association could be attempted. They have proposed that the dual mechanisms hypothesis of reading by Coltheart et al. (1993) and Price et al. (2003) applies to processing of both words and pseudowords in deep orthographic languages like English. Wilson et al. (2007) have also argued that their results are consistent with a proposal of Devlin et al. (2006) for a functional role of the left posterior fusiform gyrus as a perceptual interface between visual form and lexical representations of words. This region in the occipitotemporal cortex has been labelled The Visual Word Form Area (VWFA) (McCandliss et al., 2003; but see Price and Devlin, 2004), and it was reported to be highly sensitive to orthographic

regularity, i.e., words and pseudowords, but not to irregular letter strings (e.g., Polk and Farah, 2002).

Differences in processing of words and pseudowords are important for understanding of reading disturbances in dyslexia. There is a large body of evidence on problems that dyslexic children encounter in phonological awareness tasks, with grapheme-to-phoneme conversion (Vellutino, 1979; Nicolson and Fawcett, 1994b; Nicolson and Fawcett, 1995; Bruck, 1993b). Coltheart et al. (1993) suggested there are two types of dyslexia: phonological (difficulty with pseudowords) and surface (difficulty with irregular words). According to recent evidence (e.g., Bowey and Rutherford, 2007), however, this division may not be clear cut as relatively few cases of either type of dyslexia appeared to be 'pure'. It is well established that dyslexic children and adults have particular difficulties in reading pseudowords (Yap and Van der Leij, 1993; Snowling, 1995). Consequently the lexical decision task (in which a stimulus is presented and the participant has to classify it as word or pseudoword) is a valuable diagnostic test. Nicolson and Fawcett (1994b; 1995) established clear behavioural difficulties in this task, including slower and less accurate responses.

At a neurological level, the behavioural deficits in reading among dyslexics are usually linked to abnormalities in language areas of the cortex. The early anatomical work (Galaburda et al., 1985) and more recent neuroimaging studies (e.g., Paulesu et al., 1996; Shaywitz, 1998b) support the notion of dysfunction in the perisylvian areas of the left hemisphere. Price and Mechelli (2005) reviewed the evidence of abnormalities in dyslexia, both structural and functional in some of these areas, including occipitotemporal, that correlated with reading disturbance. They suggested that the damage in left occipito-temporal region (acquired dyslexia) impairs the reading more than the object naming as the right occipito-temporal activation is able to sustain object naming more than reading.

The ERPs with their high temporal resolution can elucidate the levels and stages of cognitive processing involved in reading that can be difficult to differentiate with behavioural measures and neuroimaging techniques with low temporal resolution. For example, in a recent ERP study with British English speaking healthy adults the lexical frequency effect that reflects familiarity of an individual word has been found at 110 ms from stimulus onset (Hauk et al., 2006). The activation to high frequency words was smaller than to the low frequency

words, and this effect was lateralised to the left hemisphere. Shortly after these initial effects, at about 160 ms, ERPs distinguished between familiar words and unfamiliar pseudowords. The authors suggested there is only minimal delay between processing of visual word form (110 ms) and word's lexical representations (160 ms). The lexicality effects were still present in later latency windows of ERPs, with responses to pseudowords being more negative than to words at around 400-425 ms.

The problems encountered by dyslexics in lexical decision tasks were recently studied by means of recording ERPs in German-speaking children (Wimmer et al., 2002) and in young adults with Hungarian as their first language (Csepe et al., 2003). Wimmer et al. (2002) used numberwords and corresponding pseudowords. This study was designed to test the right parietal lobe dysfunction hypothesis of dyslexia. There were between-group ERP differences, with N1 amplitude smaller in the right hemisphere in response to pseudowords for the dyslexics compared to controls. It was concluded, that the pseudowords were particularly difficult and required higher attention levels, and consequently higher demands on the right parietal lobe. However, Csepe et al. (2003) have argued that the numberwords were particularly difficult, even for the controls, as non-frequent words. In the latter study the ERPs to frequently used words, numberwords and pseudowords were recorded, and the most pronounced differences between dyslexics and controls were found for the ERPs to frequently used words. Wimmer et al. (2002) and Csepe et al. (2003) did not report any word/pseudoword specific effect or lateralisation of such effect (as in the studies described above), i.e., no ERP differences (including hemispheric) were found in the controls' or dyslexics' group depending on whether words or pseudowords were processed. However, in both these studies the activation at occipitotemporal sites was not included into analysis. Additionally, as already mentioned, German and Hungarian are languages with transparent orthography and straightforward grapheme-to-phoneme mapping, and the word/pseudoword effects may be different from those in English.

I aimed to use a lexical decision task similar to those used by Wimmer et al. and Csepe et al., only with highly frequent nouns and corresponding pseudowords. I was interested to study the dynamics of brain activation at different recording sites, including occipitotemporal regions, and to observe whether the early and late ERPs would depict any differences between English speaking dyslexic and control

participants in visual word form processing or later, lexical decision making stages. It was also my goal to concurrently record the behavioural measures, such as response time and response accuracy, in both participant groups, and to investigate whether there would be any correlation of behavioural performance with the ERP findings. To the best of my knowledge, no behavioural performance on word/pseudoword lexical decision task has been reported before in English speaking nondyslexic and dyslexic adolescents with simultaneously recorded brain potentials.

Thus, my aim was to study the time course and between-group variations in different stages of word/pseudoword processing, lexical decision making and response choice in English speaking dyslexics and controls by means of recording ERPs and behavioural measures. I hypothesised that the word form recognition would be impaired in dyslexics and this would be reflected in deviations of the early ERP activation when compared to controls. Also, based on the results of our previous study (Taroyan et al., 2007), where attentional processing deviations were found among dyslexics at later cognitive stages, I expected that the later ERPs and behavioural measures would be affected too.

## 4.2. Methods

### 4.2.1. Participants

Nine dyslexic adolescents (3 females) and nine age-matched controls (3 females) were tested in this study. Same participants that were involved in the second study have also participated in this study except one male control subject who was not available for this study. The procedures for ethics approval and the psychometric data evaluation were the same as for the second study. One factor ANOVAs did not show significant differences between the dyslexic and control groups on IQ scores [$F(1,16) = 1.6$, $p>.2$], but dyslexics had significantly lower RA [$F(1,16) = 19.8$, $p<.0005$] and SA [$F(1,16) = 31.7$, $p<.0001$] scores compared to controls.

**Table 4.1. Psychometric data of participants in lexical task**

The means for both groups are displayed (ranges in parentheses)

| | Controls (N=9) | Dyslexic (N=9) |
|---|---|---|
| Age (years) | 16.3 (15.4 -19.3) | 17.1 (15.6 – 17.8) |
| IQ (standardised IQ score) | 118.1 (103-132) | 111.5 (99 - 124) |
| Reading age (years) | 17.1 | 13.0 (9.3 – 17.1) |
| Spelling age (years) | 17.1 | 11.5 (8.6 – 17.1) |

### 4.2.2. Design/Paradigm

A similar design to that of Wimmer et al.'s study (2002) was employed in this experiment. Eighty frequent regular English nouns and 80 corresponding pseudowords were presented in a random counterbalanced order. The pseudowords were created by replacing the vowel in each syllable of the corresponding real word, e.g., 'water to 'witar', or 'service' to 'sarvuce'. The stimuli consisted of black 5-8 letters and two syllables, 2cm high, low case, presented on a light grey background. They were displayed on 20 inch PC monitor, and the viewing distance to the screen was 60 cm. On average the stimuli subtended an angular size of 10.5deg in length and 2deg in height. The experiment was designed and run on a Dell DIMENSION 8300 microcomputer (version 2002) PC using E-prime V1.0 (Psychological Software Tools, 2002).

### 4.2.3. Procedure

There were 160 trials in the experiment (80 words and 80 pseudowords), each lasting about 5 sec, and the whole recording lasting about 13.5 min. Participants were instructed to press one button on the response pad with the index finger of their right hand when they saw a word, and the other button with the middle finger of the same hand when they saw a pseudoword. As in many previous ERP research studies, where right handed people took part, our participants as well

were asked to respond to the stimulus with their dominant right hand, as this is the hand they perform the majority of motor tasks with in everyday life.

Each trial started with a fixation period (a small black fixation cross in the centre of the screen) of 1000 ms, followed by the main stimulus, either word (W) or pseudoword (PW) displayed for 2000 ms, and followed by a blank screen (2000 ms) to allow for the motor response and in order to provide a rest to eyes from fixation of the stimuli. The motor response was not delayed in time as the lexical decision task was used as a reaction time task in participants' ability to differentiate between the words and the nonwords. However, they were given 2 sec in order to make a decision about the letter string they saw, and from the pilot studies this time interval proved to be sufficient for all participants to make a choice. Additionally, the motor response was made in the same way in these two conditions (W and PW) and any differences in results would be due to the differences between the stimuli.

Participants were seated in a comfortable chair in an acoustically shielded, dimly lit room. They were asked to fixate the small fixation cross displayed in the centre of the monitor at eye level that was followed by the stimulus. They were also required to refrain from eye movements, head or other body movements during stimulus presentation. Short training sessions were provided in order to familiarise the participants with the task. There were also written instructions provided before the start of the testing (see attached in Appendix 7.5). The recording was monitored and controlled by the experimenter in the adjacent room.

### 4.2.4. Data acquisition

The EEG recording system specifications were the same as in previous two studies. For the description of recording system the reader is referred to the section 2.2.3. Trial specific information, such as condition type (W, PW), accuracy of responses, and mean reaction times (RTs) of correct responses, was recorded simultaneously with the EEG, through E-prime and NetStation 4.0 EGI software and stored on the Macintosh for the further analysis of EEG. This information was also recorded and stored through Eprime on the PC for further analysis of the behavioural performance.

### 4.2.5. Data analysis

The EEG and behavioural data were further processed and analysed off-line using NetStation and Eprime. Mean RTs from the whole experiment, the number of false alarms (commission errors) and misses (omission errors) were determined for each participant.

The EEG data were digitally processed as described in the first study (see section 2.2.4). On average, 90% of the trials (epochs) were retained. The ERPs were computed by averaging all remaining trials accompanied with a correct response (about 60-70 for each condition), time-locked to stimuli, lasting 1200ms including 200 ms prestimulus baseline.

The group average ERPs were computed separately for the dyslexic and control participants in the Word and Pseudoword conditions. Several ERP components were identified by visual inspection of group average and individual participant data that can be observed in the upper, middle and lower larger scale waveforms on the left side of Figs. 4.1 & 4.2. Two early ERP peaks, P1 with a latency of 115 ms (from stimulus onset), and N1 with a latency of 180 ms were found in each participant waveforms and were best defined and with a maximal amplitude in occipital areas (lower circled channel groups in Figs. 4.1 & 4.2, labelled OL and OR, see Fig. 4.1 for symbol explanations). These peaks can be seen more clearly in the lower larger scale waveforms from one of the occipital group's channels. There was also a late positive complex with two peaks, P3 with latency around 300 ms, and P5 with a latency of about 500 (about 600 ms for dyslexics), found in both participant groups. These late peaks were most clearly present and with maximal amplitude at parietal sites (see the upper circled channel groups in Figs. 4.1 & 4.2, labelled PL and PR) and can be observed more clearly on the larger size waveforms in the upper left corner of Figs. 4.1 & 4.2.

I was also interested in the ERPs recorded at the channels circled into groups as shown on left and right far sides of Figs. 4.1 & 4.2. These channel groups approximately correspond to the left and right occipitotemporal regions (labelled OTL and OTR in Figs. 4.1 & 4.2), i.e., to the approximate location of the VWFA. Electrophysiological methods, such as ERPs, do not usually provide a reliable spatial resolution, however, the visual inspection of group average ERPs showed word/pseudoword specific effects in this area only, with amplitude to pseudowords

being larger than to words in the left hemisphere (see Fig. 4.1 for controls). As can be seen in Figs. 4.1 & 4.2, the ERPs in these areas were characterised with distinct components of large amplitude that are described below. The early ERP peaks, P1 and N1, were identified in these regions with the same latency and amplitude as the P1 and N1 in occipital channels (see Tables 4.3 – 4.6). There was also a late positive ERP peak identified in this group of channels, P4, with latency around 400 ms for both groups. These components can be observed more clearly on the middle larger scale waveforms on the left side of Figs. 4.1 & 4.2, from one of the channels in the groups labelled OTL and OTR. The early ERP peaks (P1 and N1) from occipital electrodes and occipitotemporal electrodes (separately) and the late peaks, P4 from occipitotemoral area, and P3 and P5 from parietal regions were submitted to further analysis.

### 4.2.6. Statistical analysis

The mean RTs to correct hits for each participant were subjected to repeated measures analysis of variance (ANOVA) with 1-between subjects factor Group (dyslexics versus controls) and 1-within subjects factor Condition (Word versus Pseudoword) mixed measures design. The numbers of omission and commission errors were statistically analysed as one 1-between factor (Group) and 2-within factors, Condition (W, PW) and Incorrect Responses (omission, commission), ANOVA.

The amplitude and latency of the early (P1 and N1) and late (P3, P4 and P5) ERP components from the respective regions of interest were analysed separately for the left and right areas. As in previous two studies, a group of channels in selected regions (described above) was averaged in order to improve the signal to noise ratio. Similar channel grouping has been used elsewhere (e.g., O'Connor et al., 2007). Thus, the upper two channel groups (circled as shown in Figs. 4.1 & 4.2) correspond to the left and right parietal regions, the lower two groups correspond to the left and right occipital areas, and the channel groups circled on sides correspond to the left and right occipitotemporal areas. The labelling is as explained in Fig. 4.1.

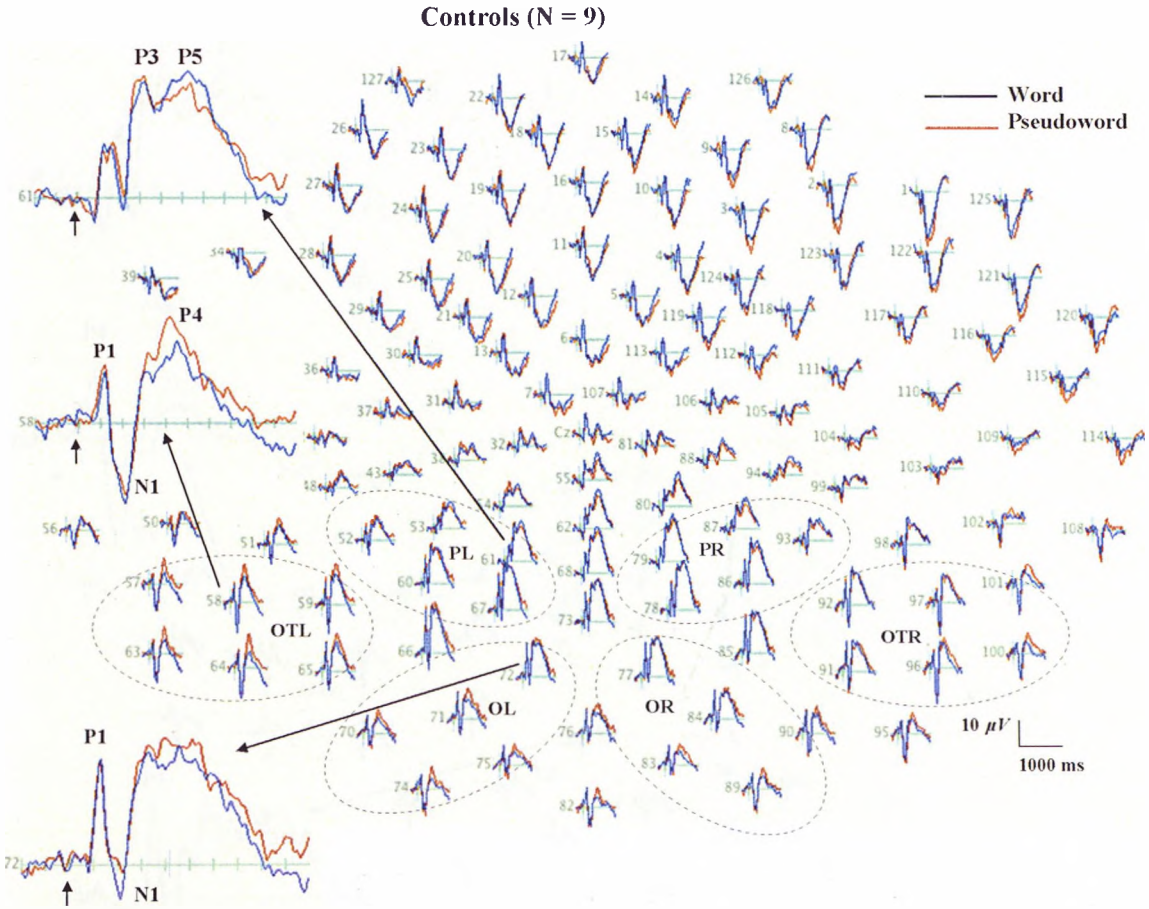


**Figure 4.1. Control group average ERPs for words and pseudowords**

The waveforms are shown for control participants in Word (—— ) and Pseudoword (—— ) conditions at all electrode sites. OL – occipital left, OR – occipital right, OTL – occipitotemporal left, OTR – occipitotemporal right, PL- parietal left, PR – parietal right. The larger scale waveforms in the left top and bottom corners show the representative ERPs and characteristic peaks from parietal (upper circled channels) and occipital (lower circled channels) regions. The vertical lines on waveforms (arrows on larger scale ERPs) indicate the stimulus onset at 0 ms.

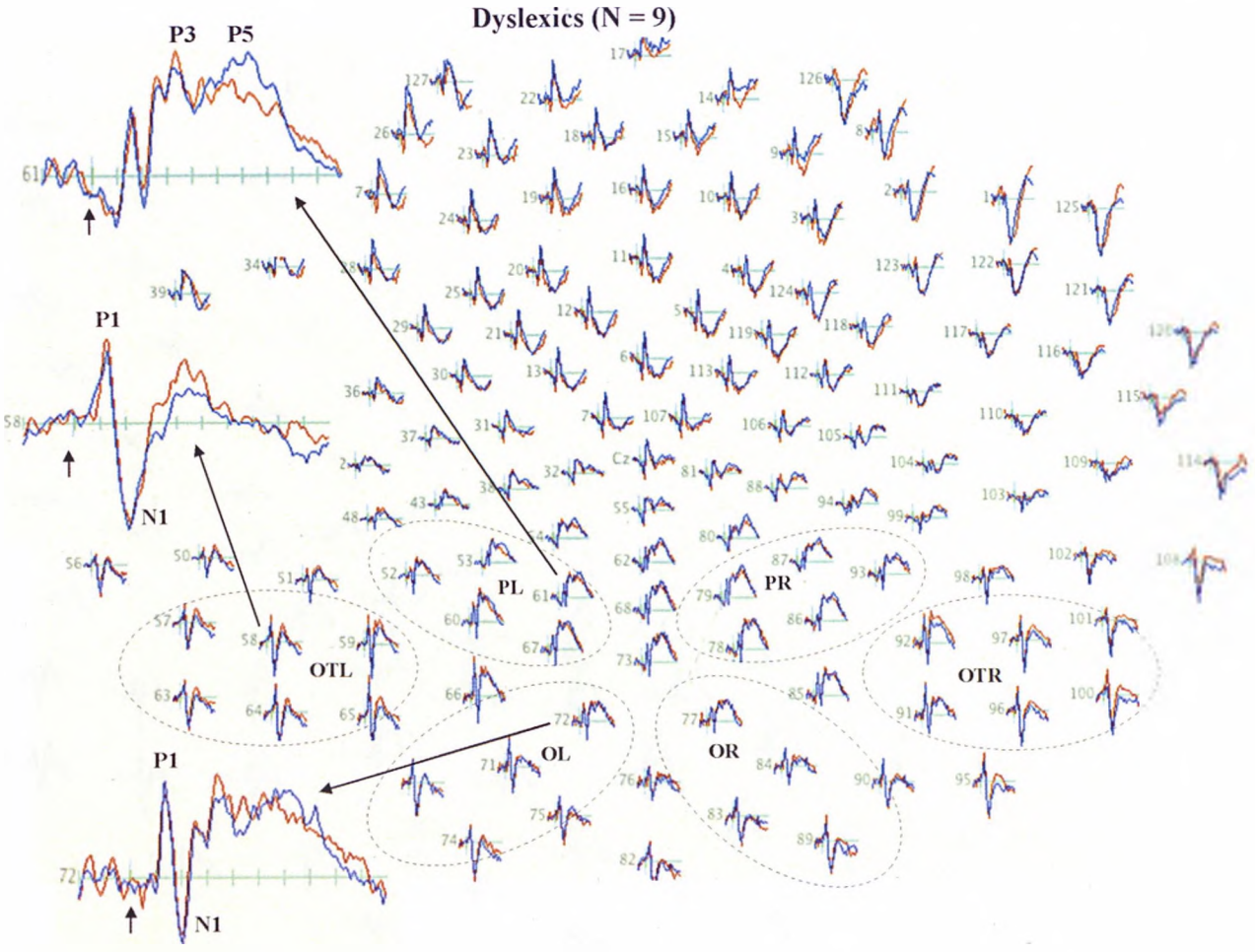


**Figure 4.2. Dyslexic group average ERPs for words and pseudowords**
The waveforms are shown for dyslexic participants in Word ( ——) and Pseudoword (——) conditions at all electrode sites. All labels and the format are the same as in Fig. 4.1.

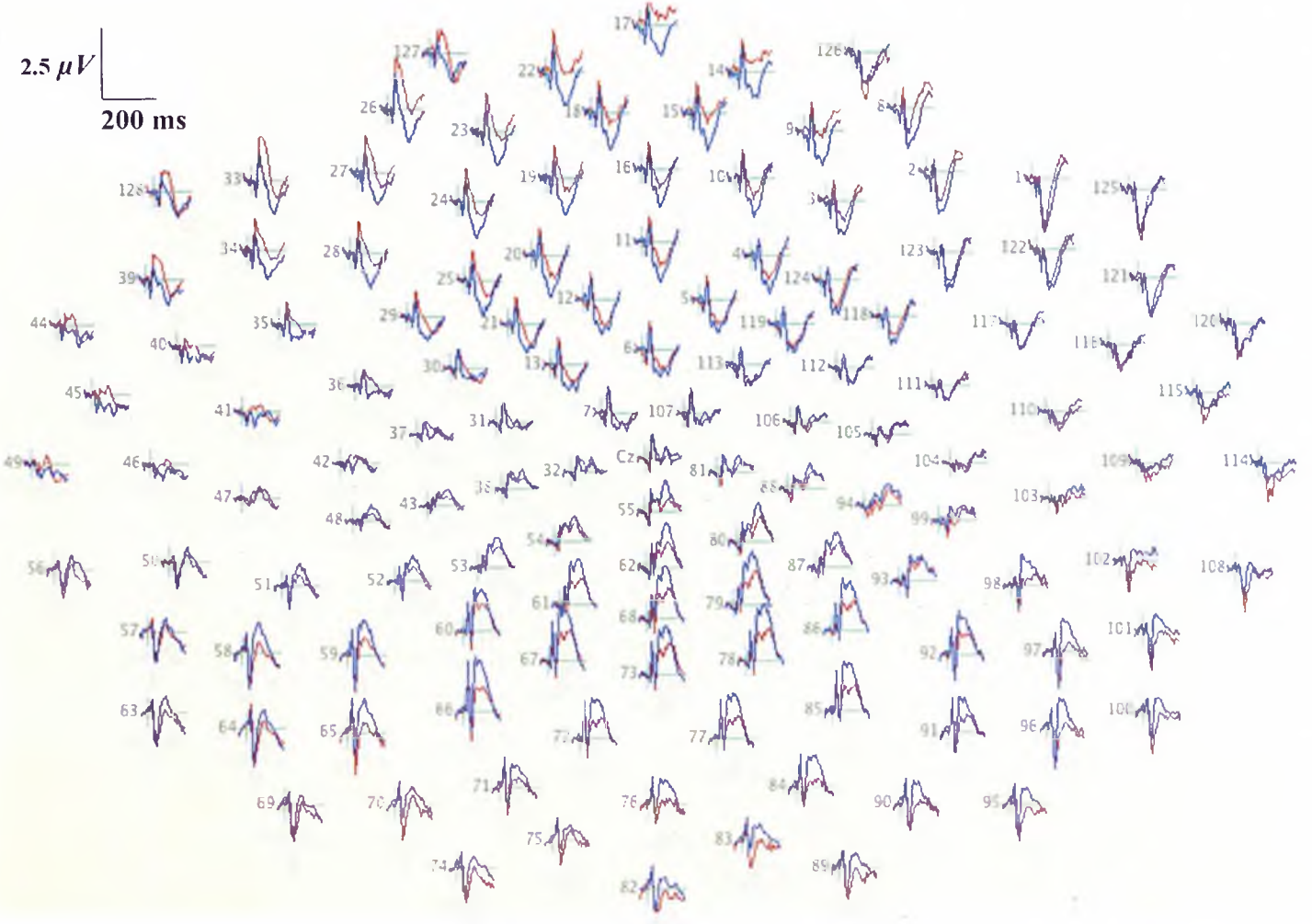


**Figure 4.3. Control (—) and Dyslexic (—) groups average ERPs for words**

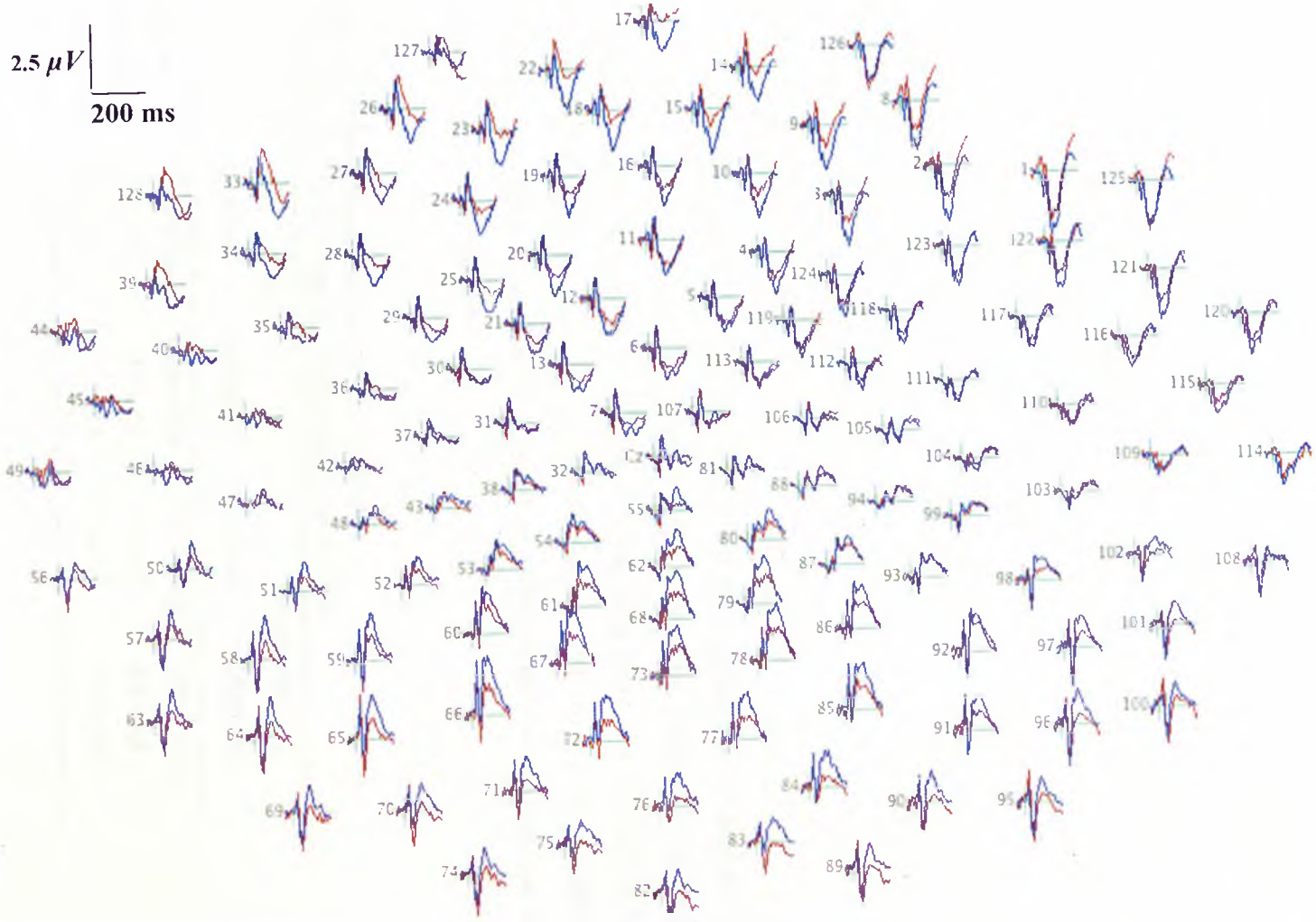


**Figure 4.4. Control (—) and Dyslexic (—) groups average ERPs for pseudowords**

The amplitude of the peaks in individual subject ERPs were found in the time windows defined by the peaks in group average ERPs and automatically measured relative to the pre-stimulus baseline. The latency of the peaks was computed relative to the stimulus onset. The peak amplitude and latency values from all electrodes in a group were averaged.

The average amplitude and latency values of ERP components from each group of electrodes and for each participant were submitted to ANOVA with 1 between-subjects factor Group (dyslexics versus controls) and 2 within-subjects factors Condition (W versus PW) and Hemisphere (left and right).

The criterion for statistical significance was $p < 0.05$. The statistical analysis was performed using StatView (SAS Institute, 1998).

## 4.3. Results

### 4.3.1. Behavioural data

The statistical analysis of mean RTs revealed significant differences for both main factors, Group and Condition. The RTs were longer in dyslexics compared to controls ([$F(1,16) = 6.3$, $p<.05$], and they were also delayed in the Pseudoword condition compared to the Word condition [$F(1,16) = 73.87$, $p<.0001$]. No interaction effects were observed. The mean values of RTs for both groups and conditions are shown in Table 4.2.

**Table 4.2. Behavioural data in the lexical task**
The values for both groups are displayed (means ± SD)

| | Word | | Pseudoword | |
|---|---|---|---|---|
| | Controls | Dyslexics | Controls | Dyslexics |
| RT (ms) | 776.4 ± 107.6 | 895.9 ± 83.6 | 924.5 ± 168.0 | 1058.4 ± 70.7 |
| Omissions | 0.5 ± 0.5 | 4.2 ± 5.0 | 1.2 ± 1.7 | 8.6 ± 5.8 |
| Commissions | 0.9 ± 1.3 | 3.2 ± 3.4 | 0.9 ± 0.9 | 6.1 ± 7.8 |

For the number of incorrect responses, the 1-between (Group) and 2-within (Condition, Incorrect Responses) factor ANOVA revealed both main factor and interaction significant effects. The number of incorrect responses was larger in dyslexics compared to controls [$F(1,16) = 22.9$, $p < .0005$] as a main factor, and it was also larger in the Pseudoword compared to the Word condition [$F(1,16) = 10$, $p < .01$] as a main factor. However, there was a Condition x Group interaction effect [$F(1,16) = 6.5$, $p < .05$], and subsequent analysis showed that the number of incorrect responses was larger in the Pseudoword compared to the Word condition in the dyslexics group mainly. The mean values of the number of incorrect responses for both groups are also displayed in the Table 4.2.

### 4.3.2. ERP data

The grand average waveforms in the Word and the Pseudoword conditions are presented for the Control group in Fig. 4.1, and for the Dyslexic group in Fig. 4.2. The expanded waveforms displayed in the left lower, middle and upper corners in both figures show the characteristic ERP components, P1 and N1 from selected occipital, P1, N1 and P4 from occipitotemporal, and P3 and P5 from parietal channels. The mean values of the amplitude and latency of the ERP peaks are shown in Tables 4.3 – 4.6, for both groups and conditions.

**Table 4.3. The amplitude of the ERP peaks to words and pseudowords**
The group mean values are shown in μV (mean ± SD)

| Group | Word | | Pseudoword | |
|---|---|---|---|---|
| ERP peak | Left | Right | Left | Right |
| Controls | | | | |
| P1 | 4.7 ±2.4 | 5.0±2.6 | 4.7±2.9 | 4.8±3.1 |
| N1 | -4.7±2.6 | -4.6±2.8 | -4.6±2.9 | -4.5±3.0 |
| P3 | 5.9±1.8 | 6.4±2.6 | 6.2±2.1 | 6.1±2.5 |
| P5 | 5.9±2.1 | 6.6±2.4 | 5.8±2.3 | 5.9±1.8 |
| Dyslexics | | | | |
| P1 | 4.6±2.6 | 4.1±2.3 | 4.0±1.5 | 4.1±1.4 |
| N1 | -4.9±1.9 | -4.7±2.2 | -4.5±2.4 | -4.3±2.5 |
| P3 | 4.4±1.9 | 4.3±1.7 | 4.8±1.8 | 4.7±1.4 |
| P5 | 4.1±1.4 | 5.0±1.9 | 3.3±1.0 | 4.5±1.2 |

**Table 4.4. The latency of the ERP peaks to words and pseudowords**
The group mean values are shown in ms (mean ± SD)

| Group | Word | | Pseudoword | |
|---|---|---|---|---|
| ERP peak | Left | Right | Left | Right |
| Controls | | | | |
| P1 | 120.2±15.9 | 115.6±13.1 | 113.5±16.8 | 110.7±14.5 |
| N1 | 181.8±20.4 | 182.8±19.7 | 180.5±20.9 | 182.2±20.0 |
| P3 | 298.7±36.6 | 308.5±31.3 | 308.6±32.1 | 312.4±42.9 |
| P5 | 495.4±56.3 | 489.2±65.0 | 486.7±42.3 | 517.5±62.3 |
| Dyslexics | | | | |
| P1 | 115.0±23.3 | 111.3±22.3 | 119.0±18.8 | 116.8±19.2 |
| N1 | 187.7±36.7 | 188.4±36.5 | 192.3±32.8 | 191.6±32.9 |
| P3 | 331.6±36.5 | 340.4±56.5 | 326.8±43.6 | 345.8±61.7 |
| P5 | 584.8±75.7 | 602.0±69.3 | 558.7±61.0 | 565.1±60.8 |

**Table 4.5. The amplitude of the ERP peaks in occipitotemporal area**
The group mean values (mean ± SD) in μV

| Group | Word | | Pseudoword | |
|---|---|---|---|---|
| ERP peak | Left | Right | Left | Right |
| Controls | | | | |
| P1 | 3.2±1.7 | 3.7±2.1 | 3.8±1.6 | 3.4±2.3 |
| N1 | -5.4±2.7 | -5.2±3.4 | -5.1±2.6 | -5.3±2.8 |
| P4 | 4.9±2.4 | 5.3±2.7 | 6.3±2.9 | 5.8±1.8 |
| Dyslexics | | | | |
| P1 | 4.1±1.9 | 3.7±2.0 | 4.1±1.8 | 4.1±1.5 |
| N1 | -5.6±3.0 | -5.3±2.2 | -5.0±2.9 | -4.7±2.3 |
| P4 | 2.8±1.3 | 2.9±1.4 | 3.5±1.4 | 3.6±1.1 |

**Table 4.6. The latency of the ERP peaks in occipitotemporal area**
The group mean values (mean ± SD) in μV

| Group | Word | | Pseudoword | |
|---|---|---|---|---|
| ERP peak | Left | Right | Left | Right |
| Controls | | | | |
| P1 | 116.2±13.6 | 115.3±17.7 | 111.7±14.9 | 112.4±14.7 |
| N1 | 199.1±41.7 | 203.0±31.0 | 205.0±48.3 | 201.7±21.8 |
| P4 | 390.1±77.0 | 384.4±86.1 | 387.0±59.0 | 404.3±100 |
| Dyslexics | | | | |
| P1 | 121.4±15.1 | 118.0±19.2 | 125.5±8.4 | 119.1±12.1 |
| N1 | 219.3±37.6 | 211.6±35.3 | 217.1±34.4 | 208.5±31.4 |
| P4 | 400.5±72.4 | 408.2±67.1 | 402.3±68.5 | 401.3±106 |

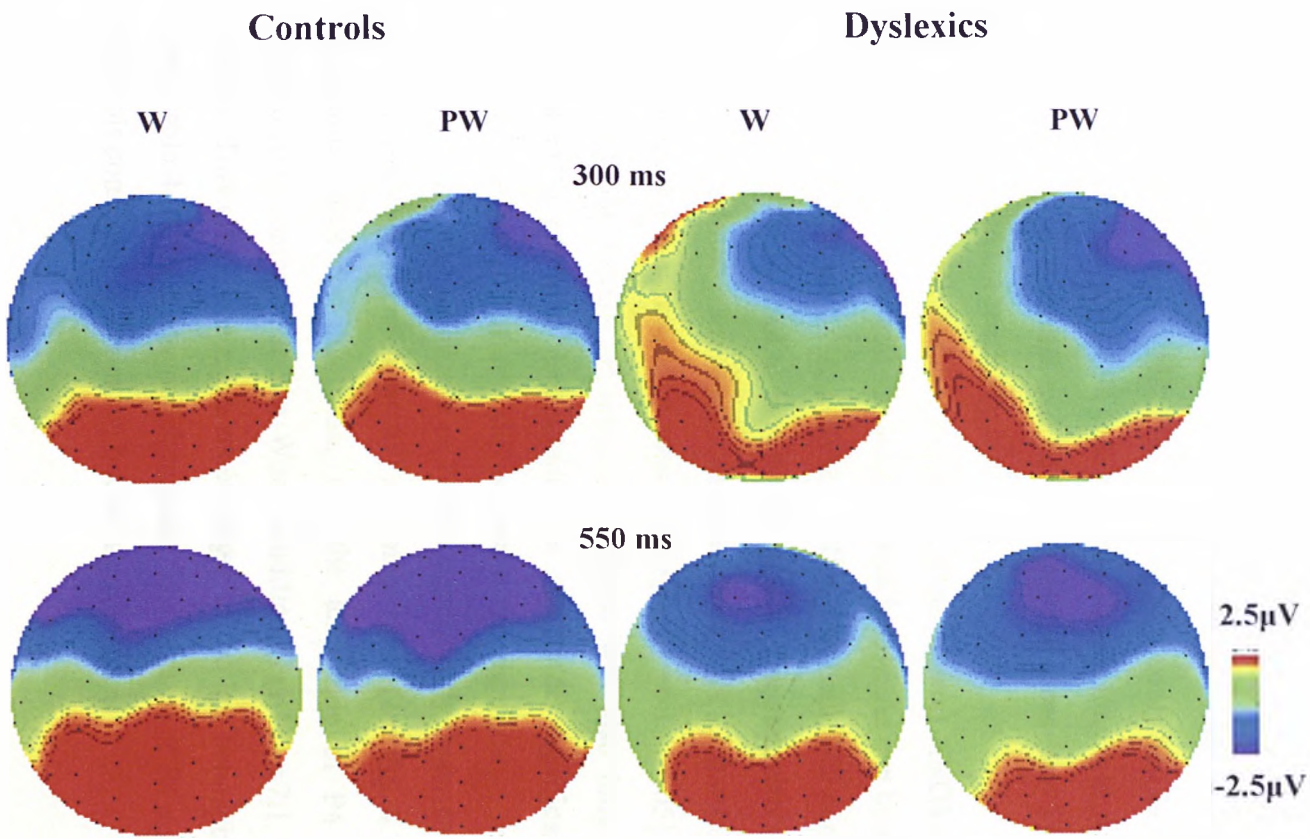


**Figure 4.5. Topographic ERP maps for words and pseudowords**
Activation maps captured at point of maximal voltage for the P3 peak at 300 ms and the P5 peak at 550 ms in both conditions for Control and Dyslexic groups. The black spots represent individual channel from 128 electrodes GSN net.

The statistical analysis did not show any significant effects for the early ERP components P1 and N1 in occipital areas [largest $F(1,16) = 4.4$]. There were no significant main effects for the early ERP components in the occipitotemporal area either, however, I found a significant interaction effect for the amplitude of P1, Condition x Hemisphere x Group [$F(1,16) = 7.1$, $p < .05$]. Subsequent ANOVA showed that the P1 amplitude in the left occipitotemporal area was significantly larger for the pseudoword than for word condition for the controls only [$F(1,8) = 5.5$, $p < .05$]. No such condition differences were found for the right hemisphere, or for the dyslexic group. There were also some consistent trends for the early ERP peaks in occipital channels. For example, as can be seen in Tables 4.3 & 4.5, the amplitude of P1 was slightly larger in controls compared to dyslexics in occipital areas, and the latency of P1 and N1 was slightly longer in dyslexics compared to controls both in occipital and occipitotemporal areas (see Tables 4.4 & 4.6), but these effects did not reach significance.

The 3 factor (Group, Condition, Hemisphere) ANOVA results for the late ERP components, P3 and P5, are described below. As can be seen in the Table 4.3 and in the topographic maps of Fig. 4.3 (for P5), both ERP components were larger in the control compared to the dyslexic group. The statistical analysis showed that this effect did not reach significance for the P3 [$F(1,16) = 4.0$, $p = .06$], but it was significant for the later ERP peak, P5 [$F(1,16) = 6.1$, $p < .05$]. As can be seen in Table 4.4, the latency of these components was also longer for the dyslexics compared to controls. And again, this effect was significant for the P5 peak [$F(1,16) = 9.9$, $p < .01$], but it did not reach the significance level for the P3 peak [$F(1,16) = 2.3$]. The amplitude of P4 was significantly larger for Controls compared to dyslexics [$F(1,16) = 9.6$, $p < .01$] as a main effect (see Fig. 4.3). There was also a condition effect for this peak, i.e., the amplitude of P4 was larger in the Pseudoword compared to the Word condition [$F(1,16) = 7.1$, $p < .05$] across both groups. This effect was again much larger in the left hemisphere for the controls (see Table 4.5) but it was not significant. The latency of P4 was slightly shorter in Controls compared to dyslexics, but not significantly.

## 4.4. Discussion

In the current study I investigated the dynamics of brain electrical activation during processing of words and pseudowords in English-speaking dyslexic adolescents and age-matched controls, with a concurrent recording of the behavioural performance in this lexical decision task. In summary, the results of this study showed significant differences between the two groups in behavioural data, where the dyslexics were significantly slower and significantly less accurate than the controls. The behavioural measures also indicated a better performance in the Word compared to the Pseudoword condition, especially in the dyslexic group. The amplitude of the early ERP peak, P1, was significantly larger in the Pseudoword compared to the Word condition in the left occipitotemporal area for the control group. The amplitude of P4 was larger in the Pseudoword compared to the Word condition across both groups. The late P4 and P5 peaks were significantly attenuated, and P5 was significantly delayed for the dyslexics compared to controls.

Firstly, I discuss the results of the condition and hemisphere factors. The statistical analysis of the behavioural data showed highly significant differences between word and pseudoword conditions. The RTs were faster and the number of the errors, omission and commission, was smaller in the Word compared to the Pseudoword condition in both participant groups. However, there was Condition x Group interaction effect and the subsequent analysis showed that the number of errors was larger in PW compared to W condition in the dyslexics group mainly. Significant word/pseudoword differences were also found for the early and later brain activation, i.e., an increase in the amplitude of P1 (only for the controls) and P4 (in both groups) recorded at occipitotemporal sites was observed in response to pseudowords. Similar word/pseudoword differences in the early brain activation were found in other ERP studies (Sereno et al., 1998; Hauk et al., 2006). For example, Sereno et al. (1998) reported larger P1 (112 ms post-stimulus) amplitude to pseudowords than to words over posterior parietal regions, whereas Hauk et al. (2006) showed larger brain activation for pseudowords than for words in the left lateralised regions of the posterior temporal cortex at about 160 ms. In our study the word/pseudoword differences were found for the amplitude of P1 as early as 110 ms in the left occipitotemporal region for the controls' group only. However, some other studies found an opposite effect, i.e., a larger activation for words than

pseudowords in this area (e.g., Fiez et al., 1999; Fiebach et al., 2002). As suggested by Mechellie et al. (2003) various methodological differences could e the reason for differences in these studies. In a more recent study it was suggested that the increase of activation in response to pseudowords may be due to the greater processing demands needed for unfamiliar pseudowords compared to familiar and frequently used words (Kronbichler et al., 2004).

It is of interest to attempt to relate these findings to converging studies involving functional MRI studies on VWFA. In this context, it is important to acknowledge the danger of attempting to infer regional activation from the electrodes located at the surface of the head, especially for the regions distal from the scalp. As already mentioned, the ERP methods are known for a reliable temporal but not spatial resolution. However, the modern high density sensor nets provide finer spatial as well as temporal resolution (Srinivasan et al., 1998). In the current study this is further supported by the fact that significant word/pseudoword differences were found in the occipitotemporal region only (and not in parietal, for example). Our and previous ERP findings may be related to the results from neuroimaging studies of word/pseudoword activation in VWFA and may serve as electrophysiological correlates of visual word form recognition.

However, unlike the controls, no reduction in the amplitude of P1 in response to words was observed among the dyslexic participants. This absence of word/pseudoword effect in P1 amplitude (together with absence of asymmetry) indicates deviations in the early brain electrical activation related to visual word form processing. This suggests that, unlike the controls, the dyslexic group were not able to discriminate between familiar words and unfamiliar pseudowords at this time point in brain activation. The results suggest abnormalities in the left occipitotemporal area of dyslexics and show deficits in word/pseudoword processing at an early stage of 110 ms from the stimulus onset among English speaking dyslexic adolescents that took part in this study.

In the later ERP activation, however, the amplitude of P4 was larger to pseudowords than to words both in controls and in dyslexics. This result replicates the findings from the previous MEG (Wilson et al., 2007) and ERP (Hauk et al., 2006) studies where the amplitude for pseudowords was found to be larger than to words until about 400 ms. This effect has been interpreted as indicating that the lexical status of the stimulus is not completely resolved until that time. Since a

similar effect, i.e., a reduction in amplitude to words, was observed for the P4 amplitude of the dyslexic participants, I suggest that although they showed deficits in the early visual word form recognition, at the later stage of the lexical decision the brain activation was similar to that of the controls (but see the later discussion of the attenuated amplitude of P4 and P5 in the dyslexic participants). Thus, both participant groups differentiated between the two conditions and experienced more difficulty when processing pseudowords, even at later lexical stages. This was reflected in increased brain activation, i.e., larger P4 amplitude, and worse behavioural performance for pseudowords compared to words, including longer RTs and less accurate responses in both groups.

The 'wordness' effect was not present for P3 and P5 ERP peaks. These late deviations were recorded at parietal sites, unlike P1 and P4 from occipitotemporal sites, and may not reflect specifically reading related activation. These late positive waves at parietal regions are normally attributed to decision making and executive function related activations, particularly so for the P5 (e.g., Hauk et al., 2006). As can be seen in Tables 4.4 & 4.2, there was a time interval of at least 300 ms between the latency of the latest ERP peak, P5 (around 500 ms for controls), and the RTs ( about 800 ms). This gap was even longer in the pseudoword condition, and particularly so for the dyslexic participants (500 ms). Without doubt additional decision making and response planning processing took place after the first 600 ms of stimulus onset that were not reflected in the ERP components. It is during this 200 to 500 ms interval between the latency of the ERPs and average RTs that the final decision making and response choices were completed, as the RTs are recorded at 800 to 1060 ms on average.

The ERP analysis showed between group differences not only in the word/pseudoword effect but also in the hemispheric distribution of activation. According to the statistical analysis, unlike controls, there was no left hemispheric lateralisation of function in the dyslexic group, i.e., the amplitude of P1 to words and pseudowords was of the same magnitude in both hemispheres and the two conditions. Both in recent ERP and neuroimaging studies (as described above) normally achieving English speaking readers have been shown to have a left hemispheric lateralisation in visual word form recognition. This was also found in the control participants. The absence of asymmetry in the dyslexic participants' data and the even distribution of activation in two hemispheres supports previous

reports of atypical symmetry and disregulated interhemispheric function in dyslexia (e.g., Taroyan et al., 2007). In a recent behavioural study by Rutherford (2006) it was suggested that familiar words invoke lexical processing by both hemispheres, whereas unfamiliar pseudowords invoke non-lexical processing by the left hemisphere. Since dyslexics have difficulties with pseudoword processing, i.e., with non-lexical processing in the left hemisphere, they show more reliance on the right hemisphere, hence absence of asymmetry in their behavioural responses. It has been also proposed by Price and Mechelli (2005) that damage in the left occipitotemporal area impairs reading more than object naming because the right ocipitotemporal area does not compensate for reading as much as for object naming.

I now return to the between-group differences in the late ERPs recorded in occipitotemoral and parietal channels. There were significant deviations in the brain activation of the two groups in the later ERP peaks, with significantly larger amplitudes of P4 and P5 and shorter latency of P5 for the controls. The between-group amplitude effects of the late ERP peaks recorded in the current study replicated similar findings from our previous ERP study of the Continuous Performance Task (an attentional task not using words) in dyslexia (Taroyan et al., 2007) where the amplitude of the late positive peaks was also found to be attenuated in dyslexics. The late between-group ERP latency differences in the current study were paralleled by significant differences in behavioural data, with the dyslexic group showing slower and less accurate responding both for words and pseudowords. The delay and reduction in the ERP peaks as well as poor behavioural performance may indicate general decision making problems in addition to literary difficulties that they encounter and that become apparent at a later stage of stimulus categorisation and response choice.

In conclusion, these results suggest abnormalities among dyslexics at the initial word/pseudoword processing stages, i.e., in visual word form recognition, and as early as 110 ms, in the occipitotemporal region, in terms both of lateralisation and differentiation between words and pseudowords. The dyslexic group were also impaired in the later, cognitive stages of lexical decision making and response choice.

# 5. BRAIN-BEHAVIOUR CROSS-STUDY CORRELATION

In all three studies described in this thesis almost the same population of people participated in the tasks. I compared the results of these experiments in a cross-study correlational analysis in order to find out whether any correlations existed between various measurements used in these tasks. An additional analysis, factor analysis, was also undertaken and is described below in section 5.2. Some of the participants that helped with the first study, CPT task, were not available for the second and the third studies. However, 7 (2 females) people in the dyslexic group and 7 (2 females) people in the controls group participated in all three tasks. The number of measurements across these studies was very large, therefore I selected the conditions in each task that were most difficult, perceptually and cognitively. I expected that these conditions would prove the most informative, since they often triggered differences between the dyslexic and the control groups either on behavioural and/or electrophysiological level. Thus, in the continuous performance task (CPT) I selected the NoGo condition that triggered an asymmetrical activation in the controls but an atypical symmetrical response in the dyslexics. In the coherent motion study the 10% coherent condition was selected as it was perceptually most difficult because of the least number of coherently moving dots compared to the other coherent conditions. This condition highlighted the 'magnocellular participant' that had delayed latency of ERP and low sensitivity in his performance when compared to the rest of the group. However, the 40% coherent condition (perceptually easiest because of the larger number of coherently moving dots) was included as well. In the last study, lexical decision task, the pseudoword (PW) condition was selected as there were more errors made by dyslexic participants in this condition when compared to controls. I have selected one early and one late ERP component from each study. The P1 was selected in all three studies from occipital and P3 (P5 in PW) from parietal areas. Additionally, the N1 and P2 in the coherent 10% condition were included, as the latency of these components was delayed for the 'magnocellular' participant when compared to the rest of the dyslexic group in the motion study. In the lexical decision task P1 and P4 from occipito-temporal areas were also included. Both the amplitude and the

latency values of the ERP components were analysed, and I have included the values for both left and right hemispheres in all studies. As for the behavioural results, the RTs and errors (omission plus commission) were included from the CPT task. In the CPT experiment the response was recorded only in the Go condition, therefore, the RTs and the error rate for this condition, as well as the ERP data for this condition (together with the NoGo condition), were included. In the motion study the dprime and the RTs were selected. In the lexical decision task the RTs and the errors for the PW condition were included. One important criterion for participants was their literacy scores. I have included this criterion as a difference between their chronological age and the spelling age, i.e., CA minus SA. This discrepancy further differentiated the control and dyslexic participants. All data were analysed in SPSS, and Pearson coefficient values (range -1 to +1) were obtained for all correlations. Significant results are reported below.

## 5.1. Correlational analysis

One of the main aims of this analysis was to see whether the speed of processing correlated across conditions and various indices of brain activation and behavioural performance in different studies. I hypothesised that: 1) processing speed and magnitude indexed by the latency and the amplitude of the ERP components would be correlated across all three studies because of generic properties of the brain activation regardless the type of the experimental task; 2) poor literacy scores and poorer behavioural performance would be correlated with attenuated and delayed ERPs as found previously in the ERP studies of dyslexia.

*CA-SA.* The significant correlations of CA-SA with other conditions analysed are displayed in Table 5.1. First, for the motion study this analysis revealed that the amplitude of P1 in the left hemisphere in coherent 10% condition negatively correlated with the CA-SA ($r$= .6, p < .05). In other words, the larger P1 amplitude associated with smaller difference between the CA and the SA, i.e., with better literacy scores. For the simplicity in description of hemispheric localisation, I will refer to right (R) and left (L) components, e.g., L P1 and R P1. The CA-SA negatively correlated with the amplitude of the P3 (L & R) both in Go and NoGo conditions, and the R P4 and the L P5 in PW condition (the smallest $r$ = .6, p<.05),

whereas it correlated positively with the latency of the L P1 Go and the R P3 Go ($r$ =.6, p<.05). The CA-SA also highly correlated with the Error in PW condition ($r$ = .8, p<.01). This means that the larger was the CA-SA, i.e., the worse were the literacy scores, the smaller was the amplitude and the longer was the latency of the ERP components, and the higher was the error rate.

**Table 5.1. The significant correlations for the CA-SA**

| | CA-SA |
|---|---|
| P1 Amplitude Coherent 10% Right | -.560* |
| P1 Latency Go Left | .585* |
| P3 Amplitude Go Left | -.756** |
| P3 Amplitude Go Right | -.553* |
| P3 Latency Go Right | .556* |
| P3 Amplitude NoGo Left | -.728** |
| P3 Amplitude NoGo Right | -.671** |
| P4 Amplitude PW Right | -.601* |
| P5 Amplitude PW Left | -.701** |
| P5 Amplitude PW Right | -.555* |
| P5 Latency PW Left | .691 |
| Error PW | .763** |

* - correlation is significant at the .01 level
** - correlation is significant at the .05 level

*Motion study.* In addition to the significant negative correlation of the CA-SA with the P1 amplitude in coherent 10 % condition, there were other results found for this task. Thus, dprime in coherent 10% condition was negatively correlated with the Error rate in Go condition (CPT task) ($r$= .6, p < .05), but positively with the amplitude of the L & R P5 in PW [($r$= .6, p<.05) and ($r$ = .8, p<.01) respectively]. Both L and R P3 amplitude in coherent 10% was positively correlated with the amplitude of the P3 (L & R) in Go condition (smallest $r$ = .6, p<05), whereas the latency of the P3 (L & R) in Coherent 10% was positively correlated with the Error rate in Go condition ($r$ = .7, p<.01) and the latency of P5 in PW condition ($r$= .6, p<.05).

*CPT task.* The amplitude of P1 Go (L & R) was positively correlated with the amplitude of the P1 and P4 PW (both L & R for P4), (smallest $r$ = .5, p<.05), whereas the latency of the P1 (L & R) was positively correlated with the Error PW ($r$ = .7, p<.01). The amplitude of the NoGo P1 (L & R) was also positively correlated with the amplitude of the R P1 and P4 PW ($r$ = .6, p<.05), whereas the latency of the R NoGo P1 (similarly to the Go P1) was positively correlated with

the Error PW ($r$ = .5, p<.05). The amplitude of the P3 (L & R) Go was positively correlated with the amplitude of the P4 (L & R) and R P5 in PW (smallest $r$ = .6, p<.05), but it was negatively correlated with the Error PW ($r$ = -.5, p<.05). The correlation coefficients of the Go and NoGo ERPs with CA-SA are reported above. The amplitude of the (L & R) NoGo P3 correlated positively with the amplitude of the late PW (L & R) peaks P4 and P5 (smallest $r$ = .7, p<.01).

*Lexical decision task.* Except the correlations for the conditions of this task with components in other studies already reported above, there were significant correlations within this task found for the latency of the L P1 PW with the RT PW ($r$ = .8, p<.01), the amplitude of the R P4 PW with the Error PW ($r$ = -.6, p<.01). The amplitude of P5 PW (L & R) was negatively correlated with the RT PW ($r$ = -.6, p<.05), and the latency of L P5 PW was positively correlated with the Error PW ($r$ = .7, p<.01).

## 5.2. Factor Analysis

An exploratory Principal Components analysis was also undertaken, using 13 variables I considered to provide a good spread across the different experiments, with a view to seeing whether dyslexia (as indexed by CA-SA) was associated with a particular set of dimensions, or whether it spread across several factors. The results are by no means robust, in that there are too few participants per variable, but nonetheless they may prove of interest. The analysis was performed using StatView (SAS Institute, 1998) and the results are displayed in Table 5.2. The behavioural and ERP data of the same 14 participants as in the correlational analysis reported in the previous section were used. As can be seen on the Scree plot (the table for eigenvalues) that shows the relative importance of the factors, the Value 1 contributes to 31% of the variance in the data. In the second table (Unrotated factors) it can be seen that this factor has a weighting of .857 for the CA-SA which is the highest value in the table. These results support the findings of the previous correlational analysis as they show similar negative correlation with the amplitude of the ERPs, both early and late, and mostly positive correlation with the behavioural performance and latency of the ERPs. Thus, these results also suggest that larger CA-SA discrepancy, i.e. worse spelling ability, is associated

with attenuated ERP amplitude, delayed ERP latency and mostly worse behavioural performance, including lower sensitivity of coherent motion perception and longer Go and PW RTs.

**Table 5.2. The results of the Factor Analysis**

**Eigenvalues**

| | Magnitude | Variance Prop. |
|---|---|---|
| Value 1 | 4.029 | .310 |
| Value 2 | 1.828 | .141 |
| Value 3 | 1.744 | .134 |
| Value 4 | 1.659 | .128 |
| Value 5 | 1.324 | .102 |
| Value 6 | .986 | .076 |

**Unrotated Factors**

| | Factor 1 | Factor 2 | Factor 3 | Factor 4 | Factor 5 |
|---|---|---|---|---|---|
| RTCoh10 | -.356 | .253 | -.307 | .684 | .261 |
| P1ampCoh10 | -.714 | .279 | .440 | .192 | -.139 |
| P1LatCoh10 | .090 | .582 | .186 | .483 | -.555 |
| CA-SA | .857 | -.172 | .031 | .340 | .172 |
| P3LatCoh10 | .364 | .215 | -.632 | .369 | .207 |
| P1AmpGo | .288 | .547 | .341 | .103 | .634 |
| P1LatGo | .596 | -.277 | .546 | -.032 | .389 |
| P3AmplGo | -.617 | .178 | -.262 | -.517 | .169 |
| RTGo | .038 | -.434 | .396 | .132 | -.119 |
| P1LatPW | .645 | .455 | .318 | -.177 | -.375 |
| P4AmpPW | -.576 | .512 | .269 | -.285 | .309 |
| RTPW | .735 | .361 | .041 | -.268 | .040 |
| DprimeCoh10 | -.637 | -.278 | .453 | .435 | .149 |

## 5.3. Individual Effect Sizes for the magnocellular participant in three studies

I have also decided to calculate the individual effect sizes (IES) for the magnocellular participant based on Glass's delta (1981) and similarly to the procedure used in previous studies (e.g., Fawcett and Nicolson, 1999; Ramus et al., 2003b; Brookes et al., 2007). This is sometimes referred to as z-scores. Since this participant had markedly lower sensitivity of performance in the coherent 10% condition that was reflected in his delayed N1 and P2 latency, it was interesting to see how this participant performed in other tasks compared to controls. An identical procedure to the Glass's delta calculation is used to calculate IES but in this case

the individual participant's data is used in the equation to compare with the controls' group mean. Thus I followed the previous procedures and calculated his IES on all measures used in the correlational analysis reported above based on the following equation: IES = [Value (magnocellular dyslexic) – Mean(Control group)]/ SD(Control group). If an individual has an IES of –3 on a test, this is well outside normal variation (3 standard deviations) and could be an indicator of an impaired performance. In previous studies different cut-off criterion (such as 2 SD or 1 SD) were used. According to Fawcett and Nicolson (1999), if the IES of the individual is larger than ±1 compared to the control group he may be considered 'at risk' in his performance. I have selected the IES values from ±1.96 to be shown in Fig. 5.1 for the 'magnocellular dyslexic' because (under normal distribution) the probability of being 1.96 SDs below the mean is < .01. The sign of the effect size for the amplitude of the P5 PW ERP component shown in the Fig. 5.1 was reverted so that the positive effect size shows decreased amplitude for this participant when compared to the rest of the group. As can be seen in the Fig 5.1, the largest effect size for this participant was for the Error rare in PW condition (12.4) then for the CA-SA (5.3), and for different ERP components' latencies and amplitude shown in a decreasing order in this figure. Overall, the latency of the early and late ERP components was delayed for this participant compared to the controls' average data. It can also be seen, that his Error rate in the Go condition also had a large effect size. The amplitude of the late ERP component R P5 in the PW condition was smaller than control's average by more than 2SD.

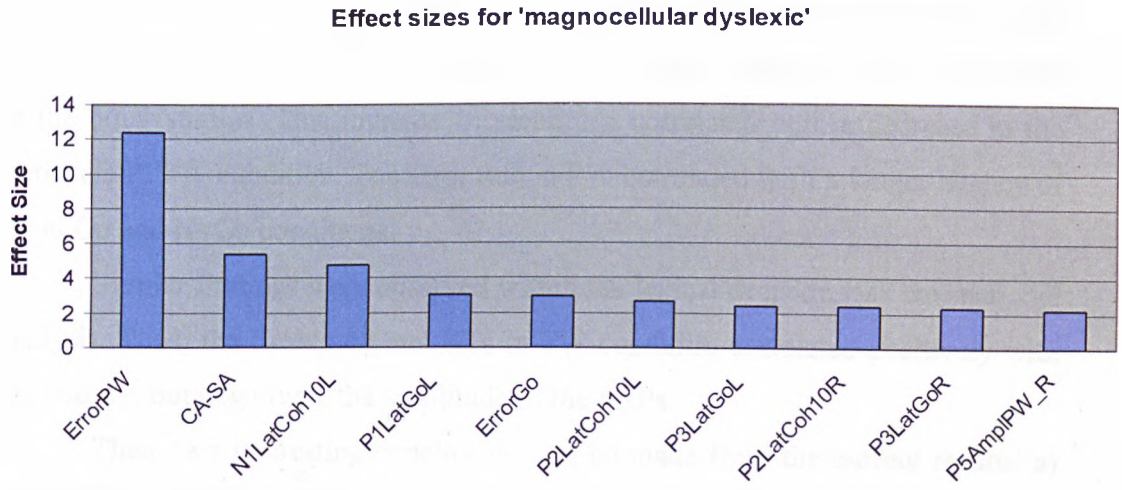


**Figure 5.1. Individual effect sizes for the magnocellular dyslexic participant**

## 5.4. Summary and discussion of the results

The results of the brain-behaviour analysis revealed some interesting correlations. First of all, the increase in CA-SA, i.e., in spelling discrepancy, correlated with a decrease in the amplitude of the early P1 (coherent motion 10%) and the late peaks P3 Go and NoGo and P4 and P5 PW. The increase in CA-SA correlated with an increase in the latency of P1 and P3 (Go) and the error rate PW. In other words, the worse was the spelling ability, the smaller was the amplitude of activation, the longer was the processing speed (both early and later stages) and the larger was the number of errors across different studies. These findings were nicely supported by the factor analysis reported in section 5.2, i.e., the poorer literacy ability associated with attenuated amplitude and delayed latency of ERPs, as well as with lower sensitivity in coherent motion study and longer RTs in the CPT and lexical decision tasks.

Another new and interesting finding from the correlational analysis was that the better sensitivity of performance in the coherent 10% condition correlated with less errors in Go condition and with the larger amplitude and delayed latency of the late ERP peak P5 in PW condition, whereas the delayed latency of coherent motion 10% P3 correlated with larger number of errors in the Go condition. These results show that the better performance in one study correlates with a large amplitude and shorter latency of the ERP potentials and less errors in the other studies.

Additional results of the comparisons of the CPT task with other studies also showed that an increase in the amplitude of ERP components in this study correlated with an increase in the amplitude of the early and later ERP components in the other studies. This increase in amplitude correlated with a decrease in the error rate in PW condition. The error rate in PW correlated with a longer latency of P1 in Go and NoGo conditions.

Similar findings were observed within the lexical decision task correlational analysis. Thus, the Error rate and RTs in PW condition correlated positively with the latency, but negatively the amplitude of the ERPs.

Thus, two interesting conclusions can be made from the current results: a) speed and amplitude of both early and late ERP components, e.g., faster and larger brain activation indexed by larger amplitude and a shorter latency of the ERPs, was

consistently associated across tasks; b) and more importantly for the current research, poorer literacy abilities, lower sensitivity of coherent motion perception, slower RTs and more errors across different studies generally correlated with attenuated amplitude and delayed latency of the ERP components. Thus, both hypotheses stated at the beginning of this section were confirmed. However, it should be mentioned, that these brain/behaviour correlations are found in a small group of 7 dyslexic and 7 control participants who took part in the current research, and these conclusions cannot be extended or generalised beyond the current work.

The individual effect size analysis for the 'magnocellular dyslexic' showed that he had markedly larger error rate in PW and Go conditions, worse spelling ability accompanied with considerably delayed latency of the ERP components across different studies when compared with the controls group average.

# 6. CONCLUDING DISCUSSION

## 6.1. The aims of the project revisited

In the current project I aimed to test some of the main hypotheses of dyslexia with simultaneous behavioural and electrophysiological methods approach. My goal was to replicate recent psychophysical and neuroimaging studies that reported various perceptual and cognitive deficits among dyslexics. These deficits included visual sensory impairment, attention deficits and abnormalities in the phonological processing of words and pseudowords, as well as in the early visual word form recognition. I wished to investigate whether some of the above mentioned abnormalities in behavioural performance and/or deviation in brain activation would be present among British English speaking dyslexic adolescents as compared to their age and IQ matched controls. The important issue was whether such deviations would be revealed both in the performance and in brain activation that were planned to be recorded simultaneously. Furthermore, I expected that even if there were no differences in the dyslexics' behavioural performance from that of the controls, the subtle deviations in their brain activation would be revealed with the help of our high density ERP recording system. This project was designed to further our understanding of the brain-based mechanisms of dyslexia in parallel with and reflected in their reportedly deficient psychophysical performance and visual perception. This, in turn, could help to improve the early diagnostic methods in order to help for early intervention programs that would improve the quality of life and education and help with the difficulties that many dyslexic children face.

In order to achieve these aims, I recorded ERPs and behavioural performance of the participants in three different tasks. In the first study I decided to investigate whether the attention deficits reported among dyslexics may be a result of the overlap with ADHD. Therefore, I tested the attentional performance of dyslexic adolescents without ADHD symptoms during CPT task. In the second study I aimed to find out whether magnocellular deficits reported in a subset of dyslexics would be present in our set of participants and in what proportion, and

whether these would be correlated with deviations, if present, in their brain electrical activation. I used stimuli that were designed to test the magnocellular function. In the third and final study reported in this thesis, I aimed to study the neurophysiological and behavioural indices of word and pseudoword processing in dyslexia, particularly the early visual word form recognition stage.

## 6.2. Summary of findings

The results of the studies undertaken in this project showed interesting deviations in psychophysical performance and EPR correlates of the brain electrical activation of dyslexics. The main findings of between-group differences in all three studies are briefly summarised below.

### 6.2.1. CPT study

There were no significant differences in mean reaction time, error rate or sustained attention between the groups. By contrast, the P3 amplitude was significantly smaller and its latency significantly longer for the dyslexic group. This component was significantly lateralised in controls, whereas in dyslexics it was symmetrical.

### 6.2.2. Motion study

In terms of behavioural results, there were no significant between-group differences in sensitivity or the response latencies of correct responses. No between-group differences were found for early (P1, N1, and P2) and late (P3) ERP peaks. However, for one dyslexic participant the sensitivity of responses was marginally worse compared to others in the group. The individual participant analysis also showed that his early ERP components were markedly delayed compared to the group average data. The additional brain-behaviour correlational between-group analysis revealed that the increase in the amplitude of the P1 ERP component in the coherent 10% condition was negatively correlated with CA-SA values, i.e., poorer literacy scores correlated with attenuated P1 amplitude.

### 6.2.3. Lexical decision task

The behavioural performance in terms of accuracy and of latency was significantly worse for the dyslexic group. The ERP analysis indicated that the early ERP component, P1 (not significantly), and the later positive peaks, P4 and P5 (significantly), were delayed and attenuated for the dyslexic group compared to the controls. Analysis of the early ERPs recorded in occipitotemporal region led to an interesting dissociation. As expected, the controls showed a left lateralised Condition effect, with the amplitude of P1 significantly smaller to words than pseudowords (attributed in the literature to more focused processing of words in the visual word form area). By contrast, there was no such lexical effect for the dyslexic group, with equal P1 amplitudes for words and pseudowords, at the control level for pseudowords.

### 6.2.4. Brain-behavioural analysis

The cross-study correlational analysis revealed that the literacy problems were accompanied by a larger error rate together with attenuated and delayed brain activation in many conditions across the studies. These findings were supported by the results of an additional factor analysis described earlier. Additionally, the larger and faster ERP activation correlated across all studies both for the early and later ERP peaks. Further individual analysis for the 'magnocellular dyslexic' revealed that he made more errors in lexical decision and CPT tasks that were accompanied by delayed latency of the ERPs across al three studies.

## 6.3. Overall Discussion

The results of these studies suggest that the behavioural performance was not different in dyslexics from that of controls in the first two studies, when compared at a group level. The absence of significant between-group differences in the behavioural indices of CPT task suggests that the attentional performance is not affected in dyslexia. Under the relatively light workload conditions of the CPT, 'pure' dyslexic participants showed no behavioural signs of attentional difficulties. The attenuated, delayed and symmetrical ERPs in our dyslexic group may reflect deviant information processing in the right parietal lobe and abnormal interhemispheric asymmetry in dyslexia. The behavioural data of the first study suggest that abnormal attentional performance is not a 'core' feature of developmental dyslexia. The presence of electrophysiological markers of dyslexia in CPT reveals the atypical brain organisation that characterises dyslexia. In the second study that tested coherent motion perception among dyslexics no between-group differences in the behavioural performance were found either. The results of this study, however, suggested that a proportion of dyslexic adolescents do suffer from magnocellular problems, and that this is associated with abnormal early ERP components. In this sample the incidence of magnocellular impairment was low (11%). The results of the last study, the lexical decision task, showed interesting between-group differences. The deviations in the early ERPs of dyslexics support the evidence of deficits in pre-lexical visual word form recognition within the first 110 ms of activation together with altered hemispheric asymmetry. In addition, the slowed and attenuated late ERP components and weaker behavioural performance of the dyslexic group highlight deficits in the later, cognitive, processing stages.

Thus, it seems that attentional deficits are not a core feature of dyslexia, although the brain activation of dyslexics in the CPT task was attenuated, delayed and atypically symmetrical among dyslexics. This study does not provide conclusive evidence in favour of any of the three major theories of Dyslexia that were briefly described in the Introduction - the phonological, the magnocellular and the automatisation deficit hypotheses. However, the deviations in activation of P3 of dyslexics, i.e., its delayed latency and attenuated amplitude, reflect a delayed cognitive processing that may be related to automatisation deficits and cerebellar

deficits as well as the right parietal lobe abnormalities and atypically symmetrical brain function. The magnocellular deficits were found only in one participant from the dyslexic group. The delayed N1 and P2 (200-300 ms) ERP components and decreased sensitivity of his performance suggest impairment of coherent motion processing and magnocellular dysfunction in this participant. The results of this study can be interpreted in favour of magnocellular hypothesis with an emphasis that these deficits probably exist only in a small subgroup of dyslexic English speaking adolescents. However, as suggested earlier, the absence of between-group differences in our study may have also been caused by insufficient demands on the attention system that was recently suggested to cause magnocellular deficits via posterior parietal input. And finally, the deviations in the brain activation of dyslexics in visual word form processing that appear as early as 110 ms suggest that they do have abnormal word/pseudoword processing as compared to the controls. The brain activation at this early stage is related to pre-lexical and pre-conscious processing of the stimuli. However, this is a skill developed by experienced readers during the long process of learning to read and is based on good orthography-to-phonology mapping ability and recognition of the visual shape of a familiar word. Therefore, according to our results, it could be concluded that there are abnormalities in the occipito-temporal area or VWFA of dyslexics, and that these ERP deviations reflect deficiencies in dyslexics' early visual word form recognition skills as indexed by their longer RTs and a larger number of errors made in response to pseudowords than words compared to the controls' group. However, the P3 and P5 deviations in dyslexics' ERP recorded in parietal sites also show abnormalities at later cognitive stages of a performance, that may also be related to suggested automatisation deficits and deficient cerebellar performance. The delayed and attenuated later ERPs both in CPT and in lexical decision studies, together with a weaker behavioural performance in the latter, confirm that dyslexics may have problems at later cognitive stages of processing regardless the type of the cognitive task they are performing. These findings show once more that dyslexia is a multisymptomatic developmental disorder and is caused by subtle changes in various interconnected areas of the brain. Additionally, the results of the cross-study correlational and factor analyses revealed that generally larger and faster brain activation was related to a better performance and higher literacy scores among our participants, whereas the 'magnocellular dyslexic' participant identified

in the coherent motion study had markedly larger error rate and delayed ERPs in the CPT and the lexical decision task.

## 6.4. Limitations of the current research

Despite the careful planning and the utmost attention to detail when designing these tests there are some shortcoming that should be mentioned in relation to this work.

### 6.4.1. Participants' sample sizes

The dyslexia research group at Sheffield University has helped immensely for this project by providing a cohort of dyslexic and control participants that were involved in other studies but had no relation to the current project. These participants were children recruited from local schools. However, some of them would not fit the criteria used for the current work, e.g., some of them had ADHD overlapping symptoms or were much younger or older than the age range of participants used in this study. As a result the number of participants in each group were slightly less than I hoped for. It would have been also better to have an equal number of male and female participants, that could have been possible provided we had a larger number of participants overall.

### 6.4.2. ADHD and dyslexia/ADHD mixed samples absence

It was also my intention to test another group of participants that had only ADHD or ADHD/dyslexia mixed symptoms. This could have been especially interesting for a concurrent testing and comparison of results with 'pure' dyslexic participants in the performance of the CPT task. The comparison in brain electrical activation between 'purely' dyslexic and ADHD/dyslexic groups could be valuable in extending our existing knowledge of similarities and differences of the origins of these overlapping developmental disorders. Unfortunately, this was not possible as

we could not find the required number of participants with ADHD that could also satisfy the criteria of age and IQ match for the dyslexic and control groups that I tested.

### 6.4.3. Different age groups of participants

In relation to the same issue of the samples of participants, it should be mentioned, that I would be extremely interested to carry out these tests in different ages of dyslexic and control children with a purpose of closer observation of the onset and development of the deviations in the brain activation of dyslexics that were found for the age group tested in this study. This is also a potential direction for the future research.

### 6.4.4. EEG recording issues

In the age of rapidly developing technology and advances in electrophysiological recording methods it is difficult to keep up with many developing improvements while working on one project. We wished to keep the specifications of our EEG system, critical for the data recording, unchanged while collecting the data for the three studies of this project. This provided a possibility for comparison between different individual recordings and for the averaging of individual participant ERPs into group waveforms. We have used EGI recording and analysis hardware and software for our experiments. The equipment provided by different companies offer different methods for dealing with eye movements and other artefacts. The better versions of these artefact removal methods would help for better filtering and improved signal-to-noise ratios when extracting EEG and ERP signals. The problems with bridging, i.e., propagation of the signals across the surface of the head from one electrode to the other, as well as slightly increased contamination of the frontal recording channels (a consequence of closer location to eyes and face muscles), could be dealt with slightly (not dramatically) better with more recently developed analysis software.

### 6.4.5. Concurrent neuroimaging recordings

Electrophysiological methods are well known for their excellent temporal resolution. However, the spatial resolution of these techniques in identifying of the regions and areas activated during the task are less advanced compared to neuroimaging techniques, such as fMRI. The project could have benefited greatly if such concurrent ERP+fMRI recording of activation was possible to carry out. Particularly, this could be important for an fMRI confirmation of the ERP results in the occipito-temporal area found in the lexical decision task. An alternative and equally informative recording technique is magnetoencephalography (MEG), which is an electrical signal recording as well, but is based on measuring the associated magnetic fields emanating from the brain in this case. Unlike EEG, it has good spatial resolution and electrical source localisation capacity (e.g., Dale et al., 2000; Cornelissen et al., 2003) that could also be very useful had we had the opportunity to employ this method in our studies.

### 6.4.6. Timing in planning the recordings

And finally I would like to mention the issues of the time in recruiting the participants and in designing the studies, as well as bookings of the experimental room. If the above were possible to carefully control and were better planned, I would have carried out the recording of all three studies in the same time interval, e.g. during the spring of the second year of the PhD. This could allow for a statistical analysis, if this was considered purposeful, and comparison of the results from all three studies. However, the first study was carried out in the first year of the PhD, and the second and the third studies were conducted in the second year of the PhD.

## 6.5. Future work

The potential future directions of this research are partly a consequence of the limitations and the concerns regarding the current project mentioned above. Thus:

1) It would be extremely interesting to carry out a comparative, between-developmental-disorder study on all three tests that were used in the current study. Dyslexia is currently considered to have somewhat common biological origins with ADHD, SLI and autism. The availability of high density ERP recording system and the tests already used in the current project could be very useful for future neurophysiological and behavioural studies and comparison across different learning disorders.
2) As mentioned earlier the tests designed during this project have a potential diagnostic role, and it would be valuable to conduct a longitudinal study and involve different age groups of dyslexic and non-dyslexic participants in order to find out the onset of the deviations that appear in brain activation of dyslexic children. For example, it would be extremely useful to find out the age of the onset in abnormalities of visual word form recognition. The differences, e.g., atypically symmetrical P1 component of ERPs, in brain activation to words and pseudowords that were found in English speaking dyslexic adolescents may have a different manifestation and age onset from those of non-English speaking children.
3) Similarly these EEG tests could be successfully used in different clinical and healthy populations, such as Alzheimer's and healthy ageing elderly populations for an early detection and intervention. As an inspiring example, these techniques are already used in a different research project here at Sheffield University that looks into the effect of omega-oils in the cognitive function of elderly individuals and could be used for an early detection of any dementia symptoms that are not recognisable at the behavioural level.
4) The potential future directions of research mentioned above and many other consecutive studies (since our road of discoveries about the human mind and behaviour is endless) would benefit greatly if the electrophysiological and neuroimaging techniques could be combined. The

current project benefited greatly by concurrent ERP and behavioural recordings, and it could benefit even further with high spatial resolution neuroimaging techniques used in combination with our high density and high temporal resolution electrophysiological methods.

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# 8. APPENDICES

## 8.1. Information sheet for participants

### EEG study of Reaction Times in Dyslexia

You are invited to take part in a study looking at changes in brain electrical activity during a reaction time test. Detailed instructions will be provided.

**What is the aim of the study?**

The aim of this study is to investigate whether there are interesting differences between dyslexic and non-dyslexic participants in the way their brains respond on seeing letters and looking for a sequence.

**What will the EEG show?**

EEG is a simple way of measuring the electrical activity of the brain. If it is recorded to a particular event, then averaging a number of trials will help to have a potential or a response related to appearance of that particular event. This is called the evoked potential (EP) technique. Another goal of study is to analyse the frequency components of EEG recording.

**What will the EEG recording involve?**

This technique involves placing on the head a 'net' of small non-intrusive pads. The current Net in use in this Department is a 128-channel cap of little plastic tubes with sponges that are placed on your head by the experimenter. The Net will be soaked in advance in a special solution that contains distilled water, a bit of lo salt and Johnson's baby shampoo in order to improve the conductivity of brain signals. It is a reasonably comfortable procedure – it doesn't hurt at all! Your hair will get slightly wet while applying the Net, so it's worth bringing a comb along for afterwards. The technique is in common use

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world-wide, even with babies. The experimenter will monitor the progress of the task in the adjacent room. You will always be able to communicate to the experimenter if you need to.

**What will I have to do during EEG recording?**

During recording, different letters will be presented in the centre of a computer screen in between two vertical lines. You will be asked to fixate these lines and attend to the letters appearing within these fixation lines. You will be also asked to refrain from blinks and head and body movements (especially when the stimulus is on) as much as possible to prevent interference of the noise with signal. You will be given full instructions before the start of the recording and have a trial run to familiarise you with the task.

**How long will the EEG sessions last?**

The task and recording itself will last about 15 min. The whole experiment including the appliance of the Net and practice session will last about 1 hour.

**Is the EEG safe?**

This type of recording is considered completely safe. It does not involve exposure to radiation; neither does it involve any injections. The sponges attached to the scalp only record the ongoing activity of the brain. You will be in a normally illuminated room and able to speak to us throughout. The study can be stopped at any time if you wish. Fully trained staff will be present. The type of EEG to be employed is in routine use in the Department of Psychology, Sheffield University.

**Will I be rewarded for taking part?**

We will pay you £5 an hour.

**What if I change my mind during the study?**

Your participation in the research is entirely voluntary. You have the right to withdraw from the study at any point, without having to give a reason and without your future study being affected in any way.

**What will happen to the information from the study?**

The EEG recorded data and information for all the participants will be analysed to see whether there are any interesting differences between groups of dyslexic and non-dyslexic participants. The results, I hope, will be published in the dyslexia research literature in order to be of maximum use worldwide. Any results about you personally will be held in the strictest confidence and not disclosed to anyone outside the project. The results will be described completely anonymously as far as participants are concerned.

**What if I have further questions?**

Please do not hesitate to contact Dr. Angela Fawcett or Naira Taroyan at:

Psychology Department

Western Bank, University of Sheffield,

Sheffield, S10 2TP

Tel (Naira Taroyan): (0114) 222 6553 or email: N.A.Taroyan@sheffield.ac.uk.

**Additional information:**

The study has been approved by Research Ethics Committee of Sheffield University Psychology Department. It would take place in the EEG lab of Psychology department at a time convenient for participants.

Naira Taroyan (Researcher)

Dyslexia Research Group

Department of Psychology

University of Sheffield

## 8.2. Research consent form

### EEG study of different types of performance in Dyslexia

**PLEASE DELETE AS NECESSARY**

Have you understood the participant information sheet? YES/NO

Have you had an opportunity to ask questions and discuss this study? YES/NO

Have you received satisfactory answers to all your questions? YES/NO

Have you received enough information about the study? YES/NO

To whom have you spoken? .....

Do you understand that you do not need to take part in the study and if you do enter you are free to withdraw -

- at any time

- without having to give a reason for withdrawing YES/NO

Do you agree to take part in this study?

YES/NO

Signed: ..... Date:

.....

.....

(NAME IN BLOCK LETTERS)

Contact phone number: .....

(As you already have parental consent to participate in the dyslexia projects, we don't need it again).

## 8.3. Instructions for the CPT study

Welcome to the Experiment

You will see a sequence of letters.

Please press first button (from left) only when you see letter 'X' preceded by letter 'O'.

Please try to refrain form blinks and other bodily movements during the recording.

Do nothing otherwise

Press any key when you are ready to start

## 8.4. Instructions for the coherent motion study

Welcome to the Experiment

You will see various combinations of small dots moving on the screen. In some cases they will move upwards, from the bottom to the top of the screen. In other cases, they will move randomly in different directions. Your task is to press the first button on your left with the index finger of the right hand, when you see dots moving upwards. When you see the dots moving randomly in different directions (like TV noise), please press the second button on your left with the middle finger of your right hand.

Please try to avoid eye blinks during stimulus display as much as possible

Press any key when you are ready to start

## 8.5. Instructions for the lexical decision task

Welcome to the Experiment

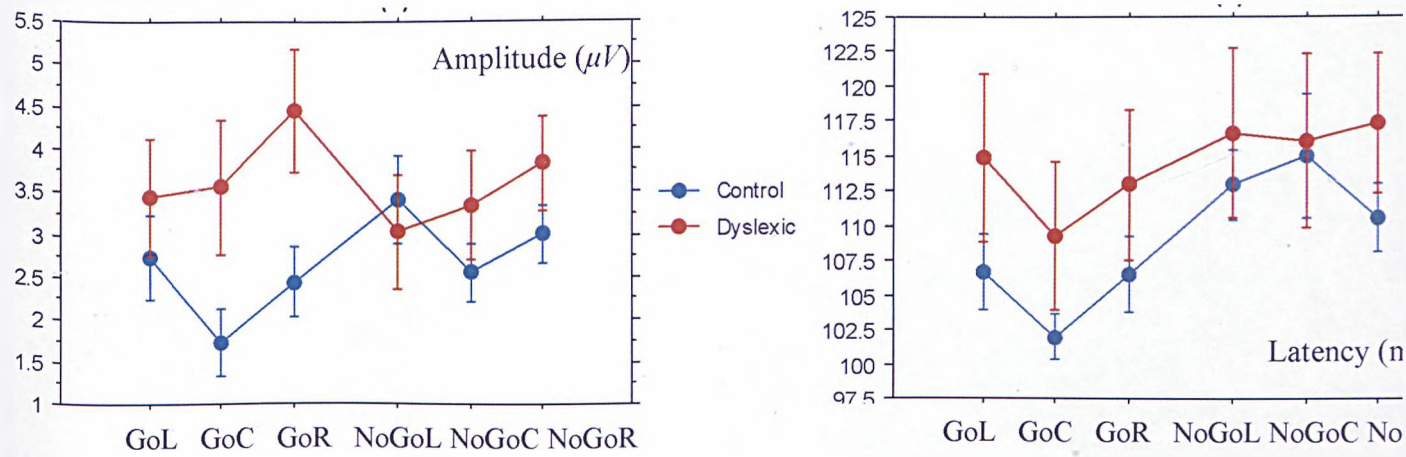
You will see a sequence of letter combinations. Some of them will be real words, others will be nonsense words, i.e., without any meaning. Your task is to press the first button on your left with the index finger of your right hand when you see a real word. When you see a nonsense word, please press the second button on your left with the middle finger of your right hand.

Please try to avoid eye blinks during stimulus display as much as possible

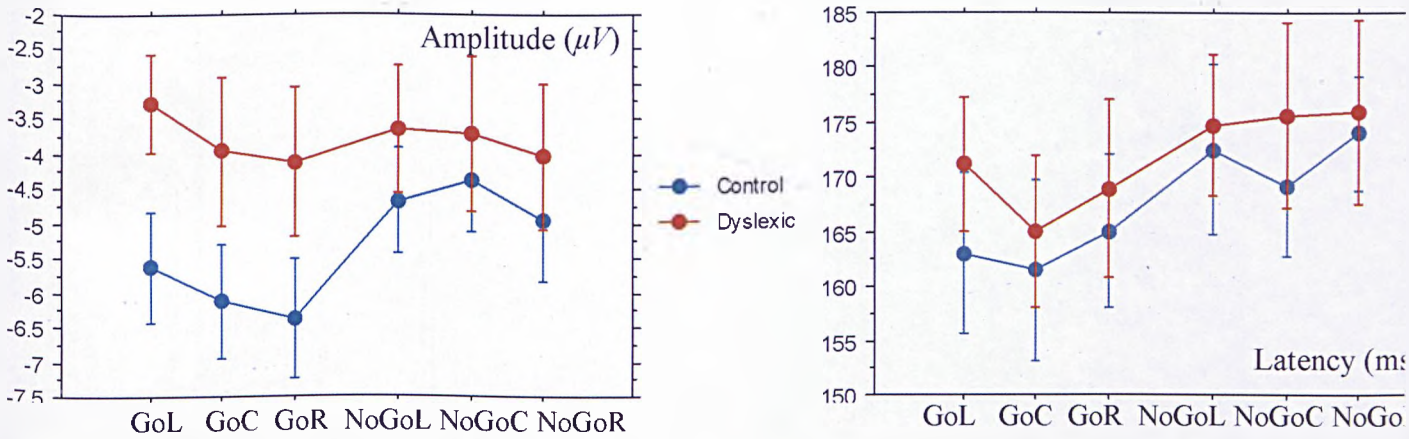
Press any key when you are ready to start

## 8.6. Graphs for the Tables 2.2 & 2.3

**P1 amplitude and latency** (with standard error bars) in CPT task in Go and NoGo conditions and left, central and right (L, C, R) areas of occipital cortex




**N1 amplitude and latency**




P3 amplitude and latency