A MAGNETOENCEPHALOGRAPHIC STUDY OF LOW-LEVEL AUDITORY PROCESSING IN DEVELOPMENTAL DYSLEXIA

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The possibility that developmental dyslexia results from low-level sensory processing deficits has received renewed interest in recent years. Opponents of such sensory-based explanations argue that dyslexia arises primarily from phonological impairments. However, many behavioural correlates of dyslexia cannot be explained sufficiently by cognitive-level accounts and there is anatomical, psychometric and physiological evidence of sensory deficits in the dyslexic population.

This thesis aims to determine whether the low-level (pre-attentive) processing of simple auditory stimuli is disrupted in compensated adult dyslexics. Using psychometric and neurophysiological measures, the nature of auditory processing abnormalities is investigated. Group comparisons are supported by analysis of individual data in order to address the issue of heterogeneity in dyslexia.

The participant pool consisted of seven compensated dyslexic adults and seven age and IQ matched controls. The dyslexic group were impaired, relative to the control group, on measures of literacy, phonological awareness, working memory and processing speed. Magnetoencephalographic recordings were conducted during processing of simple, non-speech, auditory stimuli.

Results confirm that low-level auditory processing deficits are present in compensated dyslexic adults. The amplitude of N1m responses to tone pair stimuli were reduced in the dyslexic group. However, there was no evidence that manipulating either the silent interval or the frequency separation between tones had a greater detrimental effect on dyslexic participants specifically. Abnormal MMNm responses were recorded in response to frequency deviant stimuli in the dyslexic group. In addition, complete stimulus omissions, which evoked MMNm responses in all control participants, failed to elicit significant MMNm responses in all but one of the dyslexic individuals.

The data indicate both a deficit of frequency resolution at a local level of auditory processing and a higher-level deficit relating to the grouping of auditory stimuli, relevant for auditory scene analysis. Implications and directions for future research are outlined.

KEYWORDS: N1m, MMNm, Individual Differences, Auditory Grouping, Auditory Scene Analysis

For Isabella Duncan Hogg and Thomas Maurice Fisher

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1 AIMS

1.1 General Aims

This thesis investigates auditory processing in developmental dyslexia. Its principal aim is to determine whether low-level processing of simple auditory stimuli is abnormal in compensated dyslexic adults. Furthermore, the nature of any such deficits is investigated using psychometric and physiological measures. Where differences between the dyslexic and control groups are revealed, the data of individual participants are examined in an attempt to address the question of variability within the dyslexic population. Finally, the data are considered in terms of previous findings and postulated mechanisms.

1.2 Specific Aims

The tone pair study, presented in Chapter 5 examines differences between control and dyslexic participants on a frequency discrimination task, in terms of both behavioural performance and physiological responses to stimuli. By varying the silent interval and frequency separation between tones, the relative contribution of each manipulation can be considered.

In Chapter 6 the MMNm in response to frequency deviant stimuli is measured. Differences between the dyslexic and control participant groups in terms of the latency and amplitude of MMNm in response to stimuli that differ in frequency by either a large or small degree are examined.

Data presented in Chapter 7 explore the sensory integration of brief and rapidly presented stimuli in dyslexic and control groups. As complete stimulus omissions only evoke MMNm responses if successive stimuli are integrated as unitary percepts, this paradigm provides an estimate of the time window within which successive stimuli are integrated in Sensory Memory. Stimuli are presented at rates that span the postulated duration of this integration mechanism and the presence or absence of MMNm is evaluated statistically for each participant. Furthermore, the amplitude of responses to omissions is compared between dyslexic and control groups in each condition.

2 INTRODUCTION TO DYSLEXIA

2.1 Developmental Dyslexia

2.1.1 Introduction

Developmental dyslexia is a specific learning difficulty that disrupts the normal acquisition of literacy skills. It is a developmental as opposed to an acquired disorder, in that it occurs spontaneously through development and does not originate as the consequence of insult or injury to the brain. The observed difficulties acquiring literacy skills are unusual in that they occur in otherwise able children who perform well on other cognitive tasks. Prevalence within the school-aged population is estimated at around 8% (Shaywitz, Shaywitz, Fletcher, & Escobar, 1990).

The term 'dyslexic' is often substituted in the literature for 'reading disabled', 'reading impaired', 'reading disordered' and so on. The reason for the focus on reading is that reading problems are the most obvious, and in many cases the first, behavioural manifestation of dyslexia. Children with dyslexic problems often have associated deficits in related domains, for example specific language impairment, developmental dyspraxia, dysgraphia, dyscalculia and attention deficit disorder.

2.1.2 Definition

There is considerable debate surrounding an acceptable definition of dyslexia. According to the medical model forwarded by The World Federation of Neurology, dyslexia is:

> '...a disorder manifested by difficulty in learning to read despite conventional instruction, adequate intelligence, and sociocultural opportunity' (Critchley, 1970, cited in Snowling, 2000)

However, the principal weakness of such a definition is that it defines only exclusionary criteria and fails to identify positive signs for diagnosis.

In practise it is important to discriminate between dyslexic individuals (i.e. those with difficulties specific to literacy skills) and generally backward readers (those

who read at the level expected for their intelligence). Thus, regression analyses relating IQ to literacy ability are employed and indeed dyslexia is often 'diagnosed' as a discrepancy between actual reading and spelling attainments and those predicted based by age or intelligence (e.g. Turner, 1997).

However, Snowling (2000) argues that such a practise can lead to a number of false positive and negative diagnoses as the discrepancy measure is very sensitive to environmental factors (e.g. the teaching a child has received and the use of compensatory strategies). Furthermore, the use of discrepancy based definitions fails, like the early medical model, to highlight inclusionary criterion. Frith (1999) goes further, pointing out that the absence of reading difficulties can be compatible with dyslexia (due to adequate remedial teaching), while the presence of reading difficulties may have nothing to do with dyslexia (e.g., due to a lack of teaching). In addition, while the behavioural signs of dyslexia are likely to change over time, as the result of compensation and learning, the underlying deficit will still exist. Thus, Frith argues that behavioural criteria alone cannot adequately define dyslexia.

2.1.3 Developmental Model of Normal and Failed Reading Processes

Frith (1985) has suggested that the development of reading skills can be divided into three stages. During the first stage (logographic), children use visual strategies to recognise a limited set of familiar words. Unfamiliar words cannot be decoded using phonological rules, and are often confused with similar words when fulfilling certain criteria (e.g. same length and certain letters are in certain positions). Alphabetic skills, the second stage, refers to the knowledge and use of individual phonemes and graphemes and their correspondences. At this stage, readers are able to pronounce novel and nonsense words. Finally, children progress to the orthographic stage. This refers to the instant analysis of words into orthographic units without phonological conversion. Rather, units ideally coincide with morphemes, internally represented as abstract letter-by-letter strings in the long-term lexical store. These units can be used to create an almost limitless number of words, by recombination. In psychological models of reading skills, the alphabetic and orthographic phases are represented as phonological and

lexical (whole word) reading routes, respectively (Coltheart, Curtis, Atkins, & Haller, 1993).

Frith (1985) proposes that dyslexia is characterised by arrest at stage one of the model in the normal developmental sequence. This is characterised by poor development of non-word reading skills. However, reading vocabulary does continue to grow due to functioning logographic skills, i.e. dyslexic individuals build up a large sight vocabulary, differentiating dyslexic children from younger readers at the logographic phase. While dyslexic children do eventually develop onto the alphabetic phase, they continue to make more errors in non-word reading tasks (Snowling, Stackhouse, & Rack, 1986b). Furthermore, dyslexic individuals tend to demonstrate an abnormally high number of visual reading and spelling errors. Thus, the breakdown in the normal reading process occurs as a result of an impaired ability to apply grapheme-phoneme correspondence rules.

2.2 Nature of the Deficit

2.2.1 Theoretical Framework

Frith (2001) has proposed a three level framework for considering developmental disorders. The argument for such a multi-stage model is that there will be causal links between brain and behaviour, which must be understood in order to conceptualise such disorders. Thus, it is important to seek explanations at all levels in the causal chain: the biological, the cognitive and the behavioural. Furthermore, it is important to consider how environmental factors interact at any or all of these levels.

2.2.2 Behavioural Characteristics

At the lowest level of the model are the behavioural manifestations of dyslexia, that is the common characteristics. Snowling et al. (1986b) have pointed out that it is important to be aware that the pattern of behavioural symptoms will vary according to the age of the individual, their ability and motivation and also the writing system in which they are learning.

Literacy deficits are central to the definition of dyslexia and can be considered as the principal manifestation of the disorder. However, there is abundant evidence

that the difficulties of dyslexic individuals extend beyond the domain of written language. A number of associated behavioural impairments, and also some unexpected behavioural correlates, are observed within the dyslexic population. The presence of specific behavioural correlates is the main drive behind the majority of causal theories and shall be outlined in section 2.3.

2.2.3 Cognitive Deficits

The second level of the conceptual model is related to the underlying cognitive deficits. Frith (2001) argues that it is the cognitive dysfunctions that can unite the varied symptoms of dyslexia.

Poor phonological ability is now accepted as the core deficit in dyslexia, as in the majority of cases dyslexic individuals appear to demonstrate difficulties when required to employ grapheme-phoneme conversion rules. Phonological ability is directly tapped by non-word reading tasks, as it is not possible to employ visual/ whole-word reading strategies, due to the unfamiliar nature of the words. Therefore, non-word reading tasks are commonly used for diagnostic purposes and the majority of studies report non-word reading deficits in the dyslexic individuals (for a review see Rack, Snowling, & Olson, 1992).

2.2.4 Biological Basis

The final stage of the conceptual model, and the ultimate aim of this approach to studying causality, is identification of the biological basis of the disorder. That is, how do genetic and brain based abnormalities lead to subtle impairments at the cognitive and behavioural levels?

Early evidence for a genetic involvement in dyslexia came from observations that susceptibility to reading disability may be heritable. The likelihood of a dyslexic child having an affected parent is 30-40% (Vogler, DeFries, & Decker, 1985). However, as the effects of a similar environment cannot be controlled for, a stronger case for heritability is made by studies comparing concordance rates in monozygotic (MZ) and dizygotic (DZ) twins. Results of such studies have reported a concordance rate of 68% in MZ twins, as compared to 38% in DZ twins (DeFries & Alarcon, 1996). Furthermore, a technique examining the extent

to which the co-twins of reading disabled probands regress toward the mean of a normal population has suggested a heritability of around 50% for reading disability (DeFries, Gillis, & Wadsworth, 1993).

Regarding the specific locus of the genetic abnormality, dyslexia has repeatedly been linked with chromosomes 15 (Grigorenko et al., 1997; Smith, Kimberling, Pennington, & Lubs, 1983) and 6 (Cardon et al., 1994; Cardon et al., 1995; Fisher et al., 1999; Gayan et al., 1999; Grigorenko et al., 1997). In addition, groups have made links between specific genetic loci and different aspects of reading difficulty (e.g. Grigorenko et al., 1997; Fisher et al., 2002). For comprehensive and up to date reviews of genetic studies in the field of dyslexia, see Fisher & DeFries (2002) or Grigorenko (2001).

A number of anatomical studies have also identified subtle anomalies in the brains of dyslexic individuals. These include developmental disorganisation of cell assemblies (ectopias) and abnormal placement of cells (dysplasias), particularly in the left inferior frontal and superior temporal gyri (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985; Humphreys, Kaufmann, & Galaburda, 1990).

Anatomical studies examining patterns of symmetry in dyslexic brains have reported abnormalities. Leftward asymmetry of specific cortical regions identified in the seminal works of Geschwind and Levitsky (1968) has been cited as the basis for the lateralisation of language in the left hemisphere. Atypical symmetry of the planum temporale has been reported (Galaburda, Sherman, Rosen, Aboitiz and Geschwind, 1985; Humphreys, Kaufmann and Galaburda, 1990; Larsen, Hoien, Lundberg and Odegaard, 1990; Hynd, Semrud-Clikeman, Lorys, Novey and Eliopulos, 1990) although these findings have been challenged with studies employing more up to date imaging techniques (Schultz, Cho, Staib Kier, Fletcher, Shaywitz, Shankweiler, Karz, Gore, Duncan and Shaywitz, 1994; Rumsey, Donohue, Brady, Nace, Giedd and Andreason, 1997) (for a review of studies in this area see Morgan & Hynd, 1998).

Posterior portions of the corpus callosum have been found to be exceptionally large in dyslexic participants, although negative findings have again been reported

(Robichon and Habib, 1998; Rumsey, Casanova, Mannheim, Patronas, DeVaughn, Hamburger and Aquino, 1996; Filipek, 1995; Rumsey et al., 1996).

Functional imaging studies have also provided evidence of neurophysiological abnormalities in dyslexic participants during a variety of reading related and sensory processing tasks (for reviews see Eden & Zeffiro, 1998; Pugh et al., 2000a; Temple, 2002). For example, PET studies have identified reduced glucose metabolism in right frontal regions in dyslexics during word reading (Gross-Glen, Duara, Barker, Lowenstein, Chang et al., 1991); a failure to activate left parietal and left middle temporal regions during a word reading task (Rumsey, Andreason, Zamtkin, Aquino, King et al., 1992); and evidence of disconnection between anterior and posterior language regions (Paulesu et al., 1991).

Functional MRI work has suggested visual processing deficits (Eden et al., 1996; Demb et al., 1998) and abnormalities in posterior cortical regions including the posterior superior temporal gyrus (Wernicke's area), the inferior angular gyrus and the striate cortex as the phonological demands in a discrimination task increased (Shaywitz, Shaywitz, Pugh, Fulbright, Constable et al., 1998). A Magnetic Resonance Spectroscopy study identified biochemical differences between dyslexic men and controls in the left temporoparietal lobe (Rae, Lee, Dixon, Blamire, Thompson et al., 1998).

It is worth noting that a number of these imaging studies point to lateralised abnormality of left hemisphere regions, in line with much of the anatomical data. Likewise, EEG studies have reported increased left temporal and parietal activity in alpha and theta wavebands (Duffy, Denckla, Bartels & Sandini, 1980); increased alpha activity in the left hemisphere with corresponding reductions of beta in left parieto-occipital regions (Ackerman, Dykman, Oglesby & Newton, 1995); increased frontal theta, reduced desynchronisation in beta and absent asymmetry of beta during a phonological task (Rippon and Brunswick, 1998); and reduced evidence of a left hemispheric processing advantage on a non-word task (Klimesch, Doppelmayr, Wimmer, Schwaiger, Rohm et al., 2001).

2.3 Prominent Causal Theories

An exhaustive list of causal theories of dyslexia cannot be provided in the present review. In this section, four major theories are outlined. These theories are highlighted as many of the issues raised are pertinent to the current studies.

2.3.1 The Phonological Representations Hypothesis

The Phonological Representations Hypothesis has provided the most commonly accepted account of dyslexic impairments over the past few decades, due to the fact that strong evidence has accumulated suggesting that phonological problems form the core mechanism of dyslexic difficulties (Bradley & Bryant, 1983; Snowling, 1987; Vellutino, 1987). It proposes that the key deficit in dyslexia is linguistic in nature, resulting from poorly specified abstract phonological representations (i.e. the way the brain represents the spoken attributes of words). The deficit impairs reading as a result of poor grapheme-phoneme decoding ability. Furthermore, it predicts a number of behavioural problems, not all specifically related to literacy. These include naming difficulties, verbal short-term memory deficits and poor phonological awareness.

Naming deficits are now well documented in dyslexia and have been taken as an indication that dyslexic individuals' phonological representations are poorly specified or inaccessible (e.g. Mann, 1986; Nation, Marshall, & Snowling, 2001; Swan & Goswami, 1997b). Furthermore, while the dyslexic readers are impaired in their ability to name items, they are able to define many of the same words, suggesting appropriate access to semantic representations (Swan & Goswami, 1997b).

Rapid automatized naming (RAN) tasks involve naming familiar objects (e.g. pictures, colours, digits) under timed conditions. Studies employing RAN tasks have found that dyslexic individuals take longer to name such items (Cornwall, 1992; Denckla & Rudel, 1976; Korhonen, 1995; Wolf, 1986; Wolf, Michel, & Ovrut, 1990). Rapid naming deficits are also reported in dyslexic adults (Felton, Naylor, & Wood, 1990; Kinsbourne, Rufo, Gamzu, Palmer, & Berliner, 1991; Korhonen, 1995; Pennington, Van Orden, Smith, Green, & Haith, 1990). While RAN impairments can be taken as evidence of a problem at the level of the

underlying phonological representations (Snowling, 2000), an alternative account views such deficits as the consequence of impairment in a timing mechanism, largely independent of phonological processing (Wolf & Bowers, 1999; Wolf & Obregon, 1992). Wolf and Bowers propose that in the same way as dyslexic individuals are slow to name highly familiar symbols, they will also be slow to automate reading processes, affecting the fluency of their reading. Thus, these authors propose that dyslexic children suffer from a 'double deficit' affecting both naming speed and phonological skills.

Verbal short-term memory processes involve the encoding of verbal items as phonetic memory codes and the rehearsal of such codes to keep them in mind for short periods of time, enabling further processing. During reading acquisition it is essential that the converted phonemes be kept in short term memory long enough to successfully blend isolated phonemes together to form a word. Dyslexic children have been shown to perform more poorly in a number of tasks of short-term memory (Korhonen, 1995; Mann & Liberman, 1984; Siegel & Ryan, 1989; Snowling, Goulandris, Bowlby, & Howell, 1986a). Indeed, poor performance on short-term memory tasks characterises adults with dyslexia (Pennington et al., 1990).

Phonological awareness refers to the metalinguistic understanding that spoken words can be decomposed into phonological primitives, which in turn can be represented by alphabetic characters. It can be assessed in a variety of ways; for example, detecting the number of phonemes in a word, reversing the order of phonemes, substituting phonemes within words, and putting together phonemes to form a word. The acquisition of phonemic awareness is critical if children are to abstract how written words relate to spoken words and progress to the alphabetic stage of literacy skills. Typically, phonological awareness develops in children just before the onset of reading skills and is an important predictor of literacy skills in the first few school years (Bradley & Bryant, 1983; Lundberg, Olofsson, & Wall, 1980). A number of studies have reported a difference on tasks assessing phonemic awareness between dyslexic and control children (e.g. Fletcher et al., 1994; Shankweiler et al., 1995; Stanovich & Seigal, 1994; Swan & Goswami, 1997a) and adults (Felton et al., 1990; Pennington et al., 1990; Shaywitz et al.,

1999). Furthermore, it is apparent that training in phonological skills allied to reading is the most appropriate form of remediation for dyslexic children (e.g. Hatcher, Hulme, & Ellis, 1994).

A number of neuroimaging studies in dyslexia have reported dysfunction in left hemisphere posterior circuitry during reading tasks, implicating both dorsal (including angular gyrus and supramarginal gyrus in the inferior parietal lobule as well as Wernicke's area) and ventral (including lateral extrastriate and left inferior occipito-temporal areas) regions (Helenius, Tarkiainen, Cornelissen, Hansen, & Salmelin, 1999a; Horwitz, Rumsey, & Donohue, 1998; Paulesu et al., 2001; Rumsey et al., 1997b; Salmelin, Service, Kiesila, Uutela, & Salonen, 1996; Shaywitz et al., 1998; Simos, Breier, Fletcher, Bergman, & Papanicolaou, 2000; Temple et al., 2001). Functional imaging studies of normal reading suggest that these two sites compose important circuits in the reading process. The dorsal regions appear to be involved in grapheme-phoneme decoding, while the ventral circuit appears to be more heavily recruited in tasks requiring whole-word form analysis (Pugh et al., 1996). In addition, abnormal over-activation of bi-hemispheric inferior frontal regions and right hemisphere posterior sites (Brunswick, McCrory, Price, Frith, & Frith, 1999; Rumsey et al., 1997b; Salmelin et al., 1996; Shaywitz et al., 1998) is also reported in dyslexic groups and has been interpreted as evidence of compensatory strategies. It has been proposed that there may be a breakdown in functional connectivity (as assessed by examining correlations in activation) in posterior regions in dyslexia (Horwitz et al., 1998). Interestingly, Pugh et al. (2000b) have reported evidence that functional connectivity between these regions is selectively impaired in tasks that required orthographic to phonological assembly. For a review of these studies see Pugh et al. (2000a).

2.3.2 Magnocellular Deficit Hypothesis

John Stein, the main proponent of the Magnocellular Deficit Hypothesis proposes that the literacy problems faced by dyslexic individuals are explained by impaired development of the magnocellular system, which is responsible for timing sensory and motor events, perhaps as the result of immunological attack (Stein & Talcott, 1999; Stein & Walsh, 1997). As learning to read and write requires incredibly

fine visual, auditory and manual skills, even subtle deficits in such a mechanism could disrupt the reading process. The predicted consequences of such an impairment are wide-ranging and include unstable vision leading to orthographic weakness, poor sequencing of sounds leading to phonological problems, in addition to more general difficulties with coordination and problems focusing visual and auditory attention. The evidence for low-level auditory deficits is outlined in Chapter 3. However, the majority of research cited in support of the Magnocellular Deficit Hypothesis has been conducted examining the visual deficits associated with dyslexia (for a review see Eden, Van Meter, Rumsey, & Zeffiro, 1996a; Livingstone, Rosen, Drislane, & Galaburda, 1991; Stein & Walsh, 1997).

It has been proposed that the visual system is divided into anatomically and functionally separate, although highly interconnected, ventral and dorsal streams (for an overview see Maunsell, Nealy, & DePriest, 1990; Merigan & Maunsell, 1993). Cell bodies within the ventral, or magnocellular (M), stream are typically larger with more myelination than those in the dorsal, or parvocellular (P), stream, and as such, M-cells conduct impulses faster than P-cells. Thus, M-cells deal with transient responses, while P-cells deal with sustained responses. M-cells are sensitive to stimuli with lower contrasts, higher temporal and lower spatial frequencies than P-cells. Similar subdivisions of the auditory system have also been proposed with similar M- and P- subdivisions evident in the medial geniculate nucleus (MGN).

Anatomically, it has been reported that cell bodies within the magnocellular layers of the visual (lateral) and auditory (medial) geniculate nuclei are reduced in size in the brains of dyslexic individuals (Galaburda, Menard, & Rosen, 1994; Livingstone et al., 1991) (see Chapter 3, section 3.2.3).

A large number of psychophysical studies have reported a number of deficits in functions thought to be controlled by the visual M-system. For example: eye movement abnormalities (Biscaldi, Gezeck, & Stuhi, 1998; Cornelissen, Munro, Fowler, & Stein, 1993; Crawford & Higham, 2001; De Luca, DiPace, Judica, Spinelli, & Zoccolotti, 1999; Eden, Stein, Wood, & Wood, 1994) extended visual

persistence at low spatial frequencies (Lovegrove, Martin, & Slaghuis, 1986); reduced flicker fusion rates at low spatial frequencies and low contrasts (Martin & Lovegrove, 1987; Talcott et al., 1998); reduced contrast sensitivity (Cornelissen, Hansen, Hutton, Evangelinou, & Stein, 1998; Martin & Lovegrove, 1987); reduced motion sensitivity (Cornelissen, Richardson, Mason, Fowler, & Stein, 1995; Cornelissen et al., 1998; Demb, Boynton, Best, & Heeger, 1998; Talcott, Hansen, Assoku, & Stein, 2000a; Talcott et al., 1998); deficits of visual spatial attention (Facoetti, Paganoni, & Lorusso, 2000 ; Facoetti & Turatto, 2000; Facoetti, Turatto, Lorusso, & Mascetti, 2001; Steinman, Steinman, & Garzia, 1998; Vidyasagar & Pammer, 1999). However, the importance of such deficits is contentiously debated (for a review see Greatrex & Drasdo, 1995; Skottun, 2000; Stein, Talcott, & Walsh, 2000).

Examining visual M-functioning physiologically, reduced and delayed visual evoked potentials (VEPs) have been reported in dyslexic groups (Brannan, Solan, Ficarra, & Ong, 1998; Lehmkuhle, Garzia, Turner, Hash, & Baro, 1993; Livingstone et al., 1991). In an fMRI study, Eden et al. (1996b) demonstrated a lack of activation of the motion area V5 in five dyslexic subjects in response to a moving, low contrast random dot pattern, believed to involve processing in the M-system. However, in an MEG study, Vanni, Uusitalo, Kiesila, & Hari (1997) reported similar levels of activation in this area in control and dyslexic groups, although longer latencies of activation were noted in the dyslexic group. Demb et al. (1998) and Demb, Boynton, & Heeger (1997) have reported lower levels of activation of visual areas V1 and V5 in dyslexic participants in response to moving gratings at low luminance contrast levels. In addition a strong correlation between individual differences in V5 activity and reading rate was noted. For a review of neuroimaging studies examining sensory-level processing deficits in dyslexia, see Eden & Zeffiro (1998).

In addition to the implications for the processing of low-level visual and auditory stimuli, the Magnocellular Deficit Hypothesis predicts that abnormalities will be evident in other systems. For example, there is evidence to suggest that touch sensitivity is reduced in dyslexic individuals (Grant, Zangaladze, Thiagarajah, & Sathian, 1999; Stoodley, Talcott, Carter, Witton, & Stein, 2000). Furthermore,

Stein, Talcott, & Witton (2001) have suggested that due to the large magnocellular projections to the cerebellum, deficits demonstrated by dyslexic individuals on tasks of cerebellar function (see section 2.3.3) may actually be a consequence of a deficit in the M-system.

2.3.3 Cerebellar Deficit Hypothesis

The Cerebellar Deficit Hypothesis is an extension of the Automatization Deficit Hypothesis (Nicolson & Fawcett, 1990), which proposed that dyslexic children have difficulties becoming expert in all skills, cognitive or motor. While deployment of compensatory strategies would lead to apparently 'near normal' performance in most skills (though at the expense of greater conscious effort), deficits would remain apparent in skills requiring rapid performance or fluent interplay of a range of subskills. Evidence for an automatization deficit is taken from the results of studies reporting deficits of dyslexic individuals on tasks requiring fast and fluent responses. For example, naming speed deficits (as reviewed in section 2.3.1) are predicted by this hypothesis. Further evidence for reduced automaticity comes from the observation that even when dyslexic individuals manage to acquire reasonable literacy skills, their reading remains slow and effortful (i.e. less automatic) in comparison with non-impaired individuals.

Making the link between automatization and the cerebellum, Nicolson and Fawcett have since proposed that the cerebellum plays a key role in the deficiencies of dyslexic individuals (for a review see Nicolson, Fawcett, & Dean, 2001). Further postulated links between cerebellar deficits and dyslexia propose that resulting motor skill impairments can explain writing difficulties (dysgraphia is often co-morbid with dyslexia), while phonological impairments may result from poor articulatory skills (for example, see Heilman, Voeller, & Alexander, 1996).

Anatomically, Finch, Nicolson and Fawcett (2000, cited in Fawcett & Nicolson, 2001) have reported relatively more large neurons and fewer small neurons in the cerebella of dyslexic brains (those also studied by Galaburda et al., 1994;

Livingstone et al., 1991). These differences were significant in the posterior cerebellar cortex, the anterior lobe and the inferior olive.

A number of deficits implicating abnormal functioning of the cerebellum have also been reported in dyslexic individuals. For example, deficits in motor skills (Fawcett & Nicolson, 1995), 'automatic' balance (Nicolson & Fawcett, 1990), bimanual coordination tasks (Moore, Brown, Markee, Theberge, & Zvi, 1995; Rousselle & Wolff, 1991), and tasks assessing speeded performance (Denckla & Rudel, 1976). Primary evidence for cerebellar dysfunction in dyslexia comes from the results of a large-scale study comparing dyslexic and control individuals on a range clinical tests assessing cerebellar function, conducted by Fawcett, Nicolson, & Dean (1996) including 14 tasks assessing a range of cerebellar functions. Dyslexic children were significantly worse on all tasks than age-matched controls (and on 11 compared to reading age matched controls). These results were confirmed in a follow-up study (Fawcett & Nicolson, 1999).

In a PET study examining patterns of activation during a finger movement study, known to induce strong cerebellar activation, Nicolson & Fawcett (1999) found group differences in cerebellar activation. While the control group showed relatively greater activation in the right cerebellum during performance of pre-learned and novel sequences of finger movements compared with rest, the dyslexic group showed greater activation in large areas of the frontal lobes when learning the novel sequence. This finding was taken as a sign that these individuals were bypassing the cerebellum and relying on conscious strategies. Strikingly, the dyslexic adults showed only 10% of the level of increased blood flow found in controls in cerebellar cortex and vermis when performing the task. Metabolic abnormalities of the cerebellum in dyslexic men have also been reported by Rae et al. (1998).

2.3.4 Temporal Processing Deficit Hypothesis

Paula Tallal has been the main proponent of the Temporal Processing Deficit Hypothesis in the past few decades. This account of dyslexia is based on evidence of specific deficits in responding appropriately to rapidly presented stimuli (in all sensory modalities) in dyslexic individuals. Such deficits in the

auditory domain would, it is suggested, impact upon speech perception, resulting in delayed or disordered language development. Comparable deficits in the visual and other sensory systems are considered to be another (though non-causal) manifestation of these pan-sensory temporal processing deficits. Originally the hypothesis was developed to explain the deficits demonstrated by children with specific language impairment (Tallal & Piercy, 1973a; Tallal & Piercy, 1973b; Tallal & Piercy, 1974), but more recently the hypothesis has been extended to account for the deficits of dyslexic individuals (Farmer & Klein, 1995; Tallal, 1980).

Most of the evidence cited in support of the Temporal Processing account of dyslexia comes from the results of auditory experiments, which are outlined in Chapter 3. Reviewing the evidence for temporal processing deficits, it is important to be aware that much of the evidence supporting a Temporal Processing account overlaps with evidence supporting a Magnocellular or Cerebellar Deficit account. Indeed, the Magnocellular Deficit Hypothesis, in particular, seems to extend and refine the Temporal Processing Deficit Hypothesis. Thus, the evidence reviewed so far (and in Chapter 3) concerning impairments in the processing of rapidly presented or rapidly changing stimuli are considered within this framework as evidence of a pan-sensory timing deficit.

2.4 Lack of Consensus

2.4.1 The Continuing Debate

While recent research has encouraged new ways of conceptualising dyslexia there is, as yet, a distinct lack of consensus regarding the causality of the disorder. The major division in current belief centres on the debate about whether dyslexia is a cognitive level, linguistic disorder, or the consequence of impaired sensory and/or motor processing. While the arguments for many of the causal theories are convincing, there is not one that appears able to explain all of the behaviourally observed manifestations of the disorder.

2.4.2 Heterogeneity

An additional obstacle in the search for a single causal pathway arises from the fact that dyslexia is an extremely heterogeneous condition, with individual

differences in both the severity and even the presence of certain deficits. Martin (1995) goes so far as to suggest that the group study approach to considering dyslexia should be abandoned in favour of detailed analysis of single case studies.

2.4.3 Subtypes

Indeed, the diversity of dyslexia as it manifests itself in different individuals has led to attempts to identify subtypes of the disorder. Examples of proposed sub-groups include dysphonetic and dyseidetic dyslexics (Boder, 1971, cited in Snowling, 2000) and, from the literature on acquired dyslexia, phonological dyslexics and surface dyslexics (Castles & Coltheart, 1993). However, it has been suggested that these sub-groups actually reflect different teaching methods (Thomson, 1999). Furthermore, attempts to identify subtypes within the dyslexic population have suggested that, as well as dissociations between individuals experiencing visual problems and those with auditory deficits, there are also 'mixed' cases with impairments in both domains (McAnally, Castles, & Stuart, 2000). Moreover, individual characteristics identified within such sub-groups are also prone to individual variability (Frith, 1999). Nevertheless, a subtyping approach may be important to the future study of the dyslexic condition.

2.4.4 Toward Consensus

Considering both the varied behavioural correlates of dyslexia and the large degree of individual variability observed within the dyslexic population, it seems unlikely that any one of the proposed causal theories will be able to account for all cases of dyslexia. Frith (1999) argues that the three-level framework (biological, cognitive and behavioural) can reconcile some of the ideas as rival positions can all be accounted for within this framework. For example, the Phonological Representations Hypothesis represents a cognitive level account of dyslexia, while the Magnocellular and Cerebellar Deficit Hypotheses posit explanations at the biological level. Furthermore, there is at least a moderate degree of overlap in the predictions of each of these accounts. Thus, it may be possible that certain aspects of each account will provide an explanation for the range of deficits observed in dyslexic individuals. It is important to be aware that reading (and for that matter spelling) is a complex skill, the mastery of which requires the recruitment and collaboration of an array of cognitive subskills, for example

visual and phonological processing, memory and attention. Thus, a deficit in any subskill could result in difficulties in mastering literacy skills.

3 RECENT AUDITORY STUDIES

3.1 Introduction

3.1.1 Introduction

In the previous chapter a number of causal theories of dyslexia were reviewed. At present there is still vigorous debate regarding which can best account for the range of deficits observed in dyslexic groups. The main division in the literature relates to whether the dyslexic condition results from a cognitive level disorder of language processing or more basic dysfunctions in sensory processes. In this chapter evidence suggesting anomalies of auditory processing will be reviewed.

3.1.2 Low-Level Auditory Deficit

In the past few decades auditory research in dyslexia has received renewed interest with many new findings implicating low-level auditory dysfunction. However, this research has not culminated in one specific causal theory; rather a number of theories are forwarded, many encompassed within multi-modal sensory processing accounts. The two main examples of such accounts are the Magnocellular Deficit Hypothesis and the Temporal Processing Deficit Hypothesis, although these are not necessarily exclusive. Furthermore, proponents of the linguistic/cognitive-level deficit, while accepting that such anomalies exist (at least in some dyslexic individuals), argue that low-level sensory deficits are irrelevant to the literacy problems faced by the dyslexic population.

3.1.3 The Causal Link

The majority of theories proposing an auditory processing account of dyslexia relate low-level auditory abnormalities to well-established phonological processing deficits. It is argued that deficient perception or processing of speech sounds results in weak representations of phonology. However, opponents of such theories argue that if the phonological architecture were corrupted to this extent, it would be expected that all tasks depending on this phonology (for example speech production and language comprehension) should suffer. Instead, these groups argue that the problems are purely metaphonological (cognitive), involving problems consciously segmenting words into phonemes.

3.1.4 Aim

The results of a large number of anatomical, psychophysical and physiological studies have been found to support the notion that a low-level auditory processing deficit exists in dyslexia. The aim of this review is to present the results of such studies, conducted in recent years, in order to identify the nature and mechanisms of such deficits. In addition, contradicting data are reviewed in an attempt to evaluate the weight of evidence for such processing deficits. As the studies presented within this thesis do not directly test the causal relationship between low-level auditory processing deficits and speech perception impairments, the present review will focus on research investigating the early processing of simple (i.e. non-speech) stimuli.

3.2 Anatomical Studies

3.2.1 Alterations of Cerebral Asymmetry

Findings of leftward asymmetry in a number of cortical structures have been related to the lateralisation of language functions in the left hemisphere. The seminal work of Geschwind and Levitsky (1968) provided strong evidence of anatomical asymmetry. The investigators reported finding that 65 of the 100 brains they studied at post-mortem displayed a leftward asymmetry of the planum temporale.

In an autopsy investigation of four dyslexic brains Galaburda, Sherman, Rosen, Aboitiz and Geschwind (1985) discovered atypical symmetry of the planum temporale. As the planum temporale in these subjects was larger than in normal brains it was concluded that dyslexics might suffer from an excess of language cortex, primarily in the right hemisphere. The finding was confirmed by a second postmortem investigation in three dyslexic women (Humphreys et al., 1990).

The planum temporale (part of Wernicke's area) is a gross anatomical landmark located in the superior plane of the temporal lobes, posterior to Heschl's gyrus. This triangular region, buried within the Sylvian fissure of the brain, is the most obviously asymmetrical region of the normal brain. The asymmetry of this structure is thought to result from right-hemisphere cell death during

corticogenesis (Shapleske, Rossell, Woodruff, & David, 1999). Thus, an absence or reduction of asymmetry in dyslexic individuals may reflect diminished neural loss in the right hemisphere during prenatal development.

A number of in-vivo studies have also been used in order to investigate planum temporale asymmetry in the dyslexic population (for a review see Morgan & Hynd, 1998). Many have reported findings in line with those of Galaburda et al. (1985), for example Duara et al. (1991); Hynd, Semrud-Clikeman, Lorys, Novey, & Eliopulos (1990); Larsen, Hoien, Lundberg, & Odegaard (1990); Rumsey et al. (1986) all report a larger incidence of abnormal symmetry of this structure in their dyslexic populations, although there is some disagreement about whether the symmetry reflects reduced left or increased right plana. However, contradictory findings have also been reported (Best & Demb, 1999; Heiervang et al., 2000; Leonard et al., 1993). For example, Schultz et al. (1994) report finding no differences between dyslexic and control subjects on measures of planum temporale area once the influence of age and overall brain volume were covaried in the analysis. Furthermore, with use of 3-D surface rendering techniques, which enable more accurate measurement, in addition to better controls for sex, handedness and IQ, Rumsey, Donohue, Brady, Nace, Giedd and Andreason (1997a) have reported normal leftward planum temporale asymmetry and normal rightward planum parietal asymmetry in their dyslexic sample. Thus variation in subject selection criteria and anatomical definitions may account for conflicts.

Typically, links have been made between abnormal planum temporale findings and cognitive level deficits. Larsen et al. (1990) provided evidence of links between planum temporale symmetry and phonological processing deficits (across both dyslexic and control groups). Likewise, Sermund-Clikeman et al. (1996) have associated symmetry or reversed symmetry with verbal comprehension, phonological decoding and reading comprehension skills, regardless of group membership (dyslexic, attention deficit or control). Galaburda (1999) suggests that, as the planum temporale is only one or two synapses away from primary auditory cortex, and is still unimodal enough to be involved in early sensory or perceptual processing, its lack of asymmetry may have implications for early auditory processing in dyslexia.

3.2.2 Size of Thalamic Nuclei

There is also anatomical evidence of changes in the size of some thalamic nuclei in dyslexic brains, examined post-mortem.

Initially, Livingstone and colleagues (1991) reported reduced cell size in the magnocellular layers of the lateral geniculate nucleus (LGN) of dyslexic brains. This nucleus is connected to the retina and the primary visual cortex. It is composed of both magnocellular (M) and parvocellular (P) layers, through which the corresponding M and P visual channels pass. M and P cells respond selectively to different properties of visual stimuli. The cell bodies within the M-layers are larger than those of the P-layers and they are more heavily myelinated (Sekuler & Blake, 1994). Thus, M-cells conduct impulses much faster and as such, M-cells deal with transient responses while P-cells deal with sustained responses (Merigan & Maunsell, 1993). The findings of reduced size M-cells in dyslexic individuals, along with the population's poor performance on tasks relying on M-system functioning (for example motion detection tasks) have been the main argument forwarded in support of the Magnocellular Deficit Hypothesis (see section 2.3.2).

Galaburda et al. (1994) have reported that the anatomical abnormalities described in the visual thalamus (LGN) may also extend to the auditory thalamus (medial geniculate nucleus, MGN) in dyslexics. Cell bodies in this structure were found to be smaller than those of controls. In the control group the distribution of different sized neurons was symmetrical, whereas, in the dyslexic group, the left MGN contained more small neurons and fewer large neurons than the right MGN.

While it is not certain that the separations of M- and P- pathways in the visual system are paralleled in the auditory system, it has been argued that there are analogous divisions (Stein, 1994). The dorsal cochlear nucleus in the brain stem, which is the first auditory relay nuclea, contains cells which are bigger than those found in the ventral division. These cells seem to be responsible for tracking the time course of acoustic stimuli (i.e. the transient information). In the superior olive, the next auditory nucleus, there are large neurons that respond to the

relative timing of input to one ear, compared to that of the other. These cells, in turn, project to large neurones located in the pericentral nucleus of the inferior colliculus, cells that also respond selectively to auditory transients. The MGN is the next auditory relay nucleus and its large cells again appear to respond preferentially to auditory transients. All of this anatomical and functional evidence has been taken to suggest that there is an M-component in the auditory system, comparable to that seen in the visual system.

Regardless of similar divisions in the sensory systems, the findings of reduced cell size in the MGN have been taken as evidence of impairment in the processing of auditory transients in dyslexia (Stein & Talcott, 1999). However, caution must be exercised in interpreting the results of Galaburda et al. (1994) and Livingstone et al's. (1991) studies, as there is no evidence that any of these dyslexic individuals demonstrated impairment on tests of visual or auditory processing in life.

3.2.3 Animal Models

Other post-mortem findings in dyslexic samples have provided support for a cognitive level account. For example, Galaburda et al. (1985) and Humphreys et al. (1990) have reported the presence of focal cortical malformations consisting of bundles of ectopic neurons and glia in the first cortical layer of perisylvian language areas (e.g. Wernicke's and Broca's areas), particularly in the left hemisphere.

Ectopias arise normally in early development before the period of neuronal migration to the neocortex (between 16-20 weeks of gestation in humans) and their connectivity to other cortical areas is wide-ranging. In contrast, alterations in cell size can occur at any time in life. Galaburda (1999) suggests that the ectopias may alter cerebral connectivity enough to affect the development of sensory areas. This has led Galaburda and colleagues to question whether the ectopic anomalies found in dyslexic brains may have a downstream effect on the changes observed in thalamic neurons (Sherman & Galaburda, 1999). This would suggest that the cognitive changes would come first and the sensory changes would result from secondary changes in the thalamus.

The group have investigated such possibilities with use of animal models. Inducing migrational anomalies in rats, equivalent to those observed in dyslexic brains, they have demonstrated that changes in neuronal size consequently appeared in thalamic nuclei (Galaburda, 2001). For example, anomalies induced in the frontal lobe produced an excess of small neurons in the MGN of the rat, mimicking the findings reported in human dyslexic brains (Galaburda et al., 1994). These results suggest that the observed thalamic changes could be due (secondary) to the cortical anomalies.

Linking the observed MGN cell size changes to auditory processing deficits, the animals with induced frontal cortical anomalies and secondary changes of the MGN were found to be impaired in processing rapidly changing sounds, behaving similarly to dyslexic humans on auditory temporal processing tasks (Galaburda, 2001). In addition, auditory event related potentials, recorded in response to the second tone in a rapidly presented pair, were reduced in mice with ectopias when intervening stimuli were closely spaced in terms of frequency (Frenkel, Sherman, Bashan, Galaburda, & LoTurco, 2000), a finding similar to that previously reported in dyslexic humans (Nagarajan et al., 1999).

Interestingly, poor performance on the auditory task was not found in the female rat population with the same induced anomalies. Re-evaluating the data revealed that the secondary changes in MGN neuronal size present in the male rats were absent in the females (Fitch, Brown, Tallal, & Rosen, 1997). Thus, the thalamic changes alone appeared to predict performance in the auditory task. Furthermore, the group found that exposing pregnant rats to testosterone and inducing the cortical malformations in the female offspring now led to the secondary thalamic nuclei changes.

These results appear then, to give credence to the hypothesis that the observed sensory impairments are secondary (non-causal) to the cognitive level dysfunctions seen in dyslexic populations. In fact, data from the animal models would appear to suggest that changes in low-level sensory processors might be a consequence of the earlier changes occurring in the higher-order cortices. In addition, the findings predict, firstly that low-level auditory processing deficits

will only be evident in individuals with the secondary changes in the thalamus, and secondly that there may be a sex difference, with only males, due to exposure to testosterone, exhibiting auditory processing deficits.

3.3 Psychophysical Studies

3.3.1 Brief and Rapidly Presented Stimuli

The early work of Paula Tallal and colleagues examined the existence of 'temporal processing' deficits in individuals with language impairment and developmental dysphasia (e.g. Tallal & Piercy, 1973a; Tallal & Piercy, 1973b; Tallal & Piercy, 1974). Due to the apparent strong link between these conditions and dyslexia, the group proposed that similar deficits might be common across all conditions.

Exploring the possibility that dyslexic individuals exhibit similar deficits, Tallal (1980) examined the performance of a group of reading disabled children on temporal ordering tasks. Twenty reading-disabled children aged between 8 and 12 years were recruited on the basis of a formal diagnosis of specific developmental reading delay, at least average intelligence and a composite reading age at least one year below chronological age grade placement. The performance of these children was compared to the performance of previously tested younger controls (all 8.5 years old).

To begin, participants were trained to respond to two separate stimuli, a tone with a fundamental frequency of 100Hz (1) and a second tone with a fundamental frequency of 305Hz (2). Each tone had a duration of 75ms and participants were asked to respond to each by pressing one of two panels. After training, the two stimuli were presented in all possible sequence combinations (1-2, 2-1, 1-1, 2-2) and participants were instructed to recreate the sequences. The performance of both the reading-disabled and control groups worsened at shorter interstimulus intervals (ISIs) (8-305ms as opposed to 428ms). However, the reading-disabled children made significantly more errors than the younger controls with reducing ISIs. Reed (1989) has reported similar finding in 23 poor reading children.

While these two studies appeared to demonstrate that the dyslexic groups were impaired in tasks requiring the ordering of brief and rapidly presented stimuli, taken by Tallal to reflect temporal processing deficits, the contribution of a number of confounding factors could not be ruled out. For example, the temporal ordering task not only required that individuals be able to processes the stimuli at fast rates, but also to order the stimuli. Therefore, Tallal (1980) went on to question whether the problems evident in the dyslexic group would persist without the ordering component.

In a second condition, Tallal (1980) eliminated the ordering component by presenting a task that simply required the differentiation of the two the stimuli. Participants were simply required to judge whether the two tones were the same or different. Results again revealed that at an ISI of 428ms, the performance across groups was comparable. However, at reduced ISIs (8-305ms), performance in the dyslexic group deteriorated more. In fact, comparing individuals' performance across the discrimination and the temporal order judgement task, no significant differences were found. Reed (1989) also replicated these results, as have many other groups (for example Cestnick, 2001; Heath, Hogben, & Clark, 1999; Heim, Freeman, Eulitz, & Elbert, 2001).

These results, therefore suggest that poor performance was not dependent on the presence of a temporal ordering component. Rather, Tallal (1980) argues that the findings support the notion that dyslexic individuals suffer from a more basic perceptual deficit affecting the rate at which they can processes perceptual information. Tallal therefore argued that dyslexic individuals have a temporal processing deficit, which manifests as the impaired ability to process brief or rapidly presented stimuli. In addition, correlations between performance on the temporal ordering and discrimination tasks and tests of non-word reading led Tallal to propose that the early perceptual deficits could have consequences for acquiring accurate phonological skills, and ultimately learning to read.

3.3.2 Individuation of Stimuli

In reviewing the evidence for the existence of cross-modal temporal processing deficits in dyslexia, Farmer & Klein (1995) have further considered the separable

components involved in the processing of sequential stimuli. In addition to judgement of temporal order and discrimination of sequential stimuli, the processing of sequentially presented stimuli requires that the individual can identify them as separable.

Gap detection tasks determine the minimum ISI required for a participant to perceive that a stimulus has been interrupted by a temporal gap. The threshold at which two events closely spaced in time are perceived as separate is measured as auditory temporal resolution. McCroskey and Kidder (1980, cited in Farmer & Klein, 1995) reported that their group of reading and learning disabled children required a significantly longer ISI to perceive two brief tones as temporally separated.

However, this result is contradicted by the findings of a number of other investigators. For example, Schulte-Korne, Deimel, Bartling, & Remschmidt (1998b) examined gap detection thresholds in spelling disabled (a discrepancy of at least one standard deviation between actual spelling scores and those predicted on the basis of IQ) adults and children. Noise bursts had a duration of 400ms, including gap. Gap size was varied in a step-wise fashion to determine threshold. The participants' task was to respond to gap or no gap with a left or right button click, respectively. Examining group means for gap detection thresholds in both the child and adult sample, no differences were found between spelling disabled and non-impaired groups. Schulte-Korne et al. (1998b) have suggested that differing participant groups can account for the discrepancy between their results and those of McCroskey and Kidder. The results of McCroskey and Kidder are not specific to reading disabled children, but rather apply to an ill-defined group of reading and language impaired children. Indeed, Ludlow, Cudahy, Bassich and Brown (1983, cited in Schulte-Korne et al., 1998b) have reported impaired gap detection in language delayed but not reading disabled hyperactive children.

McAnally & Stein (1996) also report no difference in thresholds for detecting a gap in noise between dyslexics and controls. Ahissar, Protopapas, Reid, & Merzenich (2000) found that this measure did not correlate with performance on

any reading related measure. Therefore, the evidence seems to weigh towards the conclusion that the auditory temporal resolution of dyslexics is normal.

3.3.3 Rate of Perception Versus Perception of Rate

Examining the evidence forwarded in favour of the temporal processing deficit account of developmental dyslexia, Studdert-Kennedy and co-workers (Mody, Studdert-Kennedy, & Brady, 1997; Studdert-Kennedy & Mody, 1995) have stressed the need to clarify what is meant by the term 'temporal processing'. The group argue that within the literature, two concepts are commonly confused; these are 'rate of perception' and 'perception of rate'. The ability to rapidly identify or discriminate between very brief events is dependent on rate of perception, while the ability to perceive the temporal properties of events (duration, sequence, relative timing, rhythm) is dependent on perception of rate.

The evidence presented by Tallal and Reed concerns stimuli that are brief in duration or rapidly presented, as opposed to the perception of the temporal properties of stimuli. In both Tallal's (1980) and Reed's (1989) studies, removing the temporal component (i.e. the order judgement) from the task had no effect on the performance of their poor reading participants. Indeed Reed (1989) comments that the temporal tasks simply 'provide a setting where perceptual capabilities can be stressed' (Reed, 1989, p.287). Participants in both studies were just as impaired when asked to discriminate between the brief stimuli when they were presented rapidly. Furthermore, on gap detection tasks, which do directly assess temporal perception in that accurate temporal resolution is required to code onsets and offsets, the weight of evidence suggests that dyslexic individuals perform normally (section 3.3.2). Thus, Mody et al. (1997) argue that such a deficit cannot truly be considered a deficit in 'temporal processing' or 'temporal perception'.

In addition, Studdert-Kennedy & Mody (1995) point out that discrimination of brief tones of differing frequencies, requires the perception of spectral as opposed to temporal contrasts.

Thus, the conclusions to be drawn from the early work on sequential processing are that dyslexic participants are impaired on tasks requiring spectral discriminations between auditory stimuli that are brief and presented rapidly. Considering these conclusions, two separate lines of enquiry have followed. The first concerns whether dyslexic individuals exhibit poor discriminative abilities between spectrally similar sounds, the second examines whether these individuals have difficulties relating to the processing of brief and rapidly presented sounds.

3.3.4 Discrimination of Spectral Contrasts

The results of Tallal (1980) and Reed's (1989) sequential processing studies suggested that the dyslexic groups were impaired in their ability to discriminate between stimuli based on spectral difference, in conditions where these stimuli were presented rapidly. A number of researchers have since investigated whether it is the discrimination of spectral contrasts, as opposed to the timing between the stimuli, which is the critical factor resulting in the dyslexic individuals observed difficulties. While Tallal and Reed varied the ISI between stimuli, a more sensitive measure for assessing the discrimination of spectral contrasts is afforded by measuring thresholds of just-noticeable differences in frequency.

McAnally and Stein (1996) set out to assess whether it is the temporal or spectral properties of certain stimuli, which prove problematic for dyslexics. Twenty-three dyslexic adults, with a significant discrepancy between WISC PIQ and reading ability, and 26 age and IQ matched controls were recruited to take part in the study.

Using threshold measures, McAnally and Stein (1996) found that the dyslexic adults were significantly worse than controls at detecting small changes in frequency of 500ms pure tones varying around 1000Hz, suggesting a problem with spectral discrimination. In contrast, the same group of dyslexics were not different from controls in their ability to detect a gap in noise (in line with data presented in section 3.3.2), thus their coding of stimulus onsets and offsets was unimpaired.

The results of this study have been replicated for the detection of just-noticeable differences between pure tones varying around 1000Hz (Ahissar et al., 2000) and around 500Hz (France, Hansen, Rosner, Richardson, & Stein, 1997). Interestingly, France and colleagues found that this impairment was amplified as ISIs were increased, suggesting that the dyslexics' difficulty was not caused by the rapidly presented nature of the stimuli (France et al., 1997).

Thresholds for just-noticeable differences in frequency have also been examined in a study employing a 3-forced choice paradigm (Cacace, McFarland, Ouimet, Schrieber, & Marro, 2000). Four reading impaired children (diagnosed on the basis of standard discrepancy criteria) and four age-matched controls were asked to indicate which of three sequentially presented tones differed in frequency. Confirming the results of previous studies, reading impaired children were found to have significantly higher discrimination thresholds than controls. Furthermore, in line with the findings of France et al. (1997), elevated thresholds in the reading impaired group were not dependent on stimulus duration.

As noted above, Ahissar et al. (2000) found that the frequency discrimination abilities of poor readers were typically worse than those of normal readers. In order to address the possibility that such difficulties are the result of problems with short-term memory rather than spectral discrimination itself (i.e. dyslexics may simply have difficulties remembering the pitch of the first tone, which they must do if they are to compare it to the second), they included a control condition. Their participant group consisted of 102 adults with varying reading ability, separated into those who reported difficulties with reading difficulties in childhood and those who reported no such problems. In the control condition participants had to identify whether two sequentially presented tones, with adaptively varying stimulus intensity, were the same or different. The parameters of tone duration (250ms) and ISI (800ms) were the same as in the frequency discrimination task. Performance on this task was not correlated with any of the reading measures, indicating that short-term memory was not affecting the results. In addition this control task provided additional evidence that frequency discrimination was not difficult for poor readers simply because of the duration of the stimuli or the rates at which they were presented.

It was previously thought that the pitch of a tone was neurally coded in the auditory system based on place information. Place theory states that certain portions of the basilar membrane are selectively displaced in response to certain frequencies. It further predicts that the pitch perception of a stimulus is related to the activation of the corresponding sub-set of auditory nerve fibres. Tone pitch, therefore, is registered in terms of which set of nerve fibres is maximally active. While the first of these two postulates is now confirmed, the idea that pitch is encoded by the maximal activation of a certain set of nerve fibres is disputed (Moore, 1997). An alternative to place theory is temporal theory. This suggests that auditory nerve fibres discharge periodically in synchrony with the frequency of the stimulating tone i.e. they are locked to the phase of the stimulus. Therefore, it is the firing rate of auditory nerve fibres, a temporal measure, which conveys pitch information. While temporal theory does not apply to sinusoidal stimuli at frequencies over 5000Hz, as phase locking does not occur at frequencies above this level, it accounts well for the pitch perception of everyday sounds (e.g. the human voice and musical instruments) as such sounds all have fundamental frequencies below 5000Hz (Moore, 1997).

McAnally & Stein (1996) have proposed that the results relating to poor frequency discrimination abilities in dyslexic participants may result from a phase-locking impairment. According to temporal theory, the ability to discriminate between frequencies depends on the capacity of the auditory system to generate and decode phase locked discharges as well as to exploit this information at higher levels of the auditory system. Thus, McAnally and colleagues have suggested that the dyslexic population may suffer from failure in one of these processes.

However, results which contradict such a theory are reported by Hill, Bailey, Griffiths, & Snowling (1999). This group assessed frequency discrimination thresholds in a group of 12 dyslexic adults and 12 normal reading controls, matched for age and IQ. The stimuli were 400ms in duration and were presented using a four-interval (target occurring in second or third interval), two-alternative, forced choice paradigm, with ISIs of 400ms. Frequency discrimination thresholds

were measured for pure tones varying around 1000Hz and 6000Hz. While mean threshold measures were larger for the dyslexic group, the difference between groups was not significant. Furthermore, Hill et al. point out that the mean group difference is accounted for by the performance of only four of the dyslexic participants.

The failure to obtain a significant group difference in frequency discrimination thresholds for the tones varying around 1000Hz directly contradicts the results of McAnally & Stein (1996). Furthermore, considering the possibility that the difference in findings was simply due to the selection of a different dyslexic sample, Hill and colleagues point to the observation that, where individual dyslexic participants did demonstrate elevated thresholds, this was the case at both frequencies (1000Hz and 6000Hz). As noted above, phase locking does not occur at frequencies above 5000Hz. Thus, a phase locking deficit cannot account for the difference in performance demonstrated by this subset of dyslexic individuals.

3.3.5 Processing Dynamically Altering Stimuli

Rather than being static, many of the sounds that we encounter in a natural environment change dynamically over time. The perception of such sounds can be studied with use of either frequency modulated (FM) or amplitude modulated (AM) sine waves. In AM a carrier of unchanging frequency is presented while the amplitude is varied so as to follow the magnitude of a modulating sine wave. In FM the frequency of the carrier is varied in proportion to the modulating sine waves signal, with amplitude remaining constant (Moore, 1997). A number of studies have been conducted examining the ability of dyslexic individuals to track the changes in such dynamically altering stimuli.

Witton et al. (1998) set out to examine the perception of FM in dyslexia. They recruited 21 dyslexic adults (formally diagnosed on the basis of a discrepancy between WAIS-R IQ and reading and spelling performance) and 23 age matched controls. Stimuli were sets of two tones, one a pure tone and the other a FM tone. Participants were instructed to verbally report which of the two tones was the modulated tone. Estimates of threshold for detecting FM were calculated by examining performance at six depths, chosen to span threshold at equal intervals.

Modulation occurred sinusoidally at three different rates: 2Hz, 40Hz (both with a carrier frequency of 500Hz) and 240Hz (with a carrier frequency of 1000Hz). Tones were 1000ms in duration with ISIs of 500ms between tones in a pair.

FM detection thresholds were significantly higher in the dyslexic group for both the 2Hz and the 40Hz FM tones, but not the 240Hz FM tone. Thresholds of detection at 2Hz and 40Hz correlated with one another, but neither correlated with threshold measures at 240Hz. This suggests dissociation between the dyslexics' performance at slow and rapid rates of FM. Thus, the dyslexic participants appeared to be specifically impaired at detecting FM at slow rates of modulation. Furthermore, non-word reading scores were significantly correlated with FM detection at the two lower frequency modulations but not at 240Hz.

In an extension to these findings, Talcott et al. (1999) reported that sensitivity to 2Hz but not 240Hz FM was correlated with phonological skills in an unselected school sample (normal children). Forty percent of the variance on a task of non-word reading was accounted for by sensitivity to the 2Hz FM stimuli. In a subsequent study (Talcott et al., 2000b), threshold for detecting 2Hz FM was found to be the single strongest predictor of reading and spelling ability; considered together with visual processing measures in a hierarchical regression analysis, 51% of reading skill and more than 59% of spelling skill were accounted for.

The ability to detect FM at low rates is achieved by tracking the temporal changes in the pitch of the carrier; at FM rates of 2Hz, changes are perceived as 'wobble', and at 40Hz they are perceived as 'roughness'. However, at rates of 240Hz, the presence of a tone at the pitch of the modulating frequency can actually be detected (Moore, 1997). Thus, the mechanisms underlying the detection of FM at fast and slow rates are dissociated. Tracking slow rates of modulation must be dependent on the ability to follow the variations in frequency over time. The perception of a tone at the pitch of the modulating frequency with fast rates of FM, suggests that at these rates the mechanism is probably dependent on non-linearly generated cues. For tones modulated at 2Hz and 40Hz, a single critical bandwidth encompasses all spectra. The spectrum of a tone modulated at 240Hz

extends beyond a single critical band. Therefore, perceptually processing FM at 2Hz and 40Hz is dependent on temporal cues, whereas at 240Hz spectral aspects of the stimulus are coded.

The fact that the dyslexic listeners were unimpaired in the detection of 240Hz FM, therefore, contradicts the hypothesis that it is the generation or exploitation of phase locked cues, encoding the spectral aspects of the stimulus, which is dysfunctional in dyslexic individuals. As an alternative account, Witton and colleagues have suggested that the dissociation seen in the performance of the dyslexics between high and low rates of FM suggests impaired temporal processing of dynamically altering stimuli i.e. impaired perception of rate (Witton et al., 1998).

It was noted above that Hill et al. (1999) failed to find a significant group difference in frequency discrimination thresholds between dyslexic and control adults. In an additional condition, the group measured discrimination thresholds for FM tones. The stimuli and procedure used were similar to those used in the frequency discrimination task (1000Hz and 6000Hz carrier tones, 400ms duration, four-interval, forced choice, 400ms ISI) and the modulation rate was 2.5Hz. Again, threshold measures were found to be larger in the dyslexic group, with a significant group difference for the 1000Hz stimuli (outliers removed). While Hill et al. concede that these results are consistent with Witton et al's. (1998) data, they point to the fact that the group difference for the 6000Hz stimuli was not statistically significant (after the removal of outliers) in addition to the fact that individual participants obtained very different thresholds across the two conditions. Thus, Hill and colleagues suggest that the results are not consistent with Witton et al's. hypothesis of deficits in the processing of dynamic stimuli.

In addition to examining the detection of FM in dyslexic participants, investigators have also examined the detection of AM. The threshold for detecting AM can be measured by determining the minimum depth of modulation required for the difference between modulated and unmodulated white noise to be detected. The temporal modulation transfer function (TMTF) is the threshold for detection of AM as a function of modulation frequency (Moore, 1997); as

modulation rates increase, detection threshold increases, and modulation cannot be detected at all at rates above around 1000Hz (Moore, 1997).

Mennell, McAnally, & Stein (1999) measured TMTFs in 20 discrepancy diagnosed developmental dyslexics and 20 age and IQ matched controls. 500ms bursts of noise were amplitude modulated, at variable depths, with modulation frequencies of 10, 20, 40, 80, 160, and 320Hz. Presented in pairs with an ISI of 500ms, participants were required to detect which interval contained the AM burst.

As expected, AM detection thresholds increased as modulation frequencies increased. While, the dyslexic participants had significantly higher thresholds for AM than control participants, there was no interaction between modulation frequency and participant group. That is, AM detection thresholds were higher for dyslexics over the full range of modulation frequencies. Therefore, regardless of the modulation frequency, dyslexics required greater levels of AM depth in order to detect AM. In addition, task performance was significantly correlated with reading ability. The authors argue, in line with Witton et al. (1998), that the findings suggest a deficit in the dyslexics coding of temporal change.

Hari and colleagues (1999) also designed a study to examine the detection of AM noise in a group of 20 healthy adults and 13 dyslexic adults (with significantly lower reading speed and word recognition speed scores) (Hari, Saaskilahti, Helenius, & Uutela, 1999a). The stimulus in the first condition was a 1000Hz pure tone, while in the second condition it was 80Hz AM white noise. The AM of the noise stimuli produces periodicity pitch at the frequency of the modulation, here 80Hz, despite the fact that the spectral content of the stimulus remains flat across the range. Pairs of tones and pairs of noise bursts were presented to participants. Stimuli within a pair had a duration of 500ms, separated by a 300ms gap. The first sound was constant (always either the 1000Hz tone or the 80Hz AM white noise), while the pitch or modulation rate of the second sound was varied in a stepwise fashion to identify discrimination thresholds. The participants' task was to indicate, with a button press, whether the second sound was higher or lower in pitch than the first.

The group found that mean discrimination thresholds were significantly higher in the dyslexic group for both the 1000Hz tone and the 80Hz AM noise. However, differences in discrimination thresholds between dyslexics and controls were significantly greater for detecting pitch alterations in the 1000Hz pure tone than for detecting variations in the AM phase of the noise.

Hari et al. (1999a) argued that these results demonstrate that an impairment of phase locking processes are unlikely to account for the poor discrimination abilities of dyslexic individuals. The basis of their argument was that the ability to detect AM varying around 80Hz is likely to be achieved on the basis of temporal coding alone as such stimuli lack any spectral cues. On the other hand, discrimination of the tones is achieved with place coding information as these tones contain spectral information. If an impairment of phase locking is the underlying cause of dyslexics' difficulties, Hari and colleagues propose that it would follow that these individuals should be markedly more impaired where the processing of stimuli is solely dependent on temporal coding.

However, as noted above, frequencies of less than 5000Hz are temporally coded by the auditory system by means of phase locking and so the phase locking impairment hypothesis would predict that the dyslexic participants would have higher thresholds in comparison to controls on the tone frequency discrimination task (the result obtained). Nevertheless, while this study has not proved an effective challenge for the phase locking hypothesis, the weight of evidence does seem to go against such an account.

In a recent study, Witton, Stein, Stoodley, Rosner, & Talcott (2002) have measured AM and FM sensitivity thresholds in the same group of 17 dyslexic and 21 matched control adults. The aim of the study was to examine the hypothesis that dyslexic individuals are impaired in the detection of modulation rates, which are slow enough to be tracked in time. Thus, the group predicted that if dyslexia is associated with a general impairment hindering the detection of all slow changes, they should perform worse than the controls in threshold tasks for detecting both 2Hz FM and 2Hz AM. Stimuli were 1000Hz tones of 1000ms

duration, separated by 500ms ISI and presented in a two-alternative forced-choice task (detect the period of modulation). In addition, they presented FM stimuli modulating at 240Hz (previously found to be normal in dyslexic participants (Witton et al., 1998)) and 20Hz AM stimuli (dyslexic participants have been found to have increased thresholds for this stimuli, as reported by McAnally, Hansen, Cornelissen, & Stein (1997)).

As expected, the results demonstrated that the dyslexic group were significantly less sensitive to the 2Hz FM stimuli (corrected for inhomogeneity of variance) and the 20Hz AM stimuli, while there was no group difference in response to the 240Hz FM stimuli. However, contradictory to the groups predictions, there was no significant group difference in detection thresholds for the 2Hz AM stimuli. This result suggested that reduced modulation sensitivity does not extend to all slow modulations. These conclusions were supported by the results of correlational analyses, which found significant relationships between phonological measures with only the 2Hz FM and 20Hz AM stimuli. Therefore, the group concluded that dyslexic listeners are impaired in their detection of modulation only at certain rates of AM and FM, as opposed to all slow rates.

3.3.6 Exploitation of Interaural Cues in Masking Tasks

Masking refers to the phenomenon where an auditory signal is not identified when presented within (simultaneous masking) or close to (forward or backward masking) another signal, which has similar (or identical) frequency components.

Masked signal detection thresholds (measuring the volume of signal relative to that of noise required for accurate detection) can be markedly lower if information from the two ears is used. Where the signals from the tone and the noise are identical in both ears, detection of the tone is dependent on the bandwidth of the auditory filter tuned to the tone and the relative intensity of the tone and noise signals. However, for a tone at masked threshold (i.e. just masked by the noise), inversion of the interaural signal phase (a phase shift of 180°) results in the audibility of the tone. The etiological importance of this phenomenon is thought to be related to the detection and discrimination of signals (e.g. speech) occurring

against a noisy background (Moore, 1997). Humans also exploit interaural timing differences in order to localise sound sources (Bregman, 1990).

McAnally and Stein (1996) employed such a task in order to further test their hypothesis of impaired phase locking in dyslexics. They tested their participants' detection of a 328ms 1000Hz tone presented against a background of noise. The tone was presented either dichotically (interaural phase of 0°) or in antiphase (interaural phase of 180°). Dyslexic participants did not differ from controls in their ability to detect the tone in masking noise in the 0° interaural phase condition. However, they were much worse than controls at detecting the same tone presented in antiphase. Masking Level Difference (MLD) is a measure of the difference in threshold between these phase conditions. The average MLD for the dyslexic group was significantly smaller than that of the controls. MLDs are likely to measure the accurate transmission of temporal information to a neural centre responsible for comparing such information from the two ears (Moore, 1997). McAnally and Stein (1996) suggested that these results provide further evidence of a phase locking deficit; the exploitation of neural codes between the ears is impaired.

Hill et al. (1999) have reported contradictory results. This group assessed the MLD in their group of dyslexic adults and matched controls using 200ms duration, 200Hz tones. Threshold measures for detecting the tone within the noise did not differ between groups in either the 0° or 180° interaural phase conditions and, as such, neither did MLDs. Witton, Richardson, Griffiths, Rees, & Green (1997) also recorded normal detection of interaural phase modulation in their dyslexic group; the authors report that while the dyslexics were poorer than controls in their ability to detect frequency modulations, the group demonstrated no impairments on a number of tasks requiring accurate phase locking, e.g. interaural AM.

The ability of the auditory system to exploit binaural phase cues in order to extract signals from background noise can also be measured with dichotic pitch. Dichotic pitch is a perception of pitch generated from two binaurally presented noise sequences, neither of which independently contains any cues to pitch. When

identical noise is presented to the auditory system dichotically, the brain detects that the temporal structure of the noise in each ear is the same, and fuses it into a single perceived sound (i.e. the perception is noise). However, if the phases in a narrow frequency band are shifted in the signal delivered to one ear, that interaural phase shifted frequency band will perceptually segregate from the rest of the noise. As a result, the listener perceives a faint pitch against the background of noise (Moore, 1997).

Dougherty and colleagues (Dougherty, Cynader, Bjornson, Edgell, & Giaschi, 1998) used dichotic pitch to examine the ability of dyslexic and control children to detect phase shifted frequency. Participants were eight dyslexic children (with reading skills at least 1.5 standard deviations below age norms) and eight controls. To obtain threshold measurements, signal to background ratios were varied in a stepwise fashion from 0 (no signal present) to 1 (full dichotic pitch signal). Setting the signal-to-background ratio higher than one produces monaurally detectable cues to pitch. In order to obtain a threshold measure for detecting the phase shift, participants were asked to perform two different tasks. Firstly, they were asked to indicate on which side the dichotic pitch melody came from, and secondly, they were asked to indicate whether the dichotic pitch was rising or falling. Dichotic pitch detection thresholds were significantly higher in dyslexics than in controls with six of the eight dyslexics unable to detect dichotic pitch whatsoever.

A possible explanation for the results is that the dyslexics were impaired in their exploitation of interaural timing cues (consistent with McAnally & Stein's (1996) hypothesis of impaired exploitation of phase locked cues). However, Dougherty et al. (1998) found that the dyslexic listeners were able to localise the melody at signal-to-background ratios greater than 1. While pitch information is monaurally audible at these high levels of signal-to-background ratio levels, the ability to localise sound is served by exploiting interaural timing cues. Indeed, there are no reports that dyslexics are impaired in their ability to localise sound. Dougherty et al. (1998) argue that the results reflect an impairment in the extraction of sound signals from noise. Such an impairment could impact upon the development of appropriate phonological awareness by impeding the accurate perception of

speech sounds against noisy backgrounds during critical stages of language development.

3.3.7 Forward and Backward Masking

While the results of Tallal and others did identify that dyslexic individuals have difficulties processing brief and rapidly presented stimuli (see section 3.3.1), the mechanism of such difficulties was not clearly outlined. Hari and colleagues (Hari, 1995; Helenius, Uutela, & Hari, 1999b) have proposed that the nature of the deficit might be an extended time window within which percepts can influence one another. Evidence for such a proposition shall now be outlined.

The time window within which successive stimuli can interfere with one another is directly measured in forward and backward masking paradigms. If a distracter stimulus with similar properties is presented before or after the presentation of a target stimulus, within a specific time window, the accurate perception of the target is disrupted.

Wright et al. (1997) examined masking effects in a group of learning impaired children by measuring masking level detection thresholds. The target tone was presented before, during or after noise that was bandpassed to include frequencies at and near the tone frequency. The target tone intensity was then varied in order to obtain detection thresholds. Wright and colleagues found that the learning impaired children required a higher tone level than control children in each of the masking conditions, but that this was markedly true in the case in the backward masking condition (tone immediately preceding noise). The researchers also report that preliminary data from a group of 12 reading impaired participants demonstrated that a similarly disruptive effect of backward masking was found in five of these individuals, although none were as impaired as the learning impaired children.

Ahissar et al. (2000) investigated the effect of backward masking on the frequency discrimination abilities of their group of 102 adults with varying reading ability. The two stimuli were pure tones, one with a frequency of 900Hz and the other with a frequency of 1100Hz. Tones were each presented for 20ms

and followed by a 300ms bandpass noise masker (with bandpass filtering centred around the frequency of the tones, 600-1400Hz). The ISIs between tones and maskers were adaptively varied in order to obtain threshold measures and participants were asked to make same-different judgements. Threshold measurements on this task were significantly correlated with reading ability (i.e. poorer readers needed longer ISIs in order to discriminate the tones).

3.3.8 Perception of Sound Sequences

The poor readers' increased thresholds in the backward masking task of Ahissar and colleagues, suggest that the disruptive effect of the masking noise on the accurate perception of the preceding stimuli occurs at longer separations in the dyslexic participants. Hari and Kiesila devised an elegant study to detect the influence of surrounding sounds on one another (Hari & Kiesila, 1996). Their sample comprised 20 healthy adults and 10 dyslexic adults, recruited on the basis of an early childhood history of difficulty in learning to read or spell and the provision of special tutoring in school. The dyslexic group were poorer on measures of digit span forwards and backwards, rapid stimulus naming and oral reading speed. Deficits in these areas are commonly found to persist in dyslexia into adulthood (see Chapter 2).

Stimuli were binaurally presented click trains, each containing eight clicks. The clicks within trains were presented with small (0.8ms) interaural time differences; clicks 1-4 led from the left ear and clicks 5-8 led from the right ear. Due to the very short interaural time difference, presenting the left ear leading clicks alone results in the perception that the stimuli originate from the left field of hearing, while presenting the right ear leading clicks in isolation results in the perception of stimuli originating in the right field of hearing. However, with short ISIs between individual clicks, presenting the left ear leading clicks, immediately followed by the right ear leading clicks results in a directional hearing illusion; the clicks are perceived as skipping from the left side of the head to the right in equidistant steps. As the ISI between clicks increases, so does the jump in perceived location across the midline, until the illusion dissipates (typically at ISIs of 150ms and above) (Hari, 1995).

The participants listened to the click trains and were asked to mark the perceived spatial locations of each click on a 20-point response scale (0 corresponding to the leftmost location, 20 to the rightmost location). The responses of the dyslexic and control participants were equivalent at very short ISIs (45ms). At this ISI, both groups perceived the illusorily jumping of clicks. At an ISI of 150ms, controls perceived more closely spaced steps at far lateral positions and a longer jump across clicks 4-5. At longer ISIs this midline jump increased and 11 of the controls reported that this jump equalled the total left-right distance. However, the responses (and presumably the perception) of the dyslexics at an ISI of 150ms were similar to those at an ISI of 45msec. Eight of the dyslexics continued to perceive the illusion at the longest ISI (500msec). Examining the mean data, differences between the groups were apparent at ISIs of 90ms and were highly significant for ISIs of 150, 250 and 500msec.

Essentially, these results demonstrate that the dyslexics needed a longer ISI in order to process the incoming stimuli in a manner similar to that of the normals. Thus, the study appears to demonstrate slower processing of dynamic auditory stimuli in dyslexics. However, the possible contribution of working memory deficits cannot be ruled out as participants had to respond after hearing the eight-click train (Helenius et al., 1999b).

Auditory stream segregation occurs when sound sequences consisting of alternating high and low pitched tones are presented with large frequency separations or at fast presentation rates. Under such conditions, listeners perceive the connected series of tones as separate sound streams, one high-pitched stream and one low-pitched stream. The perception of segregation reflects the tendency of the auditory system to assume that a sound sequence originating from the same source does not abruptly change its properties (Bregman, 1990). Measuring the threshold at which the sound stream is perceived as connected estimates the participant's temporal coherence boundary.

Auditory stream segregation was investigated in 18 normal and 13 dyslexic adults (diagnosis of dyslexia being solely based on self report of literacy problems) (Helenius et al., 1999b). Behavioural measures demonstrated that the dyslexic

participants were slower on tests of oral reading, naming and word recognition. Stimuli were sequences of 49ms duration tones alternating between 1000Hz and 400Hz. Stimulus onset asynchronies (SOAs) were shortened or lengthened as a result of reported perception in order to obtain an estimate of temporal coherence boundaries.

The average coherence boundary was significantly higher for the dyslexic group than for the control group. While controls did not perceive the tone sequence as segregated until SOAs were as short as 130msec, dyslexics perceived segregation at SOAs as long as 210msec. Thus, the influence of surrounding sounds was influential on the dyslexic participants' perceptual experience at slower presentation rates than for the control participants.

Again this result suggests sluggish auditory processing in the dyslexic population. All individuals 'hear backwards in time' within a time window of 400-500ms (Hari, 1995), and as a result, later sounds affect the perception of previous ones. Considering the evidence, Hari and colleagues have proposed that this time window is extended in dyslexic individuals (Hari, 1995).

Sutter and colleagues (Sutter, Petkov, Baynes, & O'Connor, 2000) have further investigated the relative effects of timing and frequency separation on the accurate perception of sound sequences in dyslexic adults. Their group consisted of eight dyslexics and 11 controls. The dyslexic individuals had previously received a clinical diagnosis of dyslexia or language learning impairment and their performance was worse than that of the controls on a measure of reading rate. Stimuli were 50ms tones consisting of one of three different frequencies. 'Background' tones were 1000Hz sinusoids, which repeated throughout the sequence. 'Middle' tones were 1030Hz sinusoids, occurring randomly in the sequence immediately before 'high' tones, which were presented at varying frequencies. The middle and high tones comprised the targets and the participants' task was to judge whether two (one target) or three (two targets) tones were presented within each sequence. In addition to varying the frequency of the high tone, the ISI between tones, while constant within a sequence, was

varied across trials (between 25ms and 225ms). The ability to correctly identify three tones in the three tone sequence was measured in the participant groups.

The ability to perceive both of the target tones is dependent on the ISI between tones and the frequency separation between the middle and high tone. Thus, with short ISIs and large frequency separations, the perception of the middle tone is impaired as it is perceptually grouped, or 'captured' within the sequence of repeating background tones.

Sutter et al. found that the dyslexics were worse than the controls at correctly identifying the three tones and that this group difference was frequency dependent. While performance was similar across the groups with small frequency separations between middle and high tones (100Hz and below), at higher frequency separations the performance of the dyslexic group dropped dramatically and significant group differences were obtained. Across both groups, performance improved with longer ISIs and smaller frequency separations. However, within the dyslexic group the interaction between frequency separation and ISI was significant, suggesting that the group differences in performance depended on the frequency separation alone.

The results suggest that dyslexic individuals suffer from disruptive capture effects, leading to impairments in the appropriate grouping of sounds. Sutter and colleagues point out that the dyslexics' difficulties were not related to the timing of the auditory stimuli, but rather in perceiving the sound frequency. Furthermore, the frequency processing deficits were not related to local frequency processing but rather global processing, as the dyslexic group's problems became more severe with increasing as opposed to decreasing frequency separations between tones. The authors argue that such grouping differences can account for the reduced frequency discrimination abilities of dyslexic groups (see section 3.3.4), as the stimuli may be captured inappropriately by one another. Sutter et al. (2000) relate these results to the findings of Dougherty et al. (1998) who also found that dyslexic individuals were impaired in their ability to extract signal from noise. The group argue that these results, in addition to the streaming results of Helenius et al. (1999b), may reflect that dyslexic individuals have difficulties

constructing scenes of the auditory world, which may in turn lead to problems extracting speech streams for noisy backgrounds. The mechanism for such a deficit, they suggest could be an extended time window within which the interference effects of surrounding auditory inputs impair the perception of one another (in line with Hari & Kiesila, 1996).

Considering the hypothesis that dyslexic individuals have a prolonged time window within which subsequent stimuli interfere, Hari and colleagues have proposed that this prolongation could be related to impairment of attentional mechanisms (Hari & Renvall, 2001; Hari, Renvall, & Tanskanen, 2001; Hari, Valta, & Uutela, 1999b). The result of such impairment would be sluggish attentional processing, i.e. dyslexic individuals take longer to disengage attention from previous targets. Data from a visual study (Hari et al., 1999b), which found that attentional blink times were prolonged in their dyslexic group, have led the authors to propose that such deficits could be present throughout sensory modalities. Considering the relationship between magnocellular systems and the control of covert (automatic) attention (Steinman, Steinman, & Lehmkuhle, 1997), Hari et al. go on to suggest that prolonged attentional dwell times could result from inefficiencies in the magnocellular system. Furthermore, data suggesting a right visual field advantage for visual temporal ordering tasks (Hari et al., 2001), have been interpreted as reflecting a mild left-sided 'minineglect', or right-sided spatial bias, in dyslexia. A review of this account is provided in Hari & Renvall (2001).

3.4 Physiological Studies

3.4.1 Organisation of the Auditory System

Kaas and Hackett (2000) and Kaas, Hackett and Tramo (1999) have reviewed a number of studies exploring the cortical auditory system of monkeys and considered evidence for a hierarchical model of auditory processing. Within auditory cortex, three fields with similar primary features form an auditory core, which is immediately surrounded by a narrow belt of secondary fields. In addition a more lateral parabelt of fields reflects a third level of auditory processing.

The three core fields are distinguished by different systematic representations of the cochlea, they behave like areas of primary sensory cortex and have dense thalamic inputs. These core areas are highly interconnected and so must influence one another strongly. Each core area projects to and appears to be responsible for activation of adjacent belt areas. Belt areas can therefore be considered to represent an obligatory second stage of cortical processing. Belt areas in turn connect with adjoining and distant belt areas in addition to areas of the parabelt and frontal lobe. The parabelt fields have few connections with core fields and activation of this area appears to depend largely on belt inputs. Functional distinctions in the parabelt may exist but are not evident in the architecture. The parabelt's interconnections with portions of the temporal, parietal and frontal lobe can be considered as evidence of additional fourth levels of auditory processing.

The spectral, temporal and spatial features of auditory inputs modify the rate and timing of activity of individual neurons in core and belt areas. While neurons in the core respond preferentially to pure tone stimuli, those in the belt respond preferentially to narrow band noise. In addition, these lateral belt neurons fire more vigorously during stimulation with species-specific noise. The results reviewed appear consistent with the view that spectral and temporal features of sound are encoded in core areas and then integrated in belt and parabelt areas to form representations of auditory objects (including spatial locations). The parabelt's connections with heteromodal and supramodal cortices may reflect multimodal integration and higher level influences on the formation of auditory percepts.

Equivalent evidence of hierarchical organisation of processing exists in the human auditory cortex. Scott and Johnsrude (2003) review evidence with specific reference to speech perception. While tuning of the speech signal probably occurs earlier, speech-specific operations are unlikely to occur prior to the signal reaching cerebral cortex. Activation of HG (identifiable as 'core' auditory cortex in humans) is evident in response to any auditory input and not specific to speech.

Functional imaging studies examining the perception of speech and other complex sounds in humans suggest a hierarchy of processing extending from human

equivalents of core regions, through belt, parabelt and more distant areas (see review by Scott and Wise, 2003). Regions immediately anterolateral to the core (possibly in the belt or parabelt) appear to be selective to inputs with spectrotemporal structure e.g. harmonic complexes, frequency modulated, and amplitude modulated sounds. Phonetic cues and intelligible speech activate regions of the superior temporal gyrus at the possible location of human parabelt cortex. However, these activations can not be spatially distinguished from responses to harmonic tones, frequency-modulated tones and sounds with a changing spectral structure suggesting a degree of parallel processing of the speech input. Activation specific to intelligible speech is measured in the left anterior superior temporal sulcus. Activation of this area, which responds to multimodal stimuli, appears to reflect an anterior route to processing beyond auditory cortices. Evidence suggests that parallel posterior routes extending to parietal cortex and ventrolateral and dorsolateral frontal cortex may also exist. While the anterior system may be vital for the mapping of acoustic-phonetic cues onto lexical representations, the posterior system may process articulatory-gestural representation of speech acts.

3.4.2 The Auditory Evoked Response

The auditory evoked response (AER) is constructed of several components, which can be divided into those constituting early latency responses (the auditory brainstem response), middle latency responses and late latency responses.

The auditory brainstem response consists of seven positive waves occurring within 10ms after presentation of auditory stimuli. The scalp measured response represents far field potentials generated by fiber tracts and nuclei of the ascending auditory pathway, although there is still some dispute concerning the exact origin of each waveform (Moeller, 1998). Depth electrode recordings in humans have suggested that wave components II and I are generated by sections of the eighth cranial nerve and that wave III appears to arise from the cochlear nucleus. Later waves may share multiple generators as opposed to a single anatomical source. For example, wave IV may receive contributions from the superior olivary complex, cochlear nucleus and lateral lemniscus. Wave V is likely to arise primarily from the lateral lemniscus as it enters the inferior colliculus.

Middle latency auditory responses occur between 10-80ms after the onset of an auditory stimulus and are characterised by multiple components. Liegeois-Chauvel, Musolino, Badier, Marquis and Chauvel (1994) examined the generator locations of middle latency components with use of intracerebral recording procedures, by exploiting variable latencies recorded across neuroanatomical regions. They found evidence that distinct but spatially overlapping subpopulations of neurons within the auditory cortex contribute to the measured potential. An early sequence of negative-positive waves, on which oscillatory activity is superimposed, was recorded from primary auditory cortex located in the dorso-posterior tip of Heschl's Gyrus (HG). The first three components (N13, P16 and N30) characterise the primary response to click stimulation.

The generator of the P50 component was more laterally and widely distributed, its generator was localised in the primary area, close to the boundaries between the primary and secondary auditory areas. Later components (N60 and N75) originated from lateral parts of HG in secondary auditory areas. Generators of N30 and P50 appeared to be more focal than the later peaks (N60, N75 and N100). The AEPs recorded in right and left primary auditory cortices had similar latency and amplitude characteristics confirming that the primary cortices of the two hemispheres are similarly organised.

Liegeois-Chauvel and colleagues proposed that evidence of parallel and sequential processing in the auditory system was available in the data; the focal localisation of early generators may reflect stimulus-specific thalamo-cortical projections, while the distributed localisation of later waves may reflect a combination of thalamo-cortical projections and widespread cortico-cortical connections.

3.4.3 The N1 and MMN Components

In the present studies two components of the late latency evoked response (N1 and MMN) are investigated and as a forward to the following review of physiological studies, it is useful to briefly review these two components.

Furthermore, Näätänen's (1990) model of auditory attention is outlined as theorists proposing that low-level auditory deficits reflect impaired attentional processes in the dyslexic population often cite it.

The N1 response is a late exogenous (i.e. stimulus driven) component of the auditory evoked response, which has a negative peak when recorded electrophysiologically. It is primarily sensitive to level changes and typically peaks 100ms after the onset of a sound (or for sounds with long enough durations, after the offset) (Näätänen, 1992).

Vaughan and Ritter (1970, cited in Näätänen & Picton, 1987) proposed that the generator of the N1 response was located in the primary auditory cortex. However, there is now evidence of multiple generators (Liegeois-Chauvel et al., 1994). Reviewing the evidence from a number of early studies, Näätänen & Picton (1987) concluded that the 'true' N1 response consists of three independent components. The first has a generator located in the primary auditory cortex (the supratemporal component), which is tangentially oriented. MEG recordings have localised this generator to the lateral part of Heschl's gyrus. The second generator is located in auditory association cortex with a radial orientation (thus, it may not be measured in MEG recordings). The third constitutes the non-specific component i.e. the onset of a stimulus in any modality will trigger activation of this component. The location of this generator is not certain, although Näätänen (1992) postulates that it may be located in frontal motor or premotor areas. Again, evidence from simultaneous EEG and MEG recordings has suggested that this generator does not contribute to the magnetically recorded N1m (Näätänen & Picton, 1987). Therefore, MEG recordings reflect only the contribution of the supratemporal N1m component.

N1 amplitude rapidly deteriorates over the first few stimulus repetitions, stabilising after two or three stimulus presentations. With rapid rates of stimulation (e.g. below 2s) the amplitude of the response to the second stimulus is around half of the original amplitude (Ritter, Vaughan and Costra, 1968, cited in Näätänen & Picton, 1987). When the first stimulus in a sequence is preceded by a visual stimulus, the amplitude of N1 in response to the auditory stimulus is greatly

reduced, suggesting that the exceptionally large response to the first stimulus in a sequence is mainly due to a large nonspecific N1 component, which is not elicited by subsequent stimuli.

Temporal recovery function refers to the progressive increase in amplitude of an evoked response as ISI increases. Hari et al. (1987, cited in Näätänen, 1992) demonstrated that N1m amplitude increased as SOAs between noise bursts increased from 1-9s. The reduction in N1m amplitude at faster rates of presentation is not thought to reflect habituation processes, as it cannot be reversed by dishabituating procedures i.e. recovery with no change in the stimulus eliciting the response (Budd, Barry, Gordon, Rennie, & Michie, 1998). Therefore, N1 amplitude reduction over the stimulus sequence must reflect refractoriness within the neural generators. However, the physiological mechanisms underlying these rate effects are not well understood. It is unlikely that they reflect true refractory periods, as synapses do not tire so quickly or recover so slowly. Rather, it is likely that complex neuronal circuits resulting in inhibitory processes underlie these effects (Näätänen & Picton, 1987).

Variations in N1 amplitude are directly related to detection ability. N1 amplitude is typically enhanced when the participant attends to the stimuli. Furthermore, higher levels of alertness lead to enhanced N1 amplitude even in unattended conditions. However, Näätänen & Picton (1987) argue that the excitability increase should not simply be interpreted as increased arousal, but also as being mediated by a general increase in sensory sensitivity.

In addition to marking the onset of a stimulus, N1 can also be evoked in response to a change in the frequency of a continuous stimulus. However, this is likely to reflect selective refractoriness of generators as opposed to a specific response to the stimulus change (Näätänen & Picton, 1987). The new stimulus appears to activate 'fresh' neuronal elements, not active in response to the preceding stimuli. Näätänen, Sams et al. (1987, cited in Näätänen & Picton, 1987) demonstrated the stimulus specificity of N1. Test tones of 1000Hz were presented alongside intervening tones, which varied in frequency between blocks. The N1 amplitude increased as the frequency separation between test and intervening tones was

increased. These effects are probably mediated by the degree of overlap between the neuronal populations activated by the two stimuli. Indeed, studies of source localisation for N1 in response to stimuli with different frequencies demonstrate tonotopic mapping of the auditory cortex (Pantev et al., 1995). Thus, N1 amplitude is mediated by both the time from last stimulus and similarity between stimuli.

The N1 component is not directly related to perception of pitch. Butler (1972) found that the presentation of a 1000Hz AM tone with a modulation frequency of 200Hz affected N1 to a subsequent 1000Hz tone much more than it affected N1 to a subsequent 200Hz tone, despite the fact that the perception was of a 200Hz tone

In stark contrast to the attenuation of the N1 response with presentation rates below 9s, Loveless, Hari, Hamalainen, & Tiihonen (1989) noted enhancement of the response to the second stimulus of a pair separated by short SOAs (below 300ms). The authors related this enhancement with psychoacoustic parallels occurring within the same time frame. For example loudness enhancement refers to the phenomenon by which the perceived intensity of a second tone in a pair is increased when the stimuli are separated by between 50-150ms (Irwin and Zwislocki, 1971, cited in Loveless et al., 1989).

Investigating the enhancement effect further, Loveless, Levanen, Jousmaki, Sams, & Hari (1996) determined that the supratemporal N1 response is actually generated by two components: The first, $N1m^P$, peaks at a latency of around 90ms; The second, $N1m^A$, peaks at a latency of around 140ms and in a slightly more anterior location. In most situations the relative contribution of $N1m^A$ is relatively very weak, explaining why the supratemporal N1m is well modelled by a single pair of bilateral ECDs. However, in a tone pair paradigm with SOAs below 300ms, the contribution of this component is enhanced.

McEvoy, Levanen, & Loveless (1997) investigated the temporal recovery properties of these two components. They presented participants with tones separated within pairs by a constant ISI of 210ms and between pairs by a variable ISI. For the $N1m^P$ component, the defining variable was the time elapsed since

the presentation of an identical stimulus. Thus this response is always reduced to the second stimulus with a 'same' tone pair or in response to single stimuli presented with fast repetition rates. This is in line with the previous literature on the recovery function of the supratemporal N1. In contrast, the $N1m^A$ component demonstrated very complex temporal dependency. In response to a single stimulus or to the first stimulus in a pair, it had a longer recovery function than $N1m^P$. However, in response to the second stimulus in a pair the $N1m^A$ component actually increased as SOAs decreased. Thus, the authors concluded that temporal integration processes govern the activity of $N1m^A$.

McEvoy et al. (1997) have suggested that complex excitatory and inhibitory responses govern the activation of the $N1m^A$ component. They propose that a stimulus driven volley of excitation activates a large response in a population of neurons, which spread excitation via association fibres to surrounding neurons. In addition, activation spreads to inhibitory interneurons. The spread of excitation would develop over a few hundred milliseconds and would serve to integrate perceptual inputs over a few hundred milliseconds. In turn, the subsequent spread of inhibitory activation would result in the inhibition of the original pool, gradually deteriorating over time. Any inputs occurring during the secondary excitation caused by the initial stimulus, but before the onset of inhibition will result in an enhanced response due to the summation of successive responses; hence the enhancement of supratemporal N1 in response to successive stimuli occurring within 200ms. Inputs arriving after the onset of inhibitory activation will result in a response decrement due to inhibitory action; hence the attenuation of supratemporal N1 in response to successive stimuli occurring within 200ms-9sec. Finally, inputs arriving at even greater intervals will result in larger responses as the inhibitory action decreases over time; hence the recovery of supratemporal N1 with ISIs exceeding 9sec. Thus the enhancement of the $N1m^A$ component seems to reflect persistence due to temporal integration (Loveless et al., 1996).

The MMN is a negative component of the auditory evoked response, elicited in response to a change in the ongoing auditory environment i.e. when a 'deviant' stimulus is embedded in a sequence of frequent 'standard' stimuli (Naatanen,

1997). It typically peaks between 100-200ms from change onset (Sinkkonen & Teraniemi, 2000).

MMN can be elicited in response to any discriminable change, for example; frequency, duration, intensity, sound origin. It can also be elicited in response to violations of abstract rules (e.g. by a descending tone pair in a sequence of ascending tone pairs (Tervaniemi, Maury, & Näätänen, 1994)). As the magnitude of stimulus deviation increases, the MMN component increases in amplitude and decreases in latency. Furthermore, detection accuracy is related to the amplitude of the response, suggesting a link between the processes underlying MMN and perceptual change detection (Jaramillo, Paavilainen, & Näätänen, 2000). Importantly, MMN can be measured with complete absence of attention (Winkler et al., 1995) and is thought to be largely unmodulated by attention. Thus, it reflects pre-attentive processing in the auditory system (Näätänen & Tecler, 1991).

Evidence to suggest that the MMN does not simply reflect the activation of new afferent elements comes from the observation that the response can be elicited by a complete stimulus omission (Yabe et al., 1995). Rather, MMN is generated by a process that compares auditory inputs against a trace of recent inputs stored in Sensory Memory (Näätänen & Alho, 1997). MMN is not elicited in response to deviants separated from standards by more than 10 seconds (Sams, Hari, Rif, & Knuutila, 1993), thus suggesting that the neural representations of standards decay over this time period. This estimate is close to Cowan's (1984) estimate of the duration of the active phase of Sensory Memory.

The MMN response does not only reflect transient sensory traces but also long term ones (Huotilainen, Kujala, & Alku, 2001). The response demonstrates long-term training effects; responses evoked toward the end of an extended session with complex stimuli are enhanced relative to those measured at the start of the session. This enhancement is directly related to improved detection accuracy (Näätänen, Schroger, Karakas, Tervaniemi, & Paavilainen, 1993).

Two distinct generators contribute to the electrically recorded MMN. The first mediates the change detection mechanism and originates on the supratemporal plane in the auditory cortices, slightly anterior to the supratemporal N1 component with a tangential orientation (Alho et al., 1998). The specific locus of this generator is believed to be mediated by the type of stimulus change (Schairer, Gould, & Pousson, 2001). The second generator is located in frontal cortex, mainly in the right hemisphere. This generator is triggered by the temporal change detection mechanism and appears to be associated with the initiation of an attention switch to the change (Rinne, Alho, Ilmoniemi, Virtanen, & Näätänen, 2000). Studies employing simultaneous EEG and MEG recordings have determined that the generator is probably either radially oriented or located deep in the brain as it does not contribute to the magnetically recorded response (Rinne et al., 2000).

Näätänen (1990) has developed a model of auditory attention. It posits that auditory stimuli receive complete encoding of all physical characteristics (e.g. frequency, duration) via a 'Permanent Feature-Detector System'. Processing of such stimulus characteristics can occur in the absence of directed attention. During the encoding phase, the outputs from different feature-specific analysers and their combinations are integrated in the time domain into unitary stimulus 'events' and the outcomes of this analysis enter Sensory Memory, where they are stored and remain active for a short time. In parallel, a 'Transient-Detector System' encodes the onsets and offsets of stimulus energy but not the qualitative aspects of these events. As new auditory events are encoded into Sensory Memory, they are compared to current events already held within this system whose representations are active. If a difference is detected, a change detector mechanism will register this mismatch. When the outputs of the Transient-Detector System and the change detection system exceed a certain threshold, conscious perception is triggered, causing executive mechanisms to examine the contents of Sensory Memory.

The event-synthesis stage of the Permanent Feature-Detector System's processing reflects Cowan's (1984) short phase of Sensory Memory, which lasts only 200-300ms (Näätänen, 1990). This phase is regarded as an intermediate phase

between perception and memory. The time period of integration constitutes the Window of Temporal Integration. It is likely to be this integration process, which mediates the N1m enhancements to second stimuli occurring within 300ms of initial stimuli, as observed by Loveless et al. (1989) and Loveless et al. (1996).

The proposed attention trigger mechanism of the Transient-Detector System may be related to the N1 response (Näätänen, 1990). The supratemporal generator (that recorded with MEG) would provide an estimate of the strength of the attention trigger signal generated by the Transient-Detector System mechanism. In addition, the generator mechanism of the frontal nonspecific component (not measured with MEG) may be involved in the attention switch function. The threshold of the attention trigger response would be mediated by anticipatory attention (top-down) for example, related to the nature of the task. Therefore, when attention is directed to the stimuli, the threshold will be low and the signal will be facilitated (for example, the enhancement of N1 in active task conditions).

A second route to attention triggering is also proposed in the model, via the Sensory Memory store. Thus, stimulus change detection (against the neural representation in Sensory Memory) occurs initially and preconsciously at the generator of the supratemporal MMN subcomponent. In turn, the frontal MMN component may underlie the attention-switching function.

The long-term effects of Sensory Memory evidenced by training effects on the MMN suggest that there is also a long-term system of storing purely sensory information. Näätänen (1992), therefore, argues that the separation of Sensory Memory should be understood in functional as opposed to anatomical terms as the trace system forms the neuroanatomical basis of both short term and long term memory. Thus Sensory Memory can be divided into three consecutive phases, occurring within the same system: the very short phase, associated with encoding stimulus characteristics and integrating events over 200-300ms; the short phase, associated with the active duration of traces in Sensory Memory (accounting for the absence of MMN with ISI greater than 9sec); the long or permanent phase, associated with the passive, inactivated system for long term storing of sensory information.

3.4.4 Responses to Brief and Rapidly Presented Stimuli

Section 3.3.1 reviewed evidence that suggested dyslexic individuals are poorer than controls in tasks requiring the processing of brief and rapidly presented stimuli. A number of studies have also been conducted to examine the physiological responses of dyslexic groups to such stimuli.

In order to examine the effects of stimulus timing Neville, Coffey, Holcomb, & Tallal (1993) presented sequences of tone stimuli at varying ISIs to a group of 22 learning impaired children and 12 age, sex and IQ matched controls. While these individuals were not specifically selected for their reading abilities, all of the learning impaired participants had severe reading impairments. Standard stimuli were 2000Hz tones, while deviants (presented with a probability of 10%) were 1000Hz tones. The participants were asked to indicate when they detected a deviant in the stimulus sequence.

Neville and colleagues found that the learning impaired group were significantly slower at detecting the deviant tones across all ISI conditions, although the interaction between ISI and participant group was not significant. Furthermore, ERPs evoked in response to the stimuli were equivalent across the groups.

However, when Neville et al. reclassified these participants into those who did and did not perform well on Tallal's repetition test, they found that those learning impaired children with poor scores on repetition tests also performed more poorly as ISIs decreased in the present task. In addition, the N140 component (the child equivalent to the adult measured N1 response) recorded in response to standard tones was significantly reduced and delayed in this group.

Considering the fact that low-level auditory processing anomalies were only observed in a subset of learning impaired children who performed poorly on repetition tasks, the group concluded that deficits in the processing of stimuli which are rapidly presented only exist in a sub sample of the learning impaired and reading disabled population.

Duffy, McAnulty, & Waber (1999) also examined the effects of presentation rates on auditory ERPs in a group of learning impaired children. The large population of 136 children were taken from a clinic treating learning impaired individuals and from a normal school population. The entire participant pool was grouped in terms of their reading abilities, and then separately in terms of scores on Kaufman Matrices (a test of non-verbal reasoning). ERPs were recorded in response to the presentation of brief complex tones either alone or in pairs with varying ISIs.

The group analysed ERP responses in terms of regions of interest, employing t-statistic significance probability mapping techniques in order to elucidate group differences. The ERPs evoked by tone pair stimuli were better able to predict reading group membership than ERPs evoked to single stimuli presented in isolation. In contrast ERP data were not able to separate the children on the basis of matrices scores. Thus, the authors proposed that the disruptive influence of presenting stimuli within pairs led to inaccurate processing of the individual stimulus components, perhaps due to forward and backward masking effects.

The group replicated these results in a study that also included a verbal stimulus condition (Valencia, McAnulty, Waber, & Duffy, 2001). However, in a subsequent study (Duffy, Valencia, McAnulty, & Waber, 2001) the same group found that, employing regression analyses, ERP responses to the verbal stimuli were more successful at predicting group membership across the sample (e.g. good or poor reader) than ERP responses to tone pairs. Thus, they have argued that problems with phonemic discriminations more than low-level auditory deficits are central to dyslexia.

Nagarajan et al. (1999) used a 37-channel MEG system to examine the cortical processing of brief and rapidly presented stimuli in dyslexic individuals. Seven poor readers and seven age and sex matched controls were recruited. All were adults and the majority were female (five in each group). Poor readers were selected on their poor performance on standard tests of reading words and non-words. In addition, these individuals were impaired on a temporal ordering task like that used by Tallal (1980). Selection of participants included the additional criterion that all individuals should have normal detection and discrimination

thresholds for tones at the frequencies employed. The authors justified inclusion of this criterion as a means of ensuring that participants could complete the task. However, this contradicts the findings of Tallal and others who determined that the dyslexic individuals' difficulties in tone pair ordering tasks actually reflected their inability to discriminate between the tones (see section 3.3.4). Stimuli were pairs of tones, each 20ms in duration. Two possible tones were used, one a 800Hz tone and the other a 1200Hz tone (labelled low and high, respectively). ISIs between the tones were either 100, 200 or 500msec. Tone pairs were presented in sequence combinations (either high-high, low-low, high-low, or low-high) and participants had to recreate the sequences with button presses. 100 trials were obtained at each ISI and MEG recorded responses were averaged.

Performance data corresponded with previous findings (see section 3.3.1); while control participants performed the task with almost no errors, poor readers performed poorly at short ISIs. In order to analyse evoked responses independent of spatial location, root-mean-square (RMS) waveforms were computed across the 37 channels for each point in time. The amplitude of N1m responses to the first stimuli within pairs were equivalent between groups, while response amplitudes were increased in the poor readers 150-200ms after this initial stimulus. Furthermore, differences were obtained in the N1m responses evoked by the second stimuli between groups.

N1m responses to first and second stimuli were not significantly different between the groups in the 500ms ISI condition. However, in the 200ms ISI condition the N1m response to the second tone was significantly reduced in the experimental group relative to the control group. In order to control for the fact that the response to the second stimulus in the 100 and 200ms ISI conditions would be contaminated by the ongoing response to the first stimulus, RMS difference functions were created; the RMS response evoked by a single stimulus was subtracted from the response evoked by a stimulus pair. N1m responses to second tones were significantly weaker in the dyslexic group compared to the control group in the 100ms and 200ms ISI conditions. In addition, weaker cross-sensor coherence was reported in the experimental group, particularly at shorter ISIs.

These results then, seem to support the psychophysical data suggesting impaired processing of brief and rapidly presented stimuli in dyslexic individuals. The authors have suggested that the poor readers may have a longer period of inhibition after an initial stimulus event. They argue that as the initial stimulus event appeared to generate a stronger response in the poor readers (reflected in the observation of increased response amplitudes 150-200ms after this initial stimulus), it could follow that the post-stimulus inhibition may also have been stronger in these individuals. Prolonged or deeper inhibition may lengthen the recovery time of the cortex. Hari & Renvall (2001) argue that this suppression of second tone responses can be accounted for by the dyslexic group's sluggish auditory processing, i.e. slowed attentional shifting from the first stimulus to the second.

As noted above, this study could be criticised on the grounds that it included dyslexic participants demonstrating impairments on temporal ordering tasks but excluded individuals who had difficulties with frequency discriminations, contradicting the conclusions of Tallal and others. Perhaps the poor readers did have discrimination difficulties, which were simply not identifiable with simple behavioural measures. Such deficits could surface as a result of the increased task demands, i.e. the additional stress imposed by reducing the ISI and asking participants to order the stimuli (Reed, 1989). The proposition that dyslexics' deficits in coding spectral properties of stimuli may surface as stimuli become more brief and dynamic is raised by Ahissar et al. (1999).

Considering the stimulus specificity of the N1 response (section 3.4.1), it is possible that the dyslexic group's attenuation in second tone responses reflects the fact that tones of differing frequency were not coded as 'new' stimuli. Unfortunately, Nagarajan et al. (1999) do not separately report the data for responses to same-same pairs (high-high or low-low) and same-different pairs (high-low or low-high), a comparison which may have shed some light on such a possibility.

A final criticism of the study is the nature of the temporal ordering task itself. Such a complex task confounds results as it introduces additional demands of

memory and attention. Furthermore, additional cognitive processes include the generation of motor responses and possibly even language processing (if participants were verbally labelling the stimuli in order to recall their order). A simpler task design could reduce these confounding factors.

Merzenich, Schreiner, Jenkins, & Wang (1993) have proposed that dyslexia may result from increased integration and stimulus persistence periods at preconscious levels of sensory processing, i.e. temporal integration of information into Sensory Memory (see section 3.4.1). The group argue that measures of such periods shorten throughout development and propose that the deficits dyslexic participants demonstrate in tasks requiring the perception of rapidly presented stimuli may reflect a developmental failure in the refinement of these integration periods. Considering Hari et al's. proposals that dyslexics' deficient processing of rapidly presented sounds results from prolongation in a time window within which successive inputs interfere with one another (see sections 3.3.7 and 3.3.8), Loveless & Koivikko (2000) examined whether the mechanism for such a deficit was a longer than normal time window of temporal integration into Sensory Memory.

The persistence in temporal integration processes can be directly measured by examining the enhancement of N1m in response to stimuli occurring within short time windows (see section 3.4.1). Thus, Loveless & Koivikko (2000) predicted that if the dyslexic deficits do result from an extended period of integration, this enhancement effect should be displaced to longer time intervals than in control listeners.

Their participant group consisted of 10 dyslexic and 15 control adults. 50ms noise bursts were presented in pairs with variable SOAs. Participants were instructed to ignore the stimuli while MEG responses were measured. Loveless and Koivikko then examined the amplitude of N1m responses to second noise stimuli. The averaged data to stimuli in the 500ms SOA condition were subtracted from those in the shorter SOA conditions, in order to eliminate the effects of overlapping responses. N1m amplitude values in response to the second stimuli were taken from the channel with the maximum signal and were expressed

as a percentage of the response amplitude to the first stimuli. This relative amplitude measure eliminated the effect of any overall differences in N1m amplitudes between groups or individuals (the group do not report whether there are group differences in N1m amplitudes to first stimuli).

The results did not demonstrate the predicted displacement of N1m enhancement to longer SOAs in the dyslexic group; in fact the opposite result was obtained. While N1m responses to the second noise were significantly enhanced relative to the responses to the first noise for SOAs up to 230ms in the control group, in the dyslexic group significantly larger amplitude values were only obtained in the 70 and 150ms ISI conditions. Thus, rather than a displacement of the enhancement effect to longer SOAs, the enhancement effect fell away at shorter SOAs in the dyslexic group. Loveless & Koivikko (2000), therefore, argue that sluggish auditory processing in dyslexic individuals is not explained by a longer than normal window of sensory temporal integration. As an alternative account they propose that the observed auditory deficits may be due to sluggish attentional shifting, as proposed by Hari et al. (2001). As the N1m response reflects attentional triggering mechanisms (see section 3.4.1), such a deficit could explain the absence of an enhancement effect at SOAs of 230ms in the dyslexic group (Loveless & Koivikko, 2000).

Auditory ERPs evoked in response to speech stimuli containing a transition from fricative to vowel sounds (for example 'hei') consist of an initial N1 followed by N1' (marking the onset of the transition to the vowel) (Kaukoranta et al, 1987, cited in Renvall & Hari, 2002). Renvall & Hari (2002) used MEG to measure similar N1m- N1m' responses to a noise burst immediately followed by a 400ms square wave of 250Hz in a group of nine dyslexic and 11 controls. The SOA between onsets of transitions (noise/square wave stimuli) was always 1100ms and the noise duration was varied within conditions, resulting in different ISIs between transitions. Equivalent current dipoles were modelled to explain the N1m and N1m' responses and the resulting waveforms were analysed in terms of latency and amplitude.

The amplitude of the N1m response was significantly smaller in the dyslexic group with noise durations of 200ms (both hemispheres) and 100ms (right hemisphere only). In addition, in the control group the N1m' amplitude increased with increasing noise duration, mimicking the effect observed when the duration of the fricative is increased in fricative/vowel combinations (Kaukoranta et al, 1987, cited in Renvall & Hari, 2002). However, this enhancement in N1m' amplitude with increasing noise duration was significantly weaker in the dyslexic group; no enhancement was observed in the left hemisphere and the enhancement in the right hemisphere between 100ms and 200ms noise duration conditions was only very subtly present. These results suggest deficits in the auditory cortical processing of such transitions in the dyslexic group. Renvall & Hari (2002) argue that these brief auditory stimuli are capturing less attention in the dyslexic listeners.

While the findings of the studies reviewed above provide evidence that N1 responses to low-level auditory stimuli are abnormal in dyslexic population, a contradictory result is reported by Helenius, Salmelin, Richardson, Leinonen, & Lyytinen (2002). These researchers recorded magnetic fields in response to simple 1000Hz tones, natural speech sounds and complex non-speech sounds (composed of formant frequencies contained in the speech sounds) in a group of 10 dyslexic adults and nine controls. When participants were asked to actively discriminate the speech sounds, the N1m amplitude in response to the first syllable was larger in the dyslexic group, while the N1m latency in response to the second syllable was significantly delayed. In an equivalent condition where participants were instructed to ignore the stimuli, the N1m amplitude in response to the first syllable was again significantly larger in the dyslexic group. In contrast, no group differences were observed in response to the simple and complex non-speech stimuli. Thus, the authors argue that the abnormally strong response seen in the dyslexic group reflects a speech specific deficit. They suggest that this increased level of response to speech stimuli may reflect the activation of an abnormally large non-specialised neuronal population in dyslexic individuals.

3.4.5 Responses to Spectral Contrasts

A number of researchers have argued that the problems dyslexic individuals face with temporal order judgement and tone pair discrimination tasks actually arise from their impaired ability to discriminate between fine spectral contrasts (section 3.3.4). Frequency discrimination abilities can be measured physiologically in frequency deviant MMN paradigms.

Baldeweg, Richardson, Watkins, Foale, & Gruzelier (1999) measured MMN responses to pitch deviants in 10 independently diagnosed dyslexic adults and 10 normal controls matched for age, sex and handedness. Stimuli were 50ms pure tones; the standard 1000Hz tone had an 80% probability, while each of four deviants (1015, 1030, 1060 and 1090Hz tones) had a 5% probability. In another condition, MMNs were evoked in response to duration deviants. The paradigm was identical, except that all tones had a constant frequency of 1000Hz with varying durations; standard tones were 200ms long while the four deviants were 160, 120, 80 and 40ms long. 1000 tones were presented for each condition block with ISIs of 500msec. Participants were instructed to ignore the tones and perform a visual motion detection task.

N1 amplitude and latency were measured as the maximum negativity occurring 80-140ms after stimulus onset. The average latency and amplitude of the N1 response did not differ between groups in either the frequency or duration conditions.

MMN waves were constructed and defined as the difference between the response to deviants and standards. MMN had to be identifiable as the maximum negativity after the N1 peak. MMN onset and offset were estimated visually as maximum positivity immediately before and after MMN peak.

Initially examining group mean average waveforms Baldeweg and colleagues found that the groups did not differ in their response to the largest deviants in either the frequency or duration conditions. However, differences in MMN responses between the groups were evident in response to the smallest deviants in each condition. While MMN to the lowest duration deviants could be identified

in both groups, MMN in response to the lowest frequency deviants were not visible in the dyslexic group. As the degree of deviance reduced in this condition, the abnormality of the dyslexics MMN responses increased. In contrast, MMN waveforms in response to duration deviants were largely similar across the groups

Statistical comparisons revealed that MMN onsets and peak latencies were significantly longer and MMN durations were significantly reduced in the dyslexic group relative to the controls across all frequency deviants. While there was no group difference in MMN peak amplitude, MMN area (a more sensitive measure) was significantly reduced in the dyslexics. No significant group differences were obtained for duration deviant measures.

The physiological data were supported by performance data collected during another run of the above procedure. The only modification to the study design was that ISIs were increased to 1000ms and participants were asked to push a button when they heard a deviant tone. Furthermore, significant correlations in the dyslexic group were obtained between MMN latency data and reading measures for words and non-words. No correlations were significant in the dyslexic group for duration deviant measures or in the control group for either measure.

Baldeweg et al. (1999) have interpreted the finding of normal N1 responses across conditions and normal MMN responses to duration deviant stimuli in dyslexics as suggesting normal action of the Transient-Detector System, which encodes stimulus onset and offset (Näätänen, 1992). In contrast, they suggest that the abnormal MMN wave in response to frequency deviants reflects impairment of the Permanent Feature-Detector System (Näätänen, 1992) selective to pitch. They discuss the impaired pitch deviant detection in terms of deficient encoding due to a phase locking impairment, although as noted above, evidence now suggests that such an impairment is unlikely to account for the difficulties demonstrated by dyslexic individuals.

Hugdahl et al. (1998) recorded MMN responses in a group of 25 dyslexic children and 25 matched controls. Stimuli were 50ms tones presented at ISIs of 650ms. In

one condition mismatch responses to frequency deviants were measured (1000Hz standard tone, 1050Hz deviant tone). In another condition, mismatch responses to time gap deviants were recorded (deviant stimulus occurred after an ISI of 500ms as opposed to 650ms). The deviant probability in each case was 10%. Participants were instructed to ignore the auditory stimuli and were given a visuo-spatial distracter task. MMN waves were constructed (standard-minus-deviant) and MMN data were analysed between 108-284ms post stimuli. The peak latency of the MMN response to frequency deviants was significantly delayed in the dyslexic group, while its amplitude was significantly larger. In the time gap deviant condition, MMN latencies were again delayed in the dyslexic group. Furthermore, the interaction between deviant condition and participant group was close to significance; the dyslexic participants were more impaired, relative to controls, in the time gap deviant condition.

The finding of significantly delayed and increased MMN responses in the dyslexic group is unusual. Typically, latency delays correspond with amplitude reductions and vice versa (see section 3.4.1). The finding of a delay in the latency of MMN in response to frequency deviants corresponds with the findings of Baldeweg (1999), in addition to data suggesting that dyslexic individuals are impaired in frequency discrimination tasks (section 3.3.4). However, the increased amplitude of this response contradicts the same findings. The significantly delayed MMN in response to the time gap deviant condition appears to suggest that the encoding of stimulus onsets is impaired, a result that contradicts Baldeweg et al, in addition to data suggesting normal auditory temporal resolution in the dyslexic population (section 3.3.2).

Taken together, the results of Baldeweg et al. (1999) and Hugdahl et al. (1998) do appear to suggest that MMN responses to stimuli deviating in frequency are abnormal in dyslexic groups. However, a number of researchers have failed to find such abnormalities.

Schulte-Korne, Deimel, Bartling, & Remschmidt (1998a) examined MMNs in their sample of spelling disabled and age and IQ matched control children. In a non-speech condition, standard stimuli were 90ms 1000Hz tones, while deviants

had a frequency of 1050Hz. In the speech condition, the standard stimulus was a synthetic /da/ while the deviant was a /ba/. ISI was held constant at 590ms and the deviant probability was 15%. Difference curves (standard-minus-deviant) were constructed to illustrate the MMN wave. Two distinguishable components were identified for MMN curves in response to tones, while three were identified for the speech condition. Therefore, the MMN waves were analysed in terms of time windows. Mean areas under the curves were calculated for each of the time windows.

Mean MMN area was not significantly different between participant groups in response to frequency deviant tones. On the other hand, looking at the MMNs evoked in response to deviant speech stimuli, the mean area under the MMN curve, within the 303-620msec-time window, was significantly reduced in the dyslexic group. Schulte-Korne et al. (1998a) argue that these results suggest that the dyslexics' physiologically measured deficits are specific to linguistic processing rather than general processing of auditory stimuli. These findings were confirmed in subsequent studies with both child (Schulte-Korne, Deimel, Bartling, & Remschmidt, 1999b) and adult (Schulte-Korne, Deimel, Bartling, & Remschmidt, 2001) dyslexic populations.

Reconciling the inconsistencies in findings across frequency deviant studies is difficult because of the various methodologies employed, i.e. the degree of deviance, the measures of amplitude and latency. These inconsistencies are revisited in Chapter 6 (section 6.1.5).

3.4.6 The Frequency Following Response

McAnally & Stein (1996) reported that dyslexic adults have higher MLD thresholds than matched controls (see section 3.3.6). This led the authors to suggest that such deficits could result from impairments in the generation, decoding or exploitation of phase locked discharges. In an attempt to objectively measure phase locking in the brainstem, they also recorded the Frequency Following Response (FFR). Stimuli were 100ms tone bursts with frequencies of 200Hz, 400Hz, 600Hz and 800Hz. Electrodes were fixed and the FFR was averaged over 2000 presentations for each stimulus. The far field potential

evoked by such low frequency stimuli results from the synchronous discharge of phase-locked neurons.

The average amplitude of FFR was significantly reduced in the dyslexic group and the authors argue that such a reduction could reflect impaired phase locking as it reflects reduced synchrony of the discharge. Reduced synchrony of the discharge could in turn lead to problems in the exploitation of these inputs. However, as suggested above, the results of a number of psychophysical studies now contradict the notion of impaired phase locking (see sections 3.3.5 and 3.3.6).

3.4.7 Responses to Dynamically Altering Stimuli

It was noted above that dyslexics were impaired in their ability to temporally track modulations of amplitude and frequency (see section 3.3.5). Recording scalp potentials evoked by AM stimuli (the amplitude modulation following response, AMFR), physiologically measures the ability of the auditory system to follow dynamically changing amplitude. AMFR responses follow the phase of the evoking stimuli. McAnally & Stein (1997) recorded AMFRs in 15 adult dyslexics and 15 age-matched controls. Stimuli were 200ms tone bursts with a carrier frequency of 400Hz. Modulation depth was 100% and variable modulation rates of 20, 40, 60 and 80Hz were employed.

Mean AMFR amplitudes were significantly smaller in the dyslexic group. In addition, the interaction of participant group and modulation frequency was insignificant, reflecting a reduced response across all modulation frequencies. The consistency of the findings across all rates of modulation, in addition to the fact that neither phase nor latency of the AMFR component differed between groups, suggests that the dyslexic participants did not simply have slower responses.

In order to compare the psychophysically measured thresholds for detection of AM as a function of modulation frequency (TMTFs) with physiological responses to AM, Mennell et al. (1999) recorded both TMTFs and AMFR to modulated white noise stimulus in the same group of participants. In section 3.3.5 the results of the psychophysical study were reported; AM detection thresholds were

significantly higher in the dyslexic group across the range of modulation frequencies. Results from the physiological AMFR measures were consistent with the psychophysical data as well as the findings of McAnally & Stein (1997); AMFR amplitudes were significantly smaller in the dyslexic group. Furthermore, the correlation between AMFRs and TMTFs was strong; AMFR amplitudes could predict 78% of the variance in terms of TMTF thresholds. Thus, there is physiological evidence for Witton et al's. proposal (Witton et al., 2002; Witton et al., 1998), that dyslexic individuals demonstrate impairments in their ability to temporally track dynamically changing stimuli.

3.4.8 Response to Sound Sequences

Sections 3.3.7 and 3.3.8 reviewed evidence suggesting that the time window within which successive sounds influenced one another was extended in the dyslexic population. Furthermore, it appeared that the disruptive effects of immediately surrounding sounds were amplified in these individuals.

Rumsey et al. (1994) used PET to record physiological responses during a tonal memory task in a group of 15 severely dyslexic men and 18 matched controls. The participants task was to determine whether tonal sequences presented in pairs were the same or different (response to same, no response to different). This task was difficult for both participant groups. Control participants obtained 81% mean accuracy on the task. However, the dyslexic groups performance was significantly worse, achieving only 68% accuracy. Furthermore, while both control and dyslexic groups activated right and left temporal and right frontal cortex, significantly reduced activation was measured in the right temporal and right frontal cortex sites in the dyslexic group.

Considering their findings that dyslexic individuals demonstrated abnormal MMN responses to speech stimuli but not tone stimuli (Schulte-Korne et al., 1998a; Schulte-Korne et al., 1999b; Schulte-Korne et al., 2001), Schulte-Korne and colleagues went on to investigate the possibility that the speech specific abnormalities, could actually be accounted for by the complex nature of the speech stimuli (Schulte-Korne, Deimel, Bartling, & Remschmidt, 1999a). They argued that the task of distinguishing between the speech sounds, unlike that of

distinguishing between pure tones, required the detection of timing differences of complex auditory patterns within a few milliseconds (temporal pattern processing).

Tonal patterns comprising four tones (two 815Hz tones, one 720Hz tone and one 1040Hz tone) were used. The full duration of the pattern was 215msec. For standard stimuli, the pattern of presentation was as follows; 50ms of the 720Hz tone, followed by 90ms of the 815Hz tone, followed by 25ms of the 1040Hz tone, followed by 50ms of the 815Hz tone. In the deviant stimulus, the placing of the two 815Hz segments (50 and 90msec) was reversed. Importantly, the pitch pattern of the two sequences was identical; the only difference between the sequences was the durations of single tones.

MMN curves were plotted and, on the basis of distinguishable components, the peak amplitudes and latencies were assessed within three time windows (50-130msec, 130-250msec, and 250-600msec). No group differences were found 50-250ms after stimulus onset, but the area under the curve in the last time window (250-600ms after stimulus onset) was significantly reduced in the dyslexic group.

Considering the differences between the standard and deviant stimuli suggested to Schulte-Korne et al. (1999a) that it was the temporal difference between the patterns, which evoked the MMN response (other variables such as frequency and duration were held constant). The researchers argue that the attenuated MMN in the dyslexic group reflects an impairment in this group's processing of temporal information. The fact that differences occurred after 250ms is concurrent with the finding that attenuated MMNs in response to speech stimuli occurred at approx 300-600ms (Schulte-Korne et al., 1998a).

Another group has examined MMN responses to temporal pattern stimuli in diagnosed dyslexic adults (Kujala et al., 2000). Whereas Schulte-Korne et al. (1999a) varied the order of tones within a pattern this group varied the duration of gaps between tones, resulting in a deviant with a different temporal pattern (or rhythm). Participants were eight control and eight dyslexic adults (dyslexics performed poorly of reading and phonological processing tasks). Tone frequency

and duration were held constant at 500Hz and 30ms. In the four-tone pattern condition, the intervals between the four tones in the standard condition (83% of trials) were 200ms, 150ms and 50ms, respectively. In the deviant condition the intervals were 200ms, 50ms and 150msec, respectively. Again the duration of the entire sequence was not varied, but the temporal order of the gaps was varied. Tone patterns were separated by 1200ms SOAs. In the tone pair condition the same 500Hz tone was presented with an ISI of either 150ms (standard) or 50ms (deviant) (this is similar to Hugdahl et al., 1998) time gap deviant condition). Onset to onset intervals between tone pairs were 800msec.

Two consecutive MMN responses were recorded in control participants during the tone pattern condition. Kujala et al. (2000) propose that both responses are evoked as a result of the 'too early' third tone, which occurs after an interval of 50ms in the deviant pattern condition as opposed to after 150ms in the standard condition. The first MMN reflects a response to the processing of this tone as an 'addition'. The second MMN reflects a response to the processing of the subsequent absence of this tone as an 'omission'.

ANOVAs indicated that responses to deviant patterns were significantly more negative than those to standard patterns during three time windows from the onset of the too early stimulus (50-100msec, 200-300ms and 350-450msec). However, in the dyslexic group, no significant difference was found between these responses prior to the 400-450ms time window. MMN amplitudes at 200-250ms were significantly reduced in the dyslexic group. In addition, while the response in the 400-450ms time window was larger in the right hemisphere of the control group, it was distributed evenly over the cerebral hemispheres in the dyslexic group. In contrast, no significant group differences were measured in MMN responses to deviant tone pairs. The results of the physiological analyses were reflected by performance data collected to the same tasks in a separate session; group differences in hit rate were significant in the tone pattern condition, but no differences were found in performance in the tone pair condition.

Considering the latencies of MMN responses Kujala et al. (2000) conclude that MMN differences observed between participant groups resulted from the absence

of the 'addition' MMN in the dyslexics' response. Interestingly, the deviant stimuli in the tone pair condition presented a similar temporal deviation, without the corresponding abnormality of response in the dyslexic group. Kujala et al. (2000) argue that the interference caused by surrounding auditory inputs in the tone pattern condition accounted for this dissociation. Thus, the results can be related to the hypothesis that in dyslexic individuals the disruptive influence of successive auditory inputs is enhanced (see section 3.3.8).

The same group (Kujala, Belitz, Tervaniemi, & Näätänen), refer to as yet unpublished data in their review of MMN studies in dyslexia (Kujala & Näätänen, 2001). In this study participants were presented with tone pair order reversals, which occurred immediately before or after a masking tone. The authors report that MMN responses to these stimuli were diminished in the dyslexic group. Furthermore, this abnormality was enhanced in the backward masking condition. These data appear to suggest that the dyslexic group's responses were more vulnerable to the effects of the surrounding masking input. They correspond with the data of psychophysical studies that demonstrate impaired sensory processing in this population under masking conditions (see section 3.3.7).

3.5 Conclusions

3.5.1 Summary

The weight of anatomical, psychophysical and physiological evidence seems to suggest that abnormalities in the early processing of low-level auditory inputs do exist in dyslexic individuals. Anatomically this is reflected in reduced quantities of large neurons in the thalamus (section 3.2.2). Psychophysically the deficit is reflected in the impaired detection and discrimination of brief and rapidly presented stimuli (section 3.3.1), spectrally contrasting stimuli (section 3.3.4), dynamically altering stimuli (sections 3.3.5 and 3.3.6) and the interference of surrounding stimuli in rapid presentation conditions (sections 3.3.7 and 3.3.8). Furthermore, physiological evidence suggests that components of the auditory evoked potential and field are abnormal in response to the same stimulus types: brief and rapidly presented (section 3.4.4), spectrally contrasting stimuli (section 3.4.5), dynamically altering stimuli (section 3.4.7) and stimuli presented in rapid sequences (section 3.4.8).

A simple (and possibly crude) dissociation can be made between studies proposing that the critical stimulus features are brevity and rapid presentation rates, and those supporting the view that it is stimuli, which vary over time and need to be tracked temporally. The accounts forwarded to explain such differences can also be conveniently placed into the dichotomy of perception of rate and rate of perception, concepts that Studdert-Kennedy & Mody (1995) pointed out were widely confused in the early literature of auditory deficits in dyslexia. Indeed, the term 'temporal processing' is still commonly used to refer to either account. To be clear: Perception of rate refers to the ability to encode temporal aspects of stimulus properties; findings regarding the poor temporal tracking of auditory changes over time provide evidence for such deficits (see sections 3.3.5 and 3.3.6). Rate of perception refers to the speed at which sounds can be processed within the auditory system; results suggesting increased interference from surrounding auditory inputs reflect impairment of this nature (see sections 3.3.7 and 3.3.8). Each of these accounts have been related back to the Magnocellular Deficit Hypothesis, although with reference to different mechanisms. Talcott, Witton, Stein and others have referred to this system's importance in the tracking of temporal information, while Hari and colleagues have suggested that this system subserves the attentional shifting capabilities, which they argue are deficient in the dyslexic population.

3.5.2 A Causal Connection

Theorists reporting low-level auditory deficits make the causal connection between such deficits and dyslexia by implicating poor speech perception. Essentially, the groups argue that deficient auditory processing results in the inaccurate encoding of speech sounds (possibly during critical phases of development), which in turn, result in 'fuzzy' phonological representations. As noted in Chapter 2, section 2.2.3, the most widely accepted view is that poor phonological skills are at the core of the dyslexic population's literacy problems. The proposed nature of the deficit in the encoding of speech sounds differs between theorists, for example, via masking effects resulting in order confusions (Helenius et al., 2002), poor extraction of speech signal from background noise (Dougherty et al., 1998; Sutter et al., 2000), blurring of categorical boundaries

(Tallal, Miller, & Fitch, 1993). In addition some groups have claimed evidence of improvements in speech perception and literacy skills as a result of training with low-level auditory stimuli, providing strong support for such a causal link (Merzenich et al., 1996; Tallal et al., 1996). However, the results of such findings have been disputed (McAnally et al., 1997; Mennell et al., 1999).

Some other groups have suggested that any deficits in the processing of low-level auditory stimuli exist for only a very small proportion of dyslexic individuals (e.g. Hill et al., 1999; Neville et al., 1993). Others argue that problems processing speech sounds are specifically related to the linguistic nature of such stimuli and that the resulting impairments (for example categorical perception of phonemes) are metaphonological in nature (e.g. Mody et al., 1997).

In section 3.2.3 it was noted that anatomical variations in areas important for low-level auditory processing may be secondary to higher level changes. Thus, the causal connection may actually work in a top-down manner as opposed to a bottom-up one.

No attempt has been made in the present review to evaluate the causal direction between low-level auditory processing deficits and dyslexia. Rather, the aim of the review has been to consider recent evidence that such low-level anomalies exist and to attempt to characterise their nature. The justification of such a standpoint is that, regardless of the causal link, an understanding of the mechanisms underlying these deficits can aid our understanding of the dyslexic condition. Furthermore, while deficits in literacy and phonological skills cannot be identified in dyslexic individuals until relatively late in development (and possibly later than optimal for remediation), screening for low-level auditory processing deficits could potentially help to identify dyslexic individuals at an early stage (for example see the ongoing work of Leppanen, Eklund, & Lyytinen, 1997; Leppanen & Lyytinen, 1997; Leppanen, Pihko, Eklund, & Lyytinen, 1999; Leppanen et al., 2002; Lyytinen et al., 2001; Pihko et al., 1999).

4 GENERAL METHODS

4.1 Participants

4.1.1 Sample Selection

The first section (4.1) of this chapter describes the characteristics of the sample recruited for the present studies. A number of factors influenced the selection of this sample, for example the developmental nature of dyslexia complicates the interpretation of results based on any sample over a certain (though undefined) age, the heterogeneity of the dyslexic population (section 2.4.2) impacts upon the success of any group based study, and the involved nature of physiological data collection raises the issue of compliance.

One of the principle aims of this thesis is to determine whether auditory processing deficits are present in compensated adult dyslexics, a sample selected for a number of reasons. The most commonly observed deficits in dyslexia are literacy impairments (section 2.2.2). Reading and writing impairments, observed at the behavioural level, are unstable in dyslexic individuals over time; factors such as remediation, exposure, motivation and compensatory strategies all exert an influence throughout the lifespan. Indeed the process of acquiring normal literacy skills is itself mediated by complex developmental processes (section 2.1.3). Mounting evidence from genetic, neuroanatomical and neurophysiological studies now suggests that the observed literacy impairments result from core biological deficits (section 2.2.4). The presence of an auditory processing deficit in an adult population, who are largely compensated in terms of literacy skills, would provide evidence that these low-level auditory processing impairments are a core deficit in the condition. Identification of such a deficit, measured at the sensory level, could in turn advance the search for a marker of dyslexia employed in infancy to identify those with potential dyslexic problems so that intervention can be targeted.

Behavioural evidence of deficits in a population can provide useful clues about the underlying cognitive or biological impairments. However, exploration of neurophysiological profiles provides a much better insight as neural functioning can be perceived directly. MEG allows for the direct analysis of neural

functioning on a millisecond-by-millisecond timescale, which makes it perfect in the study of sensory processing. MEG is a completely non-invasive technique and is suitable for use with childhood populations. Nevertheless, the quantity of data required for evoked response paradigms means that recording sessions are often laborious and tiring. The necessity to remain still throughout recording sessions can also be problematic. Compliance is easier to achieve with an adult population. It is also easier to compare results across studies if a similar population is used, and the majority of neurophysiological studies (e.g. fMRI and PET studies) of dyslexia are conducted on the adult population.

Twenty participants (ten dyslexics) were originally recruited from an opportunity sample to participate in the studies and full psychometric profiles were obtained. Unfortunately, three participants from each group were rejected or withdrew participation prior to MEG data collection; one control and two dyslexic participants withdrew from the studies voluntarily, the helmet of the MEG dewar was too small for the head of one dyslexic participant, the remaining control participants obtained psychometric profiles indicating phonological and working memory deficits (possibly indicative of dyslexia).

A particular weakness of the studies presented is that estimates of required sample size were not obtained prior to data collection. Retrospective power calculations were conducted (Appendix 1) and reveal that the three studies were underpowered (although power does reach 80% in a number of cases). Future studies could consider the results of these analyses and modify the sample size accordingly. In view of the small sample size non-parametric statistical analyses were used.

Dyslexia is an extremely heterogeneous condition (section 2.4.2) and there is heated debate about whether the sensory abnormalities reported apply to the entire or only a sub-sample of the population meaning that the group study approach is not necessarily the most appropriate. In order to address the heterogeneity issue emphasis is placed on qualitative interpretation of data at the individual level and reconciliation of individuals' psychometric profiles with cortical profiles. The use of the same sample throughout the studies was deemed beneficial in order to consider individual profiles across the studies.

4.1.2 Recruitment

All participants were recruited from the student population at Aston University. Informed consent was obtained in each case and an example of the consent form given to participants can be found in Appendix 2.

All individuals were under 30 years of age at the time of testing. Normal audiological status was confirmed for each participant with use of standard audiometric testing, conducted with tone frequencies of 750Hz, 1000Hz and 1500Hz (covering the range of stimulus frequencies used in the experimental studies). Hearing thresholds for each of the participants were 10dB HL or less at each of the test frequencies.

Additional exclusion criteria included an IQ below 90, a history of otological disorder, neurological or psychiatric illness, serious head trauma, chronic substance abuse, and a documented history of attention deficit disorder, with or without hyperactivity.

In as much as all of the dyslexic group were studying for, and subsequently achieved, University degrees, at least at the Batchelor level, they could be considered to be 'compensated dyslexics'. However, all of these participants were taken from a group independently referred to The Dyslexia & Developmental Assessment Centre, based at Aston University, by the University's Learning and Support Services. One criterion for inclusion in the study was, therefore, a self-report of some persisting literacy difficulties, in addition to a childhood (under 16years of age) diagnosis of dyslexia or reading difficulties. A positive family history of problems in acquiring literacy skills (self-report) was also required. Five of the seven dyslexic individuals had received some form of support for their specific learning difficulties; the other two had received no extra tuition.

Control individuals were excluded if they, or members of their immediate family, had experienced literacy difficulties at any time (self-report). In addition,

individuals reporting that they had experienced problems with spoken language or had received speech and language therapy were excluded.

4.1.3 General Characteristics

In total, seven dyslexic and seven control individuals were recruited to take part in the present studies. Each group consisted of four females and three males. The mean age of participants was 24years 3months (range of 19years 5months to 29years 11months) in the dyslexic group and 24years 9months (range of 22years 8months to 29years 9months) in the control group ($t_{(12)} = 0.373$, $p=0.715$).

All Participants were right-handed, as observed over the psychometric assessment period. For the purpose of considering individual differences in performance, each of the participants were assigned codes with the prefix C for control and D for dyslexic, followed by an arbitrary number between one and seven.

Regrettably, data from one control and one dyslexic participant were incomplete in the results of each of the four studies (the reasons are provided in the relevant study chapters). Thus, complete data throughout the studies is only available for six control and six dyslexic individuals. The gender frequencies and mean ages of the participants whose data is used in each of the studies is outlined in Table 4-1.

Table 4-1 Sex and Age of Participants

Study Chapter	Participant Group	Gender		Mean Age (SD)
		Female	Male	
Overall	Control	4	3	24y 9m (2y 4m)
	Dyslexic	4	3	24y 3m (3y 3m)
Chapter 5	Control	3	3	25y 2m (2y 5m)
	Dyslexic	3	3	24y 1m (3y 7m)
Chapter 6	Control	3	3	25y 2m (2y 5m)
	Dyslexic	4	2	24y 9m (3y 4m)
Chapter 7	Control	3	3	25y 1m (2y 6m)
	Dyslexic	4	2	24y 9m (3y 4m)

4.1.4 Psychometric Testing

An extensive battery of psychometric tests was administered to each participant individually, in a single session lasting approximately three hours. The tests were: Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III); Wechsler Objective Reading Dimensions (WORD); Wide Range Achievement Test, 3rd Revision (WRAT3); Phonological Assessment Battery (PhAB); Dyslexia Adult Screening Test (DAST).

The WAIS-III (Wechsler, 1997) is a commonly-used 'closed' test of intelligence, standardised for the adult population, and comprising 14 subtests and two supplementary tests. This battery is designed to assess a wide spectrum of verbal and non-verbal ('Performance') skills. A summary of each subtest is provided in Appendix 3. Administration of these subtests provides the researcher or clinician with a set of raw scores, which can be converted to scaled scores, based on a range of scores achieved by a representative sample of people of the same age. By summing the scaled scores achieved over the Verbal and Performance tests, and comparing them to the age appropriate sample of scores, one can obtain age-corrected standardised scores for Verbal, Performance and Full Scale Intelligence Quotients (IQs). In addition, four index scores (groups of subtest scores based on factor analysis) can be derived and these reflect specific aspects of cognitive functioning (see Appendix 3).

The WORD (Rust, Golomok, & Trichey, 1993) Basic Reading and Spelling and WRAT3 (Wilkinson, 1993) Reading and Spelling tests were administered to participants in order to assess literacy skills. Both the WORD and WRAT3 tests of reading involve reading aloud single words of increasing difficulty, thus providing a test of word recognition out of context. The WORD and WRAT3 spelling tests are also very similar; participants write words of increasing complexity that are dictated and then presented in a short sentence. The standardisation of the WRAT3 tests is based on age appropriate samples, as norms are available for a wide age range (from 5 to 75 years). In contrast, norms for the WORD tests are only available for the school-aged population (from 6y 0m to 16y 11m). For the present data, calculation of standardised WORD scores was based on a population sample between the ages of 16y 8m and 16y 11m. As a

consequence, the adult population taking part in the present research, especially in the case of the control group, often reaches the tests ceiling scores. Therefore, the standard scores obtained are less representative of ability than with the WRAT3 tests. The justification for using the WORD test is that it is useful to have two separate measures of reading and spelling skills and few well-standardised adult tests exist. In addition, standardisation of the WORD test is based on a UK sample, whereas for the WRAT3 it is based on a US sample.

The PhAB (Frederickson, Frith, & Reason, 1997) contains a number of short tests that assess phonological processing; the accurate perception and manipulation of sounds within words and the speed of accessing and exploiting phonological codes. Details of the individual PhAB tests administered to participants are provided in Appendix 4. As with the WORD, this test battery was developed to examine the abilities of school-age populations and the norms provided cover only the 6y 0m to 14y 11m age range. For the present data, calculation of standardised scores was based on a population sample between the ages of 14y 6m and 14y 11m. Therefore, ceiling scores are again often reached in the case of the control group (no dyslexic participant obtained a ceiling score on any PhAB tests). As a consequence, the standard scores generated from these tests should be interpreted with caution.

The DAST (Fawcett & Nicolson, 1998) consists of a series of rapidly administered tests intended for screening an adult population for dyslexic difficulties. The tests focus on areas of dyslexic weakness known to persist into adulthood. Four tests from this battery were administered to the participants: One Minute Reading is a test of reading at speed, Two Minute Spelling is a test of spelling at speed, Phonemic Segmentation is a test involving the manipulation of sounds within words and Nonsense Passage is a test of reading multi-syllable pseudo-words in the context of a real word passage. The scores obtained on these tests indicate the percentile range the participant falls within.

Appendix 5 details the common classifications for standardised scores in addition to the percentage of the population falling within each score range.

4.1.5 Psychometric Results

The following results are based on the data of all 14 participants. However, where comparisons considering only the participants completing each of the individual studies changed the significance of results this is indicated.

Mean scores for the control and dyslexic groups on the subtests of the WAIS-III are presented in Table 4-2 in addition to p values where group differences are statistically significant.

Table 4-2 WAIS-III Subtest Mean Scaled Scores and Standard Deviations for the Dyslexic and Control Groups

Group Means and Standard Deviations (Independent t-test, 2-tailed)					
Scaled Scores					
Subtest	**Control**		**Dyslexic**		**Significant**
	Mean	SD	Mean	SD	
Vocabulary	15.71	2.21	15.00	2.89	Non
Similarities	14.57	2.15	14.86	3.24	Non
Arithmetic	13.71	1.80	11.71	2.63	Non
Digit Span	13.71	2.87	9.14	2.19	p=0.006
Information	13.86	1.46	13.29	1.70	Non
Comprehension	14.57	1.72	14.00	2.71	Non
L-N Sequencing	13.86	2.34	9.00	2.00	p=0.001
Picture Completion	12.43	2.82	11.86	2.12	Non
D-S Coding	12.00	3.00	8.43	3.26	p=0.054
Block Design	14.71	2.69	12.86	1.95	Non
Matrix Reasoning	14.71	1.98	12.86	2.34	Non
Picture Arrangement	12.57	3.05	11.43	2.30	Non
Symbol Search	12.29	1.60	10.43	2.51	Non
Object Assembly	12.57	2.70	11.57	1.72	Non

The scores obtained on the Digit Span and Letter-Number (L-N) Sequencing subtests were significantly poorer in the dyslexic group, while the difference between the group means on the Digit-Symbol (D-S) Coding test only just failed to reach significance. Scores for each of the participants across these three subtests can be seen plotted in Figure 4-1. The Digit Span and Letter-Number Sequencing subtests measure auditory working memory; in both cases participants are asked to retain, manipulate and repeat information that is presented to them orally. The Digit-Symbol Coding test is principally a test of processing or graphomotor speed as it is timed, although there are also elements of working memory involved; if the participant can retain the digit-symbol combinations in

working memory they do not have to continually re-check the code key. The group difference for scores on the Digit-Symbol Coding test was not significant when the data of the participants contributing to the results presented in Chapters 5 and 6 were considered separately. All other results remained unchanged.

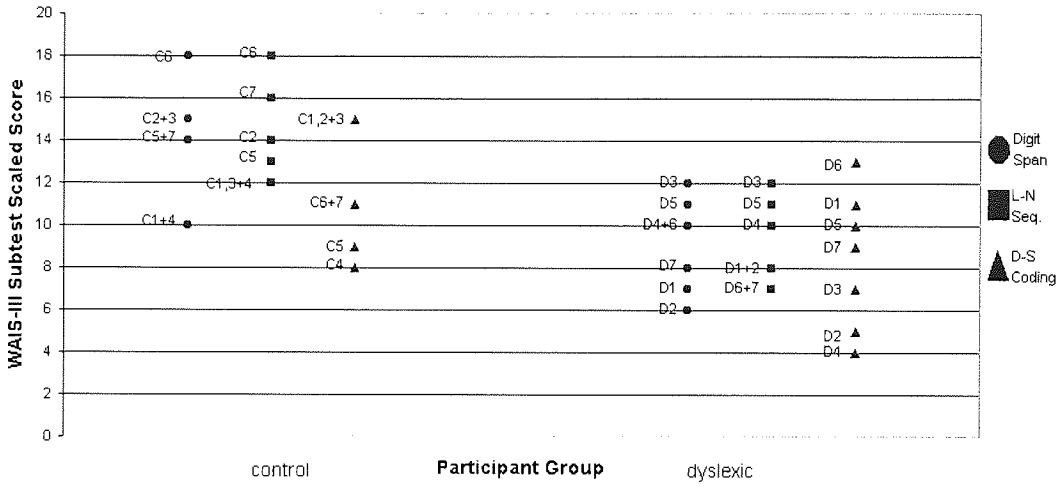

Figure 4-1 Individual Data: WAIS-III Subtests, Scaled Scores
Graph illustrating the scaled scores obtained on the Digit Span (circles), Letter-Number Sequencing (squares) and Digit-Symbol Coding (triangles) subtests for the 12 participants. Data point markers identify each of the individual subjects. As a guide, scaled scores between 8-12 fall within the average range.

The group mean WAIS-III IQ and Index scores are presented in Table 4-3 along with p values where group differences are statistically significant. The mean Full Scale IQ score for the control group is classified as 'high', while in the case of the dyslexic group it is classified as 'high average'. The discrepancy between the group average scores, which is not significant, reflects the fact that the dyslexic participants demonstrated specific difficulties on certain subtests (see Table 4-2) as opposed to a general depression across all subtest scores. This 'jagged profile' is a commonly found dyslexic trait, reflecting specific areas of cognitive weakness (Turner, 1997).

Table 4-3 WAIS-III Mean IQ and Index Standardised Scores and Standard Deviations for the Dyslexic and Control Groups

Group Means and Standard Deviations (Independent t-test, 2-tailed)					
Standardised Scores					
IQ/Index	Control		Dyslexic		Significant
	Mean	SD	Mean	SD	
Full Scale IQ	128.71	14.07	116.29	12.53	Non
Verbal IQ	129.14	13.30	119.29	14.21	Non
Performance IQ	123.14	10.25	109.43	11.46	p=0.036
Verbal Comprehension Index	127.29	11.15	125.43	13.24	Non
Perceptual Organisation Index	125.29	9.01	115.43	10.05	Non
Working Memory Index	123.00	14.22	99.43	11.49	p=0.005
Processing Speed Index	112.43	13.72	97.00	15.36	Non

A significant group difference was obtained between scores for Performance (non-verbal) IQ and for the Working Memory Index. The scores obtained by individual participants on these two scales are represented in Figure 4-2.

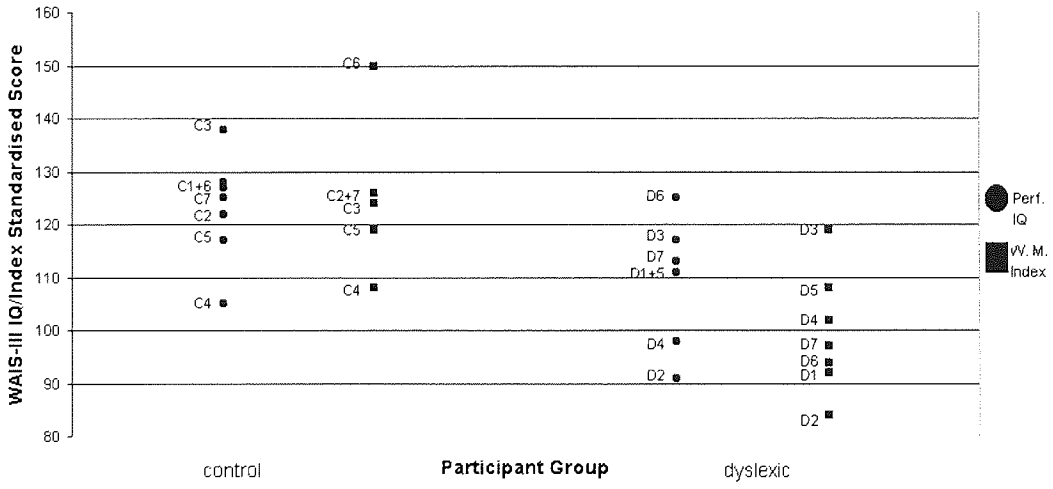

Figure 4-2 Individual Data: WAIS-III IQ and Index, Standardised Scores
Graph illustrating the standardised scores obtained on the Performance IQ (circles) and Working Memory index (squares) for the 12 participants. Data point markers identify each of the individual subjects. As a guide, standardised scores between 90-109 fall within the average range (see Appendix 5).

Performance IQ consists of tests measuring a wide range of non-verbal skills (see Appendix 3). As seen in Figure 4-2, the significantly lower group mean Performance IQ score in the dyslexic group results from the poor scores of two outlying individuals (D4 and D2) as opposed to lower Performance IQ scores in the dyslexic group overall. The group difference in Performance IQ scores was not significant when the data of participants completing the studies reported in Chapters 5 and 6 were considered separately.

The significantly lower group average Working Memory (WM) Index score in the dyslexic group appears to be representative of the data (Figure 4-2), although one of the control participants is clearly an outlier, with a standardised score on this measure more than 20 points above all other participants. The Working Memory Index is made up of scores from the Arithmetic, Digit Span and Letter-Number Sequencing subtests, all of which assess auditory working memory. The dyslexic group's scores on the Processing Speed Index, a scale directly assessing speed of processing, were significantly poorer than those of the control group when considering only the data of participants included in the results presented in Chapters 7 ($p=0.039$) and 8 ($p=0.047$).

The median cumulative percentages obtained by the control and dyslexic groups on the WAIS-III Supplementary Tests are outlined in Table 4-4. The only significant group difference was found on the Digit-Symbol Copy subtest. This involves simply copying symbols under timed conditions. Thus, the significantly poorer dyslexic group score reflects a relative deficit in perceptual and graphomotor speed.

Table 4-4 WAIS-III Median Supplementary Test Cumulative Percentages for the Dyslexic and Control Groups

Group Medians (Mann-Whitney U, 2-tailed)			
Cumulative Percentages			
Subtest	**Control**	**Dyslexic**	**Significant**
	Median	Median	
Digit-Symbol Pairing	50%	25%	Non
Digit-Symbol Free Recall	50%	50%	Non
Digit-Symbol Copy	50%	25%	p=0.025

Mean scores for the control and dyslexic groups on the reading and spelling tests of the WORD and WRAT3 are presented in Table 4-5 in addition to p values where group differences are statistically significant.

Table 4-5 WORD and WRAT3 Mean Reading and Spelling Standardised Scores and Standard Deviations for the Dyslexic and Control Groups

Group Means and Standard Deviations (Independent t-test, 2-tailed)					
Standardised Scores					
Test	**Control**		**Dyslexic**		**Significant**
	Mean	SD	Mean	SD	
WORD Basic Reading	114.00	0.00	105.29	12.07	Non
WORD Spelling	115.57	4.72	95.00	13.89	p=0.007*
WRAT Reading	117.00	2.58	107.43	8.48	p=0.024*
WRAT Spelling	115.43	4.24	95.43	10.01	p=0.001*

*Equal Variances Not Assumed

The groups did not significantly differ in terms of their performance on the WORD Basic Reading test, although the means reflect a poorer average score for the dyslexic group on this measure. In contrast, the standardised scores obtained by the dyslexic group on the other measures of reading (WRAT) and spelling (WORD and WRAT) were all significantly poorer than those obtained by the control group.

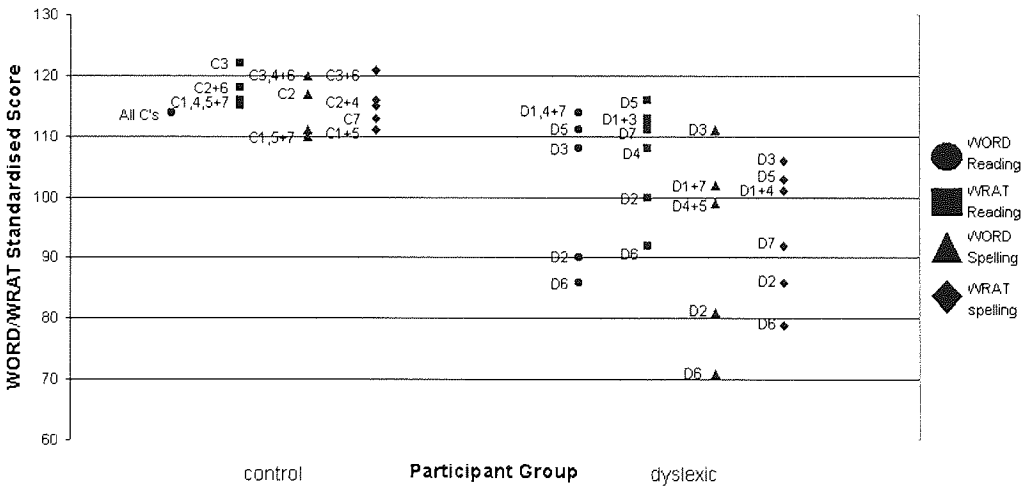

Figure 4-3 Individual Data: WORD and WRAT, Standardised Scores
Graph illustrating the scaled scores obtained on the WORD Basic Reading (circles), WRAT3 Reading (squares), WORD Spelling (triangles) and WRAT3 Spelling (diamonds) tests for the 12 participants. Data point markers identify each of the individual subjects. As a guide, standardised scores between 90-109 fall within the average range (see Appendix 5).

Looking at the scores obtained by control and dyslexic individuals on the reading and spelling measures (Figure 4-3), it becomes clear that the control participants' scores are grouping at the ceiling level. This is particularly true in the case of the WORD Basic Reading test, where the ceiling standardised score (114) is reached by all control participants (resulting in a standard deviation of zero and possibly explaining the failure to find a group difference on this measure). This reflects the limitation of the WORD tests, raised earlier, that the standardisation sample does not extend beyond 17 years of age. The 'high average/high' scores obtained by the control participants on the WRAT3 tests of reading and spelling, which do allow for standardisation with an age appropriate sample, reflect the higher than average intellectual abilities of the participant sample recruited.

The control and dyslexic groups' scores for the PhAB tests are given in Table 4-6. Significant group differences were found for all but the Semantic Fluency test (not a measure of phonological skills, see Appendix 4).

Table 4-6 PhAB Tests Mean Standardised Scores and Standard Deviations for the Dyslexic and Control Groups

Group Means and Standard Deviations (Independent t-test, 2-tailed)					
Standardised Scores					
Test	**Control**		**Dyslexic**		**Significant**
	Mean	SD	Mean	SD	
PhAB Non-Word Reading	120.00	0.00	91.00	7.30	p<0.0005*
PhAB Spoonerisms	115.57	14.68	89.00	3.00	p=0.003*
PhAB Naming Speed (Pictures)	115.57	9.73	90.00	10.92	p=0.001
PhAB Semantic Fluency	122.43	10.74	112.00	22.77	Non
PhAB Alliteration Fluency	121.00	13.56	99.71	10.27	p=0.006
PhAB Rhyme Fluency	108.71	11.07	89.29	9.43	p=0.004

*Equal Variances Not Assumed

The dyslexic group's scores on the other PhAB tests were all significantly worse than the control group's scores. The performance of all individuals across these other measures is presented in Figure 4-4.

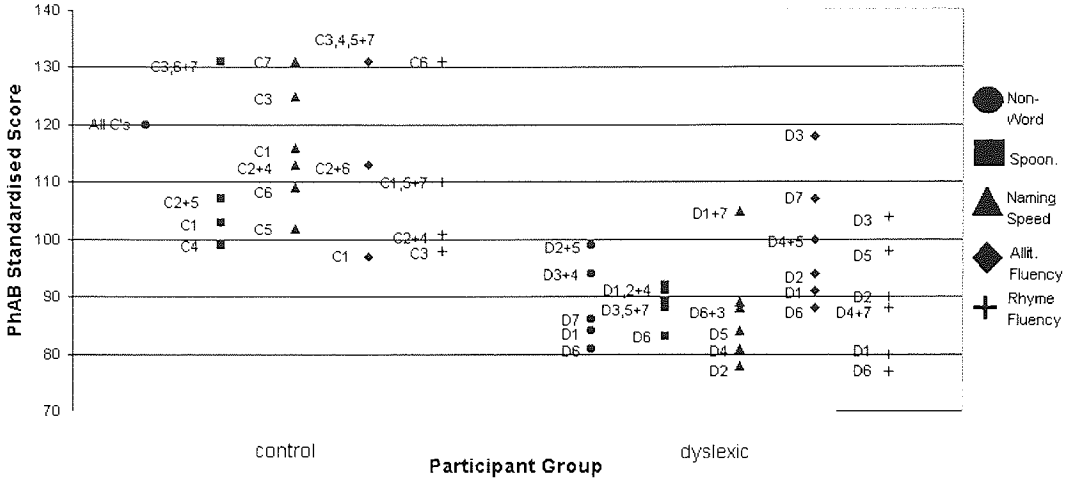

Figure 4-4 Individual Data: PhAB, Standardised Scores
Graph illustrating the scaled scores obtained on the PhAB Non-Word Reading (circles), Spoonerisms (squares), Naming Speed (triangles), Alliteration Fluency (diamonds) and Rhyme Fluency (crosses) tests for the 12 participants. Data point markers identify each of the individual subjects. As a guide, standardised scores between 90-109 fall within the average range (see Appendix 5).

When examining these data it is again important to keep in mind that PhAB standardised scores were based on a school-aged sample. Nevertheless, the data do suggest, convincingly, that the dyslexic participants were experiencing far more difficulties across this range of tests than their age and IQ matched peers.

Finally, the results of the DAST are given in Table 4-7. Significant group differences were found for all measures.

Table 4-7 DAST Tests Median Percentile Ranks for the Dyslexic and Control Groups

Group Medians (Mann-Whitney U, 2-tailed)			
Percentile Rank Range			
Test	**Control**	**Dyslexic**	**Significant**
	Median	Median	
1 Minute Reading	23-77%	5-11%	p=0.013
2 Minute Spelling	>78%	12-22%	p=0.007
Phonemic Segmentation	23-77%	12-22%	p=0.016
Nonsense Passage	>78%	<4%	p=0.002

Considering the median scores, the dyslexic group were significantly worse on every measure. All control participants obtained a score placing them in the 'average' (23-77 percentiles) or 'above average' (>78 percentile) ranges across

the test battery. In contrast, six of the seven dyslexic participants obtained scores placing them in the lowest 11% of their age group. The performance of individuals across all DAST tests is presented in Table 4-8, where scores falling below the average range are highlighted.

Table 4-8 DAST Test Individual Participant Percentile Ranges Across all Measures

Participant	Test			
	1Minute Reading	2 Minute Spelling	Phonemic Segmentation	Nonsense Passage
C1	23-77%	23-77%	23-77%	23-77%
C2	>78%	>78%	>78%	>78%
C3	>78%	>78%	23-77%	>78%
C4	23-77%	23-77%	23-77%	23-77%
C5	23-77%	23-77%	23-77%	23-77%
C6	>78%	>78%	>78%	>78%
C7	23-77%	>78%	23-77%	>78%
D1	5-11%	5-11%	23-77%	<4%
D2	<4%	<4%	5-11%	<4%
D3	12-22%	23-77%	<4%	23-77%
D4	<4%	12-22%	23-77%	<4%
D5	>78%	23-77%	23-77%	<4%
D6	5-11%	<4%	<4%	5-11%
D7	12-22%	23-77%	12-22%	12-22%

The One Minute Reading and Two Minute Spelling tests assess literacy skills with the additional pressure of a timed component. The Phonemic Segmentation and Nonsense Passage tests assess phonological skills; phoneme manipulation and grapheme-to-phoneme conversion. Thus, low scores on these two tests are consistent with the poor performance demonstrated on the PhAB measures of phonological processing.

4.1.6 Summary of Psychometric Results

The participant groups are matched in terms of Full Scale and Verbal IQ; although the dyslexic groups mean scores for each measure were somewhat lower, this difference did not reach significance. The dyslexic group's Performance IQ score was significantly lower than that of the control group. This group difference can be accounted for by the data of D4 and D2 (see Figure 4-2). In each participant's

case, at least average (scaled score of eight or above) scores were obtained for all but one of the subtests contributing to the Performance IQ score. This exception was the Digit-Symbol Coding subtest; these participants scored very poorly on this measure (D4 obtained a scaled score of four and D2 a scaled score of five).

The control group's mean Full Scale IQ score falls with the 'high' range for the individual participants' respective age groups; the dyslexic group's mean Full Scale IQ falls within the 'high average' range. These deviations from 'average' are accounted for by the fact that all participants were taken from the University student population, a sample with higher average ability than the general population.

The participant groups differed significantly in terms of their scores on the Digit Span and Letter-Number Sequencing subtests. As explained earlier in this chapter, these subtests assess auditory working memory. In addition, the group difference on the Digit-Symbol Coding test just failed to reach significance. This is principally a test of processing or graphomotor speed as it is timed, although, there are also elements of working memory involved; if the participant can retain the digit-symbol combinations in working memory they do not have to continually re-check the code key. The dyslexic group's mean score on the Working Memory Index (combining scores from the Digit Span, Letter-Number Sequencing and Arithmetic subtests) was also significantly poorer than the control group's score. Working memory deficits are well documented in the dyslexic population (see section 2.3.1).

The groups' scores on the Processing Speed Index (combining scores from the Digit Symbol-Coding and Symbol Search subtests) were significantly different when considering only the participants whose data are reported in Chapters 7 and 8. In addition, a significant group difference was obtained when comparing the two groups' (including all participants) scores on the Digit-Symbol Copy subtest, a supplementary test in the WAIS-III battery. This test involves simply copying symbols under timed conditions. While the Digit Symbol-Coding and Symbol Search subtests do contain a working memory element, the Digit-Symbol Copy subtest does not, rather it is a direct measure of graphomotor speed. Processing

speed and graphomotor speed deficits are often noted as characteristic of dyslexia (see section 2.3.3).

Examining the literacy results, significant group differences were obtained for the WRAT3 test of reading and both WORD and WRAT3 measures of spelling. The dyslexic group were significantly poorer than the control group across all of these measures and, as noted above, the failure to find a significant group difference on the WORD Basic Reading test could simply reflect the fact that all control participants obtained a score that was at the ceiling of this test.

In view of the IQ scores achieved by the dyslexic group, the poor literacy scores (in some cases falling within the 'low average' or 'low' ranges, see Figure 4-3) indicate that some of these individuals are experiencing continuing literacy deficits, despite their age and academic achievements. Literacy deficits are, of course, the most common characteristic of developmental dyslexia. Furthermore, examining the data in Figure 4-3, it is interesting to note the trend that in all but one case (D3) the dyslexic individuals' scores on spelling tests were always worse than their scores on reading tests.

Significant group differences were found for all of the tests in the PhAB, other than in the case of the Semantic Fluency test. This test is not a measure of phonological skills but, rather, serves as a useful comparison with the other fluency measures; a poor score for Alliteration and Rhyme Fluency but not Semantic Fluency suggests difficulties generating words based on phonological codes specifically (see Appendix 4). The dyslexic group's scores on the other PhAB tests were all significantly worse than the control group's scores. When examining these data it is important to keep in mind that PhAB standardised scores were based on a school-aged sample. Nevertheless, it is clear that the dyslexic groups performance on many of these tests (particularly Non-Word Reading, Spoonerisms and Naming Speed) was far inferior to that of the control group (see section 2.3.1).

The Non-Word Reading test measures the individual's ability to apply grapheme-to-phoneme correspondence rules, as the words are unfamiliar and cannot be

recognised visually. A deficit in this skill is thought to be at the core of the problems the dyslexic population face with competent literacy acquisition (see section 2.2.3). The Spoonerisms test demands the manipulation of phonemes and includes a strong working memory component, making it particularly difficult for dyslexic individuals.

Processing speed deficits have already been mentioned and are again assessed with use of the PhAB Naming Speed test, which requires the participant to rapidly name a series of common objects. The Alliteration and Rhyme Fluency tests also contain both a phonological and speed element and thus, the dyslexic group's difficulties on these tests may reflect problems with accessing phonological codes and/or processing information quickly.

A large number of the dyslexic participants also experienced problems when asked to read or spell under timed conditions (DAST One Minute Reading and Two Minute Spelling). The group's score on these measures were significantly worse than that of the control group. While, to a large extent, dyslexic individuals' difficulties with reading and spelling diminish with age, these deficits can surface when measured under pressure, for example under speeded conditions (see section 2.3.3).

The other DAST results revealed significantly lower scores in the dyslexic group on the Phonemic Segmentation and Nonsense Passage tests. These tests are very similar to the Spoonerisms and Non-Word Reading tests of the PhAB and the results provide confirmation of the present dyslexic group's difficulties with phonological skills.

4.1.7 Individual Dyslexic Profiles

A comparison of the performance of individual dyslexic participants across the range of psychometric tests reveals that specific areas of weakness vary across the group and that certain individuals experience more difficulties than others. The following provides summary profiles for each of the dyslexic participants.

D1 -WORD and WRAT3 reading scores fell within the high average range, although the performance on the timed test of reading (DAST) revealed continuing difficulties.

-Spelling was assessed in the average range with WORD and WRAT3 tests but was below average under timed conditions (DAST).

-Poor performance on some phonological tests (DAST Nonsense Passage, PhAB Non-Word Reading and Rhyme Fluency).

-Low average scores on some measures of working memory (WAIS-III Digit Span and Letter-Number Sequencing).

D2 -WORD and WRAT3 reading scores fell within the high average range, although the performance on the timed test of reading (DAST) revealed continuing difficulties.

-Spelling was low average on WORD and WRAT3 tests and below average under timed conditions (DAST).

-Poor performance on some phonological tests (DAST Nonsense Passage and Phonemic Segmentation).

-Low average scores on some measures of working memory (WAIS-III Digit Span and Letter-Number Sequencing).

-Below average scores on tests of processing speed (PhAB Naming Speed and WAIS-III Digit-Symbol Coding and Digit-Symbol Copy).

D3 -WORD and WRAT3 reading scores fell within the average/high average ranges, although the performance on the timed test of reading (DAST) revealed continuing difficulties.

-Spelling assessed in the average/high average ranges on all measures.

-Poor performance on some phonological tests (DAST Phonemic Segmentation and PhAB Spoonerisms).

-High average scores on most measures of working memory (low average for WAIS-III Digit-Symbol Coding).

-Low average score on tests of processing speed (PhAB Naming Speed and WAIS-III Digit-Symbol Copy).

D4 -WORD and WRAT3 reading scores fell within the average/high average ranges, although the performance on the timed test of reading (DAST) revealed continuing difficulties.

-Spelling assessed in the average range with WORD and WRAT3 but low average under timed conditions (DAST).

-Average scores on some phonological tests (DAST Phonemic Segmentation and PhAB Spoonerisms) but low average for PhAB Rhyme Fluency and below average for DAST Nonsense Passage

-Average scores on tests of working memory.

-Low/below average scores on tests of processing speed (PhAB Naming Speed, WAIS-III Digit-Symbol Coding and Digit-Symbol Copy).

D5 -All measures of reading indicated ability within the high average range.

-Spelling assessed in the average range on all measures.

-Poor performance on some phonological tests (DAST Nonsense Passage and PhAB Spoonerisms) but average performance on others.

-Average scores on tests of working memory.

-Low average score on a test of processing speed (PhAB Naming Speed).

D6 -WORD and WRAT3 reading scores fell within the average/low average ranges, and below average on a timed test of reading (DAST).

-Spelling assessed below average on all measures.

-Poor performance on all phonological measures.

-Average scores on most tests of working memory but low average for WAIS-III Letter-Number Sequencing.

-Low average score on a test of processing speed (PhAB Naming Speed).

D7 -WORD and WRAT3 reading scores fell within the high average range, although the performance on the timed test of reading (DAST) revealed continuing difficulties.

-Spelling assessed in the average range with WORD and WRAT3 but low average under timed conditions (DAST).

-Poor performance on most phonological tests (DAST Nonsense Passage and Phonemic Segmentation, PhAB Non-Word Reading, Spoonerisms and Rhyme Fluency).
-Low average scores on some measures of working memory (WAIS-III Digit Span and Letter-Number Sequencing).
-Average scores on tests of processing speed.

Clearly, the results of psychometric testing do confirm the heterogeneity of the current dyslexic sample (see section 2.4.2). In the majority of cases, even where the WORD and WRAT3 tests suggested average or above average reading ability, reading under timed conditions revealed continuing difficulties with reading skills. The only exception to this being D5, who performed at least within the average range across all reading measures. In this participant's case (as with D3), spelling skills were also assessed to be at least average.

All dyslexic participants demonstrated difficulties with at least some of the tests assessing phonological skills, although the severity and nature of these difficulties varied between individuals. For example, D6 obtained poor scores on all phonological measures, while other participants demonstrated problems on only two or three tests. Likewise, deficits of working memory and processing speed were not consistently found across the group.

Crudely, it appears that D3 and D5 performed better than the other dyslexic participants across the range of tests. In contrast D6 obtained poor scores on a wide variety of measures, as did D2, though to a lesser extent.

4.2 Magnetoencephalography

4.2.1 Introduction

Magnetoencephalography (MEG) is the measurement of magnetic fields generated by electrical activity within the brain. In this section the basic principles of MEG will be briefly outlined, along with the instrumentation used. In addition, the advantages of MEG, in contrast to alternative 'imaging' techniques will be highlighted.

4.2.2 Neuronal Activity

Neuromagnetism is the study of magnetic fields generated as a result of ionic current flow in the nervous system (Kaufman & Williamson, 1986). MEG relates specifically to the measurement of fields generated in the brain arising as a result of neuronal activity. Therefore, it is useful to provide a review of the mechanisms of such neural communication within the brain.

Neurons are the information-processing and information-transmitting elements of the nervous system. Largely found in the grey matter of the brain, they receive input from the environment and from other neurons (Carlson, 1994). Information is sent along neurons by means of action potentials. The membrane of the neuron separates the intracellular and extracellular fluid, each of which are made up of different ion concentrations. Protein molecules, known as ion channels, on the membrane of neurons maintain the different concentrations, by pumping selected ions against the concentration gradient or, by acting as passive channels. The membrane alters its permeability to sodium (Na+) and potassium (K+) causing signal transfer along the axon as a result of an approaching action potential (Hamalainen, Hari, Ilmoniemi, Knuutila, & Lounasmaa, 1993).

The resting potential of a neuron is -70mV. In the first stage of the action potential, the cellular membrane selectively allows Na+ ions from the outside environment to enter the cell causing a current to pass through the axon. The potential inside the cell increases to around +30mV, and the cell becomes depolarised. At this stage the interior of the cell is positive, triggering the action potential to travel along the axon with undiminished amplitude. The membrane potential then reverses itself and K+ ions flow out of the cell. The normal concentration of K+ and Na+ ions is restored by means of the Na-K pump (Romani & Pizzella, 1991).

Neurons are connected and communicate by means of synapses. An action potential in the presynaptic cell leads to the release of transmitter molecules across the synaptic cleft. Some of these molecules attach themselves onto the surface of the postsynaptic cell, leading to a change in the permeability of its membrane for specific ions. The membrane potential in this cell is altered, as is

the potential in the area surrounding the membrane, due to the ensuing flow of charge (mainly Na+, K+ and potassium chloride (Cl-) ions). An electrical field is produced and a current flows along the interior of the postsynaptic cell. This event is referred to as the post-synaptic potential. The channels are ion selective to the receptor that is activated. If the sodium channels are opened, the current flows into the cell, which becomes depolarised. The resulting postsynaptic potential is excitatory. If the potassium chloride channels are activated, the current flows out of the cell, leading to hyperpolarisation and inhibition (Hamalainen et al., 1993). The peak value of each postsynaptic potential is approximately 10mV and lasts for around 10ms.

4.2.3 Magnetic Fields

MEG signals reflect both excitatory and inhibitory depolarisations, though they are mainly associated with the excitatory postsynaptic currents (Hari, 1991). A number of cells, for example pyramidal cells, are aligned in the cortex. The sum of their postsynaptic electrical fields increase with increasing area. It is thought that around 100,000 adjacent neurons, acting in concert, are required to effect a recordable magnetic field change outside the head.

Figure 4-5 demonstrates the relationship between the electrical currents occurring as a result of neuronal activity within the brain and the resulting magnetic fields. **Q** represents the current source strength, resulting in **Jv** current flow within the brain. The potential difference **V,** which arises from this current flow, can be measured with Electroencephalography (EEG) on the surface of the scalp. MEG measures the corresponding magnetic field (**B**) from outside the head.

The magnetic fields generated by cerebral currents are minute compared with ambient magnetic-field variations; around 100 million times weaker than the earth's magnetic field and approximately 1 million times smaller than those occurring in an urban environment (Hari, 1993). Thus a number of precautions need to be taken to avoid external magnetic artefacts contaminating the neuromagnetic recording.

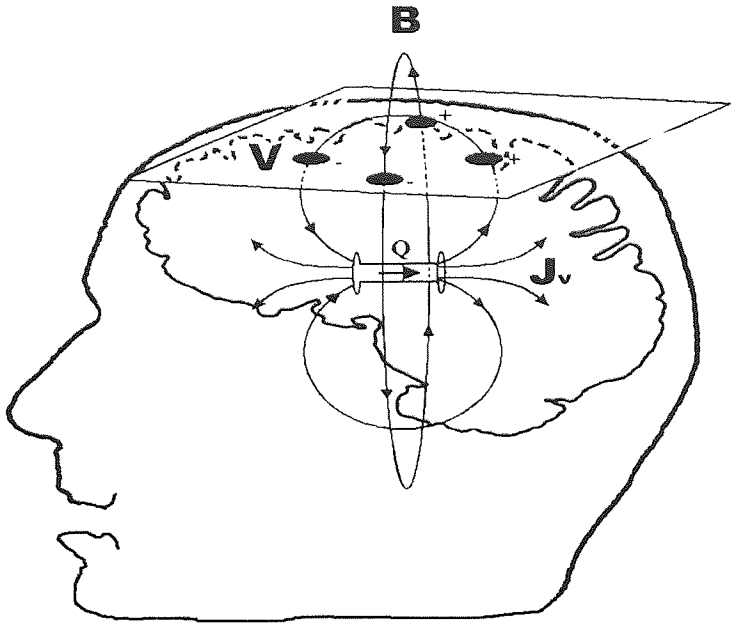

Figure 4-5 Relationship Between Electrical Currents in the Brain and Magnetic Fields Outside the Head

4.2.4 Instrumentation

The simplest way to eliminate noise contamination from external sources is to conduct recordings in a magnetically shielded room, typically made from several layers of μ-metal and aluminium (Hamalainen et al., 1993). Aston University's MEG system is placed in such a room. The μ-metal layers have a high permeability and thus shield the room from low frequency (<10Hz) fields existing outside. The aluminium plates provide eddy current shielding against higher frequency (>10Hz) magnetic interference.

Flux transformers (gradiometers) initially pick up the magnetic fields and these signals are then coupled to Superconducting Quantum Interference Devices (SQUIDs). As SQUIDs operate at superconducting temperatures of around -269°C, the sensors are immersed in liquid helium and held in a dewar.

Aston University's CTF system has 151 first order axial gradiometers; the coils are 2cm in diameter with a 5cm baseline (Figure 4-6). The first-order gradiometers play an important role in reducing noise contamination. As well as the pickup coil, the first order gradiometer contains a compensation coil, wound in the opposite direction (Hamalainen et al., 1993). This arrangement reduces the input of distant (non-neural) magnetic sources, as such sources would induce

virtually identical currents in both coils. In contrast, neural sources induce a larger current at the pickup than the compensation coil. In addition, the signal to noise ratio is further improved by introducing an additional virtual gradiometer, using a reference system. This ensures that the output is largely determined by the nearby neuronal source alone (Hari, 1993). The 151 sensors are uniformly distributed over the surface of the head.

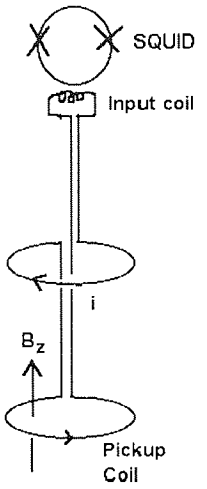

Figure 4-6 First Order Gradiometer
Schematic representation of a first order axial gradiometer (Singh, 1995).

4.2.5 Source Modelling

EEG data is recorded with use of electrodes fixed to standard scalp locations, thus one can assume that measurements taken at the same electrode site across participants or recording sessions are comparable, albeit with marginal error relating to individual variability in cortical anatomy and head shape. In contrast, MEG data is recorded from sensors that are not in direct contact with the participant. Inevitable variability in head location with respect to the dewar (orientation and distance) means that direct comparisons between sensors, either across recording sessions or across subjects, are not viable. For example, as magnetic field falls off with approximately the square of distance from a dipolar source, a small head movement of a subject between two experimental recording sessions will give rise to very large changes in amplitude at the sensor level. In

order to factor out the effects of arbitrary subject positioning in MEG it is necessary to create an estimate of the electrical current flow within the subject's head. These electrical current flow estimates will be more or less independent of the position of the head with respect to the sensors.

The accurate interpretation of MEG and EEG data relies upon the ability to localise the cortical source of measured magnetic fields or electric potentials. However, there is no unique solution to the problem of localising the source of brain activity as an infinite number of source configurations can produce an identical external magnetic field or electric potential distribution (Helmholtz, 1853, cited in Hamalainen et al., 1993). In order to solve this inverse problem it is therefore necessary to make certain assumptions.

In order to solve the inverse problem one must first be able to compute the output of the gradiometers given a certain area of active cortex (the forward problem). With knowledge of the primary source and surrounding conductivity distributions, the resulting magnetic field (MEG) can be calculated (Hamalainen et al., 1993). Therefore, a number of assumptions and simplifications are introduced; neural activity is mathematically modelled as a set of dipolar current sources and the head is modelled as a volume conductor.

The volume conductor model describes the medium of the neuronal activity, i.e. the head, and includes details of its geometry. As the skull and other extracerebral tissues do not distort magnetic fields (unlike electric potentials recorded with EEG), the conductivity of the head can be assumed to be equivalent to free space. Therefore, localisation of MEG sources can be achieved with use of a very simple spherical model, which approximates the circumference of the head (Kaufman & Williamson, 1986).

However, there are a number of points following from the assumption of a spherically symmetric volume conductor. Firstly, only currents that have a component tangential to the surface of a spherically symmetric conductor can produce a magnetic field outside, radial sources are externally silent (Hamalainen et al., 1993). Thus, magnetic fields recorded from the human brain must be

generated by current sources oriented in a direction that is at least partially tangential to the surface of the head. This poses a major limitation of MEG measurements (EEG measures sources both tangentially and radially oriented in the sphere, see Figure 4-5) as it follows that some neuronal activity will be missed. As the dendrites of pyramidal neurones tend to lie perpendicular to the cortical surface (Snyder, 1991), measured fields mainly reflect synchronous activation of cortical pyramidal cells. Because of this selectivity, it has been assumed that MEG measured fields primarily arise from activation in fissural cortex, with few gyral source contributions. However, using detection probability mapping, Hillebrand & Barnes (2002) have demonstrated that there are only very thin strips of very poor resolvability at the crests of gyri and that these strips would only account for a very small proportion of the active area required to produce sufficient net current flow. The authors conclude that around 5% of all cortical area is oriented radially below 15°. Indeed, considering the auditory recordings made in the present studies, as the auditory cortex lies within the sylvian fissure, it would appear to be well positioned for MEG recordings (Heim et al., 2000).

As magnetic field falls off rapidly with distance from an electrical source, the MEG response is relatively more sensitive to sources on the surface of the brain (it is zero at the centre of the sphere) (Näätänen, 1992). Hillebrand & Barnes (2002) argue that source depth, rather than orientation, is the main factor limiting detection probability.

A number of models have been developed in order to solve the bioelectric inverse problem each relying on different assumption sets. The most commonly used model is the equivalent current dipole (ECD). The model assumes that the measured magnetic field can be accounted for by a number of simultaneously active small regions of cortex. Mathematically these regions are modelled as an ideal electrical point sources or equivalent current dipoles (Hamalainen et al., 1993). Modelling brain activity with current dipoles is relatively successful, as at a typical measurement distance, at least 3cm from the source, many current configurations seem 'dipolar' (Hari, 1991). Also, these simplistic models are typically only used to account for relatively short (millisecond) periods of time.

Most dipole fitting algorithms minimize the difference between the theoretical and measured field patterns in a least squares sense. The minimization process is visualised in Figure 4-7. In the three schematic diagrams, the observed magnetic field (a), the model calculated magnetic field (b), and the difference or residual between the plots (c) is shown.

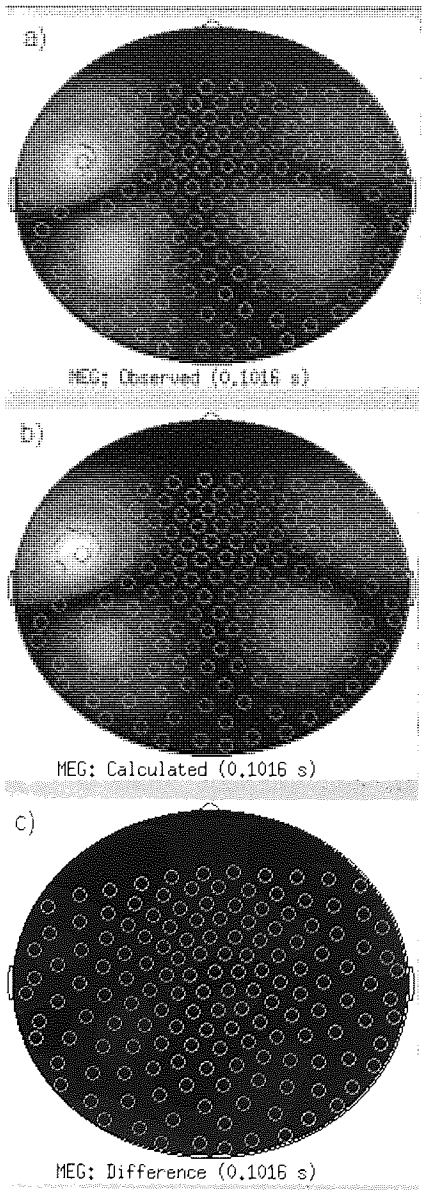

Figure 4-7 Example of Measured and ECD Modelled Field Maps
a) Field map generated in response to a single auditory tone. b) Field map of the ECD model derived by a least squares fit from the field shown in (a). c) The difference between the fields shown in (a) and (b).

The ECD model is best suited to explain signals that are precisely time-locked to sensory stimuli and which produce a distinct evoked response. In order to obtain

an adequate signal to noise ratio, data must be recorded over many repeated trials to increase the strength of the signal relative to the noise. The ECD model relies upon certain *a priori* information about the number of active sources and their time spans. Thus, critics argue that it is not well equipped to account for several temporally overlapping active sources.

An alternative class of models, which do not rely on such constraints, are minimum norm estimates (MNEs) (Hamalainen & Ilmoniemi, 1994). These models select the continuous source distribution with the minimum energy (or norm) that explains the measured field. However, the constraint of minimum energy biases all MNEs to use sources nearest the sensors to account for the data. This is because these sources can have low amplitude and produce a relatively large magnetic field (Hari, 1991). There is necessarily therefore some arbitrary weighting that must be applied in order to provide a bias toward deeper solutions. This bias could depend on anatomical or functional constraints. Another problem with the MNE is that it attempts to account for all the measured data, that is, there are no degrees of freedom with which to test how appropriate the model really is.

Stenbacka, Vanni, Uutela, & Hari (2002) have examined the relative merits of the two approaches and conclude that, while they are comparable in the evaluation of multiple sources, the ECD is more spatially and temporally accurate when modelling non-simultaneous sources. A point, which is particularly relevant for the current studies, is that ECD is more robust when the experimenter knows that a small focal field of cortex has contributed to the measured field (Uutela, Hamalainen, & Somersalo, 1999). The critical reason why MNE estimates would not be appropriate for this analysis is that the amplitudes of the current sources depend entirely on the bias weighting. That is, for each subject it would be necessary to decide on a depth or surface where one is expecting to observe a source. The amplitudes observed on this surface would be comparable across recordings on the same subject but inter subject comparisons would be strongly dependent on the arbitrary depth assumptions. The ECD model however, whilst much simpler, gives unequivocal depth and amplitude information. In addition to which, there are a number of degrees of freedom with which to test the validity of the model (Supek & Aine, 1997).

In the present studies a spatiotemporal fit algorithm was used for the ECD model. This algorithm uses both the spatial and the temporal components of the MEG signal and models them as a number of current sources whose locations, during the time interval of observation, are stationary (i.e. variations in the field are due only to variations in the strengths of sources). The sources are positioned iteratively until they account for the maximum portion of the temporal variations (Koles, 1998).

Estimates of noise levels are required in order to validate ECD models. Several approaches are used to find such noise level estimates for individual channels. For the present studies a standard anti-averaging procedure was adopted in which successive trials are alternately added and subtracted, cancelling the evoked response while retaining the noise. As the evoked responses are likely to be very similar, this method results in an accurate estimate for the noise (Hamalainen et al., 1993).

The goodness-of-fit value describes how well the field pattern of the modelled ECD agrees with the measured data. In the present studies reduced chi-square error values are considered (Supek & Aine, 1997). Reduced chi-square error values equal to one indicate that differences between modelled and measured fields are equivalent to the noise (the model and measurement are in complete agreement). Deviations of the chi-square error value from one are caused by measurement noise or inadequacy of the model; increasing values indicate modelling error is larger than measurement noise, while values very much below one suggest that the model is irrelevant (as the noise is very large).

Monte Carlo Volume analyses were performed. The Monte Carlo Volume analysis involves the computation of how stable the solution is given the measurement noise. The degree of measurement noise is assessed from the variability of the trials that contributed to the average. A dipole fit to different realisations of noisy data is repeated multiple times and the result is a cluster of fit solutions, the volume in which 95% of these solutions lie is the 95% confidence volume.

4.2.6 Advantages of MEG

There are a number of advantages afforded by using MEG over other techniques that examine neuronal processing, many of which relate specifically to the research questions posed in the present studies.

The principle benefit of MEG over other technologies is its millisecond-by-millisecond temporal resolution. This is orders of magnitude better than other methods; the resolution of both functional Magnetic Resonance Imaging (fMRI) and Positron Emission Tomography (PET) are in the order of tens of seconds. This excellent temporal resolution allows for the mapping of rapid and dynamic changes in cortical activity. The low-level auditory responses that are of interest in the present studies occur within the first 90-200ms after stimulus onset and last for only a short time; thus MEG's fine temporal resolution is essential.

MEG's spatial resolution for cortical sources can be as low as 2mm. While EEG shares MEG's fine temporal resolution, its localisation accuracy is poor unless electrodes are placed directly on the cortex itself, a highly invasive procedure. This is due to the smearing effects of the scalp and other extracerebral tissue which are practically transparent to the magnetic field, but which substantially alter current flow (Hamalainen et al., 1993). The field map obtained with MEG is around one third tighter than the EEG map, due to this smearing effect (Rose & Ducla-Soares, 1990).

MEG is a direct measure of neuronal activity within the brain. fMRI and PET however are based on correlates of neural currents such as hemodynamic and/or metabolic changes, which are only secondary consequences to changes in cortical activity. They are based on the assumption that local metabolic changes are indirectly related to increased neuronal function.

Magnetic recording is reference free. Electrical brain maps, obtained with the use of EEG, depend on the location of a reference electrode (Hari, 1993). Both fMRI and PET rely on baseline subtraction techniques i.e., an image taken before a task is subtracted from one taken during a task. There is ambiguity over whether an

area subtracted, due to being on the pre-task image, could not still be actively engaged in the task.

MEG's selectivity to magnetic fields produced by sources lying perpendicular to the surface of the modelled sphere has been forward as an advantage over EEG, which is sensitive to both radial and tangential current sources. Hari (1993) suggests that for this reason, it is often easier to interpret MEG rather than EEG data. A consequence of EEG seeing both sources is that tangential sources can be dominated or masked by radial sources (Cohen, 1987). As noted above, auditory responses are generated in fissural cortex and, as such, are theoretically well detectable with MEG measurements.

Finally, another obvious advantage arises from the non-invasive and non-hazardous nature of MEG recordings. There is no need for ingestion of trace agents, as is the case with PET, Single Photon Emission Computed Tomography (SPECT) and regional Cerebral Blood Flow (rCBF) technologies. The possible hazard resulting from exposure to high radiofrequency and magnetic fields, found with fMRI, is also avoided. Participants sit on a comfortable chair within the magnetically shielded room and place their head in the helmet at the bottom of the dewar. As the magnetic fields are measured outside the head, placement of electrodes, as with EEG recordings, is not necessary. The comfortable and time-efficient nature of this procedure, therefore, allows for extended recording sessions and the repetition of measurements over short time periods. In addition, MEG is suitable for use with a child or clinical population, thus a developmental disorder such as dyslexia could potentially be traced throughout the life span.

4.3 MEG Measurements

4.3.1 Stimuli

Auditory stimuli were generated and delivered by the STIM software provided with the CTF system. Tones, generated with a Creative AWE64, 16-bit stereo sound card (SB16 Compatible), were constructed and saved as sound files, with the parameters outlined in each of the study chapters. They were then placed in sequence files that contained the delivery parameters, for example interstimulus intervals and event probabilities. The stimulus delivery system also sends trigger

signals to the MEG acquisition computer, via a parallel port, providing precise information about the timing of stimuli.

Stimuli were introduced into the magnetically shielded room via two plastic tubes, as all materials in the MEG recording room must be non-magnetic. The Etymotic ER-1 Tubephones were calibrated prior to use, with a B and K meter with earphone coupler. The transfer functions for power spectra were found to be in line with published data (Etymotic Research). The tubes were connected to foam ear inserts, which are comfortably placed within the participants' left and right ears. The length of the plastic tubes was 30cm, resulting in a delay of approximately 2.5ms between the trigger pulse sent to the acquisition system and the actual delivery of the tones to the participant. This delay was confirmed with use of an oscilloscope set up to compare the trigger pulse and the onset of the tones via the tubes. All latency measurements are corrected for this delay.

Where videos were visually displayed to participants (Chapters 7 and 8), the monitor was placed outside the magnetically shielded room and relayed to the participant via mirrors.

4.3.2 MEG Recording Procedure

For the collection of MEG data, participants were seated in an upright position, with their heads placed in the helmet of the helium dewar. All magnetic materials (e.g. jewellery or clothing with metal elements, such as zips and underwired garments) were removed.

An essential part of MEG measurements is the accurate localisation of the head with respect to the sensors. In the case of the studies presented here, this was achieved by the placement of three coils connected to a Velcro band and attached to the scalp, roughly at the naison and preauricular points. The field pattern produced by currents led through the coils was measured, before and after recording sessions, providing information on their location within the dewar helmet and the location error produced by any movement throughout the session (recordings with movements exceeding 0.5cm were disregarded and repeated). In order to reduce head movement, a cuff was placed over the Velcro band and

inflated to firmly secure the head. The door to the magnetically shielded room was then closed.

Before the start of the data collection phase, a number of short noise tests were conducted. These involved asking the participants to breath deeply, in order to check for any further contamination for magnetic materials close to chest, and to make eye-movements (left and right and blink three times). Non-essential electrical equipment (for example, fans) were switched off before data collection commenced.

Recorded data were bandpass filtered online. Details of the width of filters, in addition to sampling rates are provided in each of the study chapters.

On completion of the recording, a digitised 3-D representation of the participant's head shape is obtained using a Polhemus Isotrak system, with reference to the three coil locations, and a bite bar (used to stabilise the head).

4.4 Data Processing

4.4.1 Initial Processing

At the first stage of data processing the raw data were corrected for DC offset based on the baseline (pre-stimulus) period. Data were then carefully inspected for artefacts caused by eye-movements or external noise sources causing 'spikes' within recording channels. Trials with such contamination were removed. Details on further data processing, specific to each of the studies, are outlined in the study chapters.

4.4.2 Averaging

Auditory evoked fields were collected in response to a number of stimulus repetitions. During the recording of evoked responses spontaneous brain activity, such as the α rhythm, is a source of noise (Hamalainen et al., 1993). To eliminate this noise averaging methods, which powerfully increase the signal to noise ratio, are employed. Averaging time locked phenomena exploits the fact that spontaneous brain activity and other sources of noise are typically not phase locked to the stimulus and can be considered independent. If we average the data

over a period of trials, the background activity will be cancelled out, enabling the evoked response to emerge.

4.4.3 Filtering

The averaged datasets were bandpass and comb filtered to remove the 50Hz powerline and its harmonics, though the specific details of filtering parameters differed between studies and are outlined in the respective chapters.

4.5 Data Analysis

4.5.1 Global Field Power

In Chapters 7 and 8 the Global Field Power (GFP) of the averaged auditory evoked fields were plotted. The GFP sums the square of the amplitude values obtained over all 151 channels at each time point. Thus, it plots absolute magnetic field power, regardless of the direction of flux (ingoing or outgoing), over time.

4.5.2 GLM

The GLM program makes use of multivariate analysis techniques in order to examine the spatiotemporal dynamics of evoked fields (Friston et al., 1996). The method is essentially a two-stage process constituting a basic dimension reduction followed by a MANCOVA. The advantages of such an approach, over more standard techniques, such as the t-test are: improved signal to noise through dimension reduction and use of multiple samples per epoch; an output in terms of canonical modes (field maps with associated time series) which are easily characterised and interpreted in an MEG framework. The data presented in Chapters 6 and 7, examining MMNm responses to auditory deviants were subjected to this analysis.

Previous studies examining MMN responses in dyslexic groups have approached the problem of quantifying mismatch responses in a number of ways. In all cases the mismatch response is considered to be the difference between responses evoked by auditory 'standards' and 'deviants'. Typically this involves subtracting the average signal to all standard stimuli from the average signal to all deviant stimuli. Some researchers have made an attempt to determine whether these

average signals are significantly different, typically at the group mean average level, thus assessing the presence or absence of a statistically significant mismatch response (e.g. Baldeweg et al., 1999; Kujala et al., 2000). Other groups have addressed the problem in a different way, considering only whether there are differences in the 'subtraction' response between dyslexic and control groups as opposed to questioning the reliability of the MMN response within the groups (e.g. Hugdahl et al., 1998; Schulte-Korne et al., 1998a; Schulte-Korne et al., 1998b; Schulte-Korne et al., 1999a). Indeed, Sinkkonen & Teraniemi (2000) argue that testing for the absence of MMN is impossible, as due to the continuous variation of both the response and noise, the probability of complete absence is always zero. These authors argue that examining the null hypothesis that an individual's response is similar to the response in a control group is more instructive.

As discussed in Chapter 2, the dyslexic population is extremely heterogeneous and, as such, a major aim of the studies presented is to consider individual differences. Therefore, considering MMN responses at the group level alone is disadvantageous. Furthermore, in a tone omission paradigm, as presented in Chapter 7, the absence or presence of a mismatch response is of principal interest. Previous tone omission MMN studies have considered the statistical difference between the standard and deviant averaged responses with use of parametric (ANOVA Russeler, Altenmuller, Nager, Kohlmetz, & Munte, 2001; Yabe, Tervaniemi, Reinikainen, & Näätänen, 1997) and non-parametric (Wilcoxon, Yabe et al., 1998) statistical tests, in addition to considering differences between stimulus conditions. Likewise, in line with Baldeweg et al. (1999) and Kujala et al. (2000), the data presented in Chapters 6 and 7 are considered, first, in terms of the presence or absence of an MMN response, and secondly in terms of group differences. For the purpose of examining the presence or absence of a mismatch response, the MMN data here were subjected to GLM analyses (as described in Friston et al., 1996).

Pre-Processing / Dimension Reduction

MEG data is multidimensional: it is recorded over 151 sensor channels, and over a number of time bins. Therefore, the first stage of the GLM analysis involves

dimension reduction; the data is filtered and resampled and then singular value decomposition (SVD) is used to further reduce the dimensionality of the data by removal of the spatio-temporal (or canonical) modes corresponding to the smallest (noise) eigenvalues. Each of the spatio-temporal or canonical modes corresponds to a set of channel time-series and implicitly a set of field maps. The relative amplitude of the mode's (or eigenvector's) corresponding eigenvalue determines its power contribution to the data. In these analyses we consistently discarded all but the largest 20 eigenvalues and their corresponding modes, the frequency bandwidth specified was always 1-30Hz, although the time period varied between studies (see sections 6.2.4 and 7.2.4).

Statistical Testing

The second stage of the GLM analysis is a MANCOVA. In the MMNm studies presented the test was simply whether the variability between two stimulus types (standard or deviant) was greater than the variability one would expect due to error. The output of the MANVOVA analysis for this basic contrast is the metric known as Wilk's Lambda. Wilk's Lambda expresses the ratio of the variability due to the effect of interest to that of the error (due to inter-epoch variability for example) and has a chi-square distribution, where the degrees of freedom (DF) are equal to the number of eigenvectors considered (here, 20). For the studies presented in Chapters 6 and 7, a probability of falsely rejecting the null-hypothesis of $p<0.01$ was taken to represent a statistically significant difference between stimulus conditions (standard and deviant).

Examination of Canonical Modes

On establishing that the effects of interest are significant it is then possible to examine the underlying canonical modes. These illustrate the distribution of the modelled effect over time and sensor channels. For the data in Chapter 7, the MMNm response is visible in the resulting modes datasets (see section 6.2.4, Figure 6-2). However, due to the short time windows employed for the GLM analysis in Chapter 7, and the small number of resulting samples, the canonical modes datasets provide little information.

It should be noted that the GLM analysis does not directly assess the presence or absence of an MMN response. Rather, it considers whether data elicited in response to standard and deviant stimuli are significantly different. The value of being able to determine this is obvious, particularly for the tone omission data presented in Chapter 7. The GLM is a parametric test, however that fact that it is used to compare artefact free epochs (at least 100) within the same scanning runs means that the assumptions associated with such tests (homogeneity of variance, normality etc) are not violated. Furthermore, the ability to explore the hypothesis on case by case basis, taking account of intra-subject variability, circumvents the need for group averaging techniques (e.g. Baldeweg et al., 1999) not amenable to MEG (section 4.2.5). This accounting for intra-subject variability means that concerns regarding the variability in both the signal and the noise, raised by Sinkkonen & Teraniemi (2000), are addressed.

4.5.3 Source Modelling

The first practical stage of source modelling involves creating realistic spherical head models. The digitised head shape files obtained after MEG measurements (section 4.3.2) were co-registered with the individual participants' structural MRI data (with reference to the common bite bar), where this was available, allowing for the construction of an accurate spherical head model. MRI images were obtained for six of the control participants and two of the dyslexic participants, using a 1.5T GE magnetic resonance scanner with 1.5mm x 1.5mm x 1.5mm voxel size. Where no MRI was available, the head model was obtained by coregistering the digitised head shape with another participant's structural MRI data. While this model cannot be considered as accurate as a coregistration with the participant's own structural information, it provides information about the head outline and positioning in relation to the sensors.

For the tone pair study (Chapter 5), N1m responses were modelled as bilateral ECDs. Taking the data from the 151 channels, a single dipole was introduced into the head model. The initial guess for the location of this dipole was based on the field maps generated at the peak of the response of interest. A spatiotemporal algorithm was used and the dipole was fitted, using a least squares search. The location of this dipole was then fixed and a second dipole was introduced in the

opposite hemisphere, the initial guess for location being based on the residual field map. This dipole was fitted and fixed and then both the left and right hemisphere dipoles were then fitted and fixed a further time. The time periods used in the spatiotemporal algorithms differed between studies and details are provided in the relevant chapters.

Dipole models were rejected where chi-square error values, at the peak latency of the response, exceeded five. In addition, only results for fits with a Monte Carlo Volume less than $5cm^3$ were reported.

Where structural MRI data were available, the modelled dipole solutions were superimposed on the MRI image. This allowed for comparisons between source estimates and actual sites of anatomical structures.

5 TONE PAIR TASK

5.1 Introduction

5.1.1 Aim

The aim of the present study is to investigate the effect of varying both the duration of the silent interval and the frequency separation (FS) between tones in a tone pair task. Behavioural and physiological responses of dyslexic and non-dyslexic groups are considered to determine the relative effects of each experimental manipulation. Do the dyslexic individuals demonstrate impairments on a frequency discrimination task and, furthermore, are any impairments related more to stimulus presentation rates or stimulus frequencies? The amplitude and latency of the N1m component, in response to simple auditory stimuli, are examined.

5.1.2 Temporal Processing Deficit Hypothesis

Paula Tallal and colleagues were among the first to make the claim that dyslexia could be characterised by impaired processing of brief and rapidly presented auditory non-speech stimuli (see sections 3.3.1 and 3.3.2). The group proposed that the inability of dyslexic and language impaired (LI) individuals to respond appropriately to rapidly changing acoustic events would affect their ability to process rapid changes in the speech stream and thus may disrupt normal speech perception resulting in delayed or impaired language development (Tallal, 1980; Tallal, 1999; Tallal et al., 1993; Tallal & Piercy, 1973b). Such basic processing deficits, they argued, would interfere with the development of phonological awareness, which has been implicated as a key component in the development of normal literacy skills (see section 2.2.3).

Evidence both for and against Tallal's Temporal Processing Deficit account of dyslexia has been presented (as reviewed in sections 3.3.1 and 3.3.2). Indeed, intense debate has been levelled at the use of the term 'temporal processing' (Mody et al., 1997; Studdert-Kennedy & Mody, 1995). However, a number of researchers have found that dyslexics' performance on tasks requiring the detection and discrimination of brief and rapidly presented non-speech stimuli is different from non-dyslexic individuals (sections 3.3.1 and 3.3.2).

One proposed neural mechanism for such deficits is a prolonged time window, within which successive auditory inputs interfere with one another (Hari, 1995; Helenius et al., 1999b).

5.1.3 Impaired Frequency Discrimination

While the temporal processing account has focussed on the dyslexic population's difficulties with auditory stimuli that are brief in nature or rapidly presented, an alternative account has questioned whether the encoding of the spectral properties of stimuli is normal in dyslexia (see section 3.3.4).

A number of studies employing threshold measures of just-noticeable differences to examine the frequency discrimination abilities of dyslexics have reported impairments (McAnally & Stein, 1996; Ahissar et al., 2000; France et al., 1997; Cacace et al., 2000). Interestingly, Cacace et al found that elevated thresholds in their reading impaired group were independent of stimulus duration and France et al. (1997) found that impairments were actually amplified at slowed presentation rates.

Considering the neural mechanism of such behaviourally observed deficits, McAnally & Stein (1996) proposed that the generation, decoding or exploitation of phase locked cues, which encode the fine spectral properties of stimuli, is impaired in dyslexia. However, there is now evidence that dyslexic individuals' phase locking mechanisms are normal (e.g. Dougherty et al., 1998; Hill et al., 1999; Witton et al., 1997; Witton et al., 1998).

5.1.4 Physiological Results

Although the results of psychophysical studies can give an insight into underlying neural processing, a more direct measure is afforded by examining physiological responses. The investigation of low-level sensory processing at a neural level requires very fine temporal resolution, thus posing a problem for hemodynamic measures of physiology. However, the use of tools such as Electroencephalography (EEG) and Magnetoencephalography (MEG) allow us to

tap into processes occurring on a millisecond-by-millisecond basis and confidently measure transient synchronous responses (section 4.2.10).

A number of features of the auditory evoked response (AER) have been examined in dyslexic groups to investigate the processing of simple auditory stimuli (as reviewed in section 3.4). For the purposes of this study, the N1 response and its magnetic counterpart the N1m is of principal interest. A brief review of N1 is provided in section 3.4.1. It is the most conspicuous deflection of the AER. The main generator source of N1 lies in the supratemporal cortex, and it is elicited by any abrupt acoustic input or change in the auditory environment.

Neville et al. (1993) recorded auditory event related potentials (AERPs) to simple tones in LI children who were also severely impaired on reading tasks. They found that the N1 component (recorded at a latency of 140ms in children) was significantly reduced and delayed when tones were presented at the shortest interstimulus intervals (ISIs) (200ms but not 1000ms or 2000ms), but only in those LI subjects who performed poorly on Tallal's Repetition Test (Tallal, 1980). Furthermore, while the LI group as a whole were worse than controls at detecting low probability target tones, the effect of shortening ISI was only significant in those LI subjects classified as poor on the temporal processing tasks. These findings would appear to imply that fast rates of stimulus presentation are selectively detrimental only to a subgroup of LI/ reading disabled individuals, rather than to the population generally.

Duffy et al. (1999) examined AERs to complex single tones and tone pairs in a group of 'learning impaired' children who had been reclassified in terms of reading ability. They found that AERs produced by tone pair stimuli presented with short ISIs (50ms and 100ms) were more successful in discriminating between the good and poor readers than AERs recorded to single tone stimuli. The group interpreted the result as evidence of interference in the perception of auditory stimuli presented in rapid succession in poor readers (perhaps due to backward/forward masking mechanisms).

Nagarajan et al. (1999) set out to determine whether cortical processing of brief and rapidly presented stimuli could differentiate good and poor readers. They presented a tone pair temporal ordering task to a group of carefully selected poor readers and matched controls and recorded MEG responses. The poor readers had all demonstrated difficulties in temporal ordering tasks, although they were able to correctly discriminate between stimuli at the test frequencies employed (800Hz and 1200Hz). Behavioural results demonstrated that the poor readers had difficulties with this task in comparison with controls across all ISI conditions, but that their performance worsened as the ISI between the tones within a pair was reduced (a trend not reflected in controls, although this may simply have been the result of ceiling level performance in the control group). In terms of physiological responses, mean RMS (root mean square) N1m responses to second tones presented at 100ms and 200ms, but not 500ms intervals were significantly weaker in poor readers. This finding suggested that the critical factor differentiating the participant groups was the presentation rate as opposed to the FS between tones.

Hari and colleagues (e.g. Hari, 1995; Helenius et al., 1999b) have proposed that impairments found in dyslexic groups in response to rapidly presented stimuli could reflect an increase in the perceptual time window within which successive auditory inputs interfere with one another. Merzenich et al. (1993) have proposed that such a disruption may be mediated by impairment at pre-conscious levels of processing. Auditory stimuli are integrated over short periods in order to form perceptual events as they are encoded into Sensory Memory. The time period over which this occurs (known as the Temporal Window of Integration (TWI)) may be extended in dyslexic individuals.

The observation that the N1 response is enhanced to the second tone in a pair when the interstimulus interval (ISI) is less than 300ms has been interpreted as evidence of persistence due to temporal integration processes (Loveless et al., 1989; Loveless et al., 1996). Loveless & Koivikko (2000) tested the prediction that the N1 enhancement effect is displaced to longer intervals in dyslexic subjects. They presented dyslexic and control groups with noise pair stimuli, separated by variable silent intervals from 70-500ms. They found that the N1m responses were significantly stronger to the second than to the first tone at all

SOAs (stimulus onset asynchrony) in the control group but that, contrary to the displacement hypothesis, this function dissipated at SOAs greater than 230ms in the dyslexic group. They concluded that an extended TWI could not account for the observed deficits in auditory processing. As an alternative account they proposed that the auditory processing deficits observed in dyslexics could be explained by reduced attentional capture.

In an attempt to mimic the N1m- N1m' physiological sequence elicited by speech sounds containing acoustic transitions, Renvall & Hari (2002) presented dyslexic and control adults with noise bursts of varying durations immediately followed by a 400ms square wave sound. The SOA between sound pair stimuli was held constant at 1.1s so that the effect of varying the duration of noise bursts was to vary the silent interval between the transitions (from 500ms-700ms). N1m amplitudes were significantly weaker in the dyslexic group compared to the control group with the shortest noise durations. Furthermore, while N1m' response amplitudes increased as a function of increased noise duration in the control group, in the dyslexic group the enhancement effect was disrupted and was only marginally evident with the largest noise durations. The authors suggest that the smaller N1m and N1m' responses in dyslexics may be due to reduced auditory capture by these stimuli. Specifically, the reduced N1m' response may result from greater inhibition of the corresponding auditory pool.

Helenius et al. (2002) report a negative result. They examined the N1m response evoked by various slowly and rapidly successive speech and non-speech sounds. While N1m responses were different between their dyslexic and non-reading impaired adults in response to speech sounds, N1m responses evoked by single tones and complex non-speech sound pairs (composed of formant frequencies which mimicked the speech sound stimuli) did not differ between groups. This result appears to suggest that the presentation rate of closely successive stimuli alone was not the determining factor in the diminished N1m response to the real speech stimuli.

Baldeweg et al. (1999) recorded the N1 responses to standard and deviant tones in their MMN study. This group found that, while MMN responses to frequency

deviant tones were reduced and delayed in the dyslexics, N1 responses were normal.

Hugdahl et al. (1998) also found that MMN peak latency was significantly delayed in their dyslexic group in response to pitch deviants. In contrast, Schulte-Korne et al. (1998a) obtained normal MMN responses in their group of spelling disabled children to frequency deviant tones but abnormal responses to deviant speech stimuli. In a follow up study, Schulte-Korne et al. (1999a) found abnormal MMN responses to tonal patterns in a group of dyslexic adults and the group concluded that the evidence suggested impairment in the dyslexic group's processing of temporal information.

5.1.5 Unresolved Issues

The principle aim of the present study is to examine the relative contribution of two factors on the behavioural and physiological responses of the adult dyslexic population; the ISI and FS between tones in a tone pair frequency discrimination task. While a number of previous studies have considered the contribution of such factors separately, no firm conclusions can be drawn across studies. Moreover, the design of the present study allows subtle manipulation of either or both of these variables in the equivalent experimental design.

While the results of Neville et al. (1993), Duffy et al. (1999) and Nagarajan et al. (1999) would seem to suggest that the impaired processing of rapidly presented auditory stimuli is related to reading ability, participant sampling issues mean that findings may not necessarily be directly extended to deficits underlying dyslexia, specifically or generally. Neville et al. (1993) and Duffy et al's. (1999) participants were taken from LI populations. Furthermore, evidence of auditory processing deficits in two of the studies (Neville et al., 1993 and Nagarajan et al., 1999) applied only to individuals who were impaired in temporal ordering tasks. The assumption that temporal processing deficits exist in all cases of dyslexia is far from established. In the present study, participants are selected purely on the basis of dyslexic difficulties.

Further caution must be exercised in interpreting the results of Nagarajan et al. (1999) as the possible confounding variable of poor frequency discrimination in the dyslexic group is not accounted for. Although the experimental group were selected on the basis that they displayed normal detection of tones at the frequencies used, Ahissar et al. (2000) have proposed that difficulties with frequency discrimination, which are 'below the surface', can emerge in dyslexics with increasing task demands. Any such deficits, masked in the behavioural data, may be apparent when examining physiological responses. Such possibilities are not addressed by the results of Loveless & Koivikko (2000) as this group's tone pairs were constructed of all 'same' tones. In the present study the contribution of any frequency discrimination impairments are addressed with the inclusion of tones at frequencies equivalent to those employed by Nagarajan et al and tones with narrower FS. Both behavioural and physiological data can be examined to consider the relative contribution of ISI and FS.

The multiple task demands placed on participants in the Nagarajan et al. (1999) study may further confound the results. The temporal ordering task involves detection and discrimination of the tones, memory of sequence (possibly including verbal labelling) and generation of a motor response. Any one of these component processes could cause problems for the dyslexic group. Such task demands are limited in the present study as groups are simply instructed to judge whether tones within pairs are the same or different, with no motor response required during physiological recordings.

While Nagarajan et al. (1999) compared actual N1m amplitudes to second tones between subject groups, Loveless & Koivikko (2000) examined relative amplitude values (N1m response amplitude to second tones were expressed as a function of N1m response amplitudes to initial tones). The advantage of such a manipulation is that the effect of varying the ISI in each participant group is discerned more clearly. According to the hypothesis that the manipulation of the timing of auditory stimuli is the key factor determining deficits in dyslexic individuals, one would predict that no differences should be observed in responses to initial stimuli (Loveless and Koivikko (2000) do not report N1m amplitude values in response to initial tones). However, although Nagarajan et al. (1999) report no significant

differences in N1m responses to initial tones between subject groups, the data they do present for the 500ms ISI condition indicates at least a subtle reduction in the amplitude of this response in dyslexic listeners (mean RMS amplitude (fT): Good Readers=130±16, Poor Readers=116±8; mean modelled amplitude (nAm): Good Readers=47±9, Poor Readers=35±7; (Nagarajan et al., 1999, table 1, page 6485). Unfortunately, amplitude values to first tones are not reported for the 100ms and 200ms ISI conditions. The significant differences observed in amplitude values for second tones could possibly reflect the fact that subtle differences, already existing in response to initial tones, were merely amplified. In order to directly assess the effect of varying ISI on N1m responses to second tones, difference values between first and second tones are compared across the groups in the present study.

5.2 Methods

5.2.1 Participants

The seven dyslexic and seven control participants from the subject pool outlined in Chapter 4 completed the study. One dyslexic subject (D7) was excluded from the analysis due to the fact that N1m responses could not be reliably modelled (section 5.2.6). In addition, a control subject's data (C7) were disregarded due to excessive eye-movement contamination in physiological data. The remaining participants were all students from Aston University and groups were matched for age, sex and IQ. The dyslexic group's performance on tests of literacy, auditory short-term memory, phonological skills and processing speed were significantly worse than the control group's performance on the same measures (see section 4.1.4).

5.2.2 Stimuli

Auditory stimuli (Figure 5-1) were tone bursts of 20ms duration (5ms Hanning Window) presented binaurally at 70dBSPL (sound pressure level). Each trial consisted of tone pairs in which there was an equal probability (p=0.25) of tones being low-low, high-high, low-high or high-low. Stimulus conditions were presented as a 2x2 factorial design; two levels of ISI (500ms or 200ms, tone1 offset – tone2 onset), by two levels of FS (400Hz or 100Hz FS, centred around 1000Hz). The inter-trial interval (ITI) was held constant at 2sec. The four tone

pair conditions were presented in separate blocks, with the order of presentation randomised across subjects. Each block comprised 200 trials.

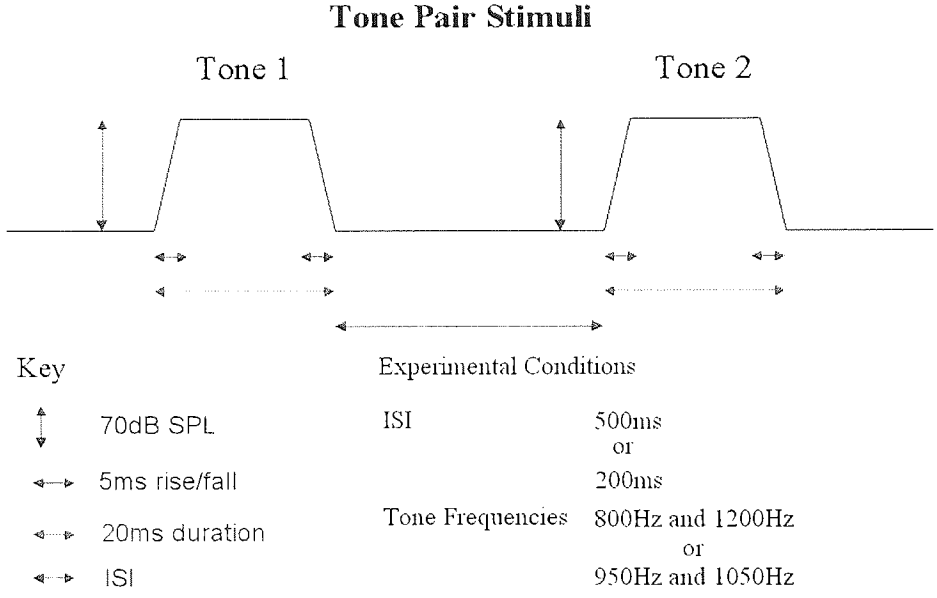

Figure 5-1 Tone Pair Stimuli
Graphical representation of the tone pair stimuli.

ISIs were selected with reference to the findings of Nagarajan et al. (1999). The group reported that while N1m responses to first and second stimuli were equivalent between groups with an ISI of 500ms, responses to second stimuli were significantly reduced in dyslexics with an ISI of 200ms. The group also report the significant group difference at an ISI of 100ms but the use of such an ISI was more complicated due to temporal overlap in responses. Nagarajan et al. employed tone frequencies of 800Hz and 1200Hz (400Hz), equivalent tone frequencies were used in the present study to enable comparisons. However, it was suggested in section 5.1.5 that reported group differences may have been confounded by subtle frequency discrimination impairments in the dyslexic group. In order to assess this possibility tones with a narrower FS (100Hz) were also included. Group differences relating to frequency discrimination impairments, which are evident at 400Hz FS, should be amplified as the FS narrows to 100Hz.

5.2.3 Data Acquisition

Behavioural and physiological data were collected for each participant within a single session, with a break of at least half an hour between behavioural and

physiological data collection. The order of administration was randomised across participants.

For the behavioural study, participants were seated comfortably in a quiet room and stimuli were presented via ear inserts, detailed in Chapter 4. They were instructed to attend to the tone pair stimuli and decide whether the tones within each tone pair were 'same' or 'different' (forced choice), regardless of the direction of change. Responses were recorded with a mouse, held between the two hands. A left thumb press indicated a 'same' response, while a right thumb press indicated a 'different' response. Participants were allowed 5mins to rest on completion of each of the condition blocks.

Physiological data were collected with the CTF 151-channel whole-head MEG system as outlined in Chapter 4, section 4.3.2. Participants were again instructed to attend to the auditory stimuli and judge whether tones within each pair were 'same' or 'different', although no physical response was made. They were asked to keep their eyes open and to fixate on a small self-selected area, at a fixed distance, in the centre of their field of vision. Data were recorded at a sampling rate of 1250Hz, with a low pass filter of 300Hz. Epochs were triggered by the first tone of each tone pair, the analysis period was 2s including a pre-stimulus period of 500ms. 5mins resting time was provided on completion of each of the condition blocks.

5.2.4 Data Processing

The mean percentage of correct behavioural responses and mean latency of behavioural responses for the 200 trials were calculated for each subject in the four stimulus conditions.

The raw physiological data were DC corrected using the pre-stimulus baseline and carefully inspected for eye-blink artefacts, epochs with large deflections were rejected; for all 12 subjects, no more than 10 trials were rejected from any one dataset (as noted above, one control participant from the original seven was excluded due to excessive eye artefact contamination). Average datasets were then created for each of the ISI and FS conditions. The data were bandpass

filtered from 1.26-70Hz and comb filtered to remove the 50Hz powerline and its harmonics.

5.2.5 Data Exploration

In order to initially explore the auditory evoked responses, raw MEG data were plotted in a number of ways; averaged data from the 151 channels were superimposed in butterfly plots, GFP plots were created over all 151 channels, and maps demonstrating the field distribution were visualised. While amplitude values cannot be compared from raw data alone (see Section 4.2.5), the latency of peak responses can be considered.

5.2.6 Source Modelling

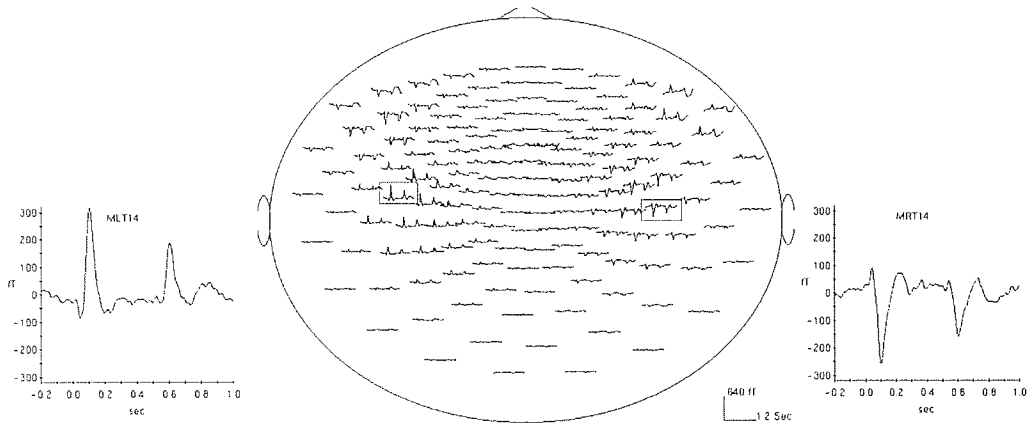

Figure 5-2 151-Channel Averaged Response to Tone Pair Stimuli
The averaged response to a tone pair with 500ms ISI across all 151 channels. Distinct deflections can be seen peaking at around 100ms after the onset of each tone and are largest over the left and right temporal lobes. The channel showing the largest response over each hemisphere is shown enlarged in the insets at the bottom of the figure.

The averaged MEG data of a representative control participant in the 500ms ISI condition can be seen in Figure 5-2. Both tones evoke a response at a latency of about 100ms. The peak amplitudes of these responses are largest over the temporal lobes and the field map (Figure 5-3) reveals dipolar patterns over the left and right temporal regions as two pairs of influx and outflux magnetic field peaks.

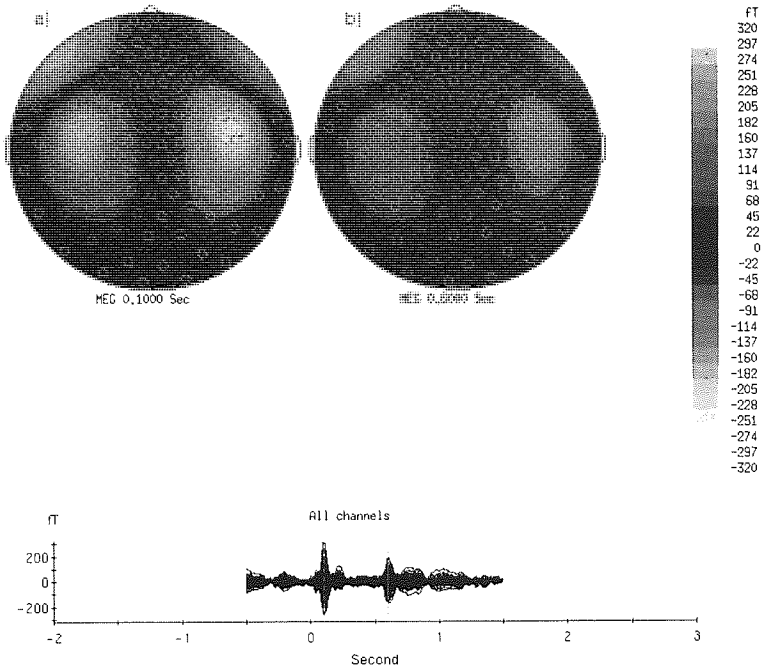

Figure 5-3 N1m Field Map at Peak of Response to Tone Pair Stimuli
Isocontour field map 100ms after the onset of the first (a) and second (b) tone stimuli. Red colours represent outgoing field values, while blue colours represent ingoing field values. Maps are shown on a schematic head.

The N1m component was identified in each participant as the first major peak in the measured signal, occurring >80ms after stimulus onset, with a field pattern of activation equivalent to that seen in Figure 5-3.

Bilateral equivalent current dipoles (ECDs) in a spherical head model were employed to explain the 151-channel field data during the N1m peak (see section 4.5.3 for details on the ECD model used). A spatiotemporal algorithm was used and ECDs were fitted, using a least-squares search, over a short time period (approximately 20ms) containing the peak of the N1m response to the first tone in each of the two experimental conditions. Firstly, a single ECD was fitted and fixed and then a second dipole was introduced and fitted in the opposite hemisphere. Each dipole was then fitted and fixed a further time. Only results for fits with a Monte Carlo Volume of less than $5cm^3$ were reported. One of the original seven dyslexics was excluded from further analysis due to the fact that N1m dipoles could not be reliably modelled (Monte Carlo Volume greater than $5cm^3$).

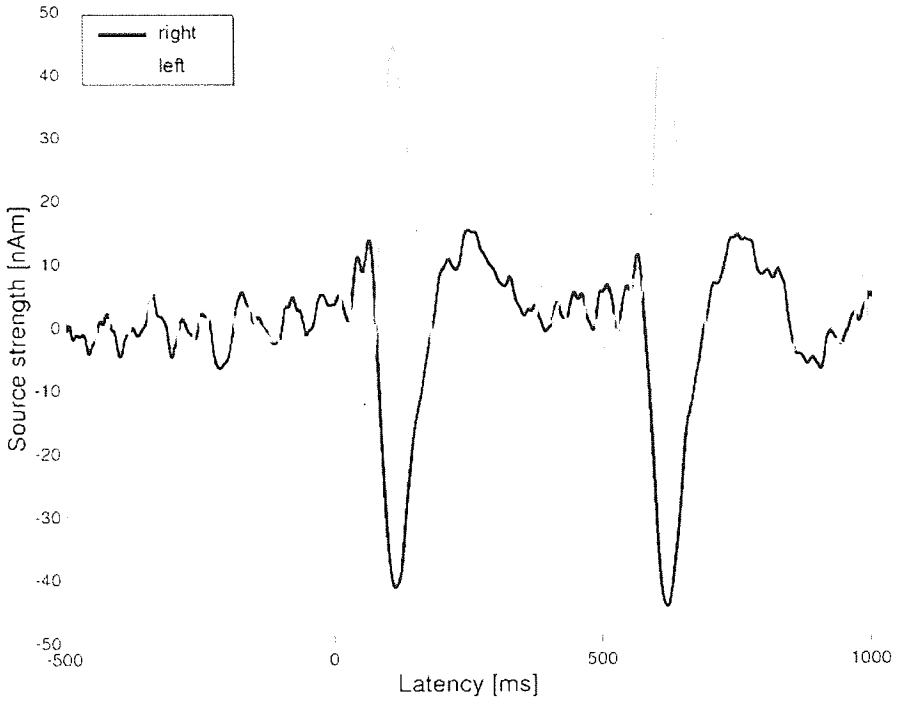

Figure 5-4 Waveforms for Dipoles Fitted to Explain N1m Responses to Tone Pair Stimuli
A plot of the time course of left and right hemisphere dipoles fitted in a representative control participant in the 500ms ISI – 400Hz FS condition. The first tone is presented at 0ms, the second at 500ms. The amplitude peaks of the dipoles occur approximately 100ms after each tone.

The analysis period was then extended to the entire 2s response, location and orientation were fixed while amplitude was allowed to vary, and the dipole waveforms were analysed (Figure 5-4). Occasionally, a third dipole was needed to explain additional noise peaks in the signal; in all cases the Monte Carlo Volume estimates for such 'noise dipoles' were greater than 20 cm^3. For all analysed datasets chi-square error values at the peak latency of the first N1m response were five or below. Figure 5-5 demonstrates the fit of the model to the field pattern 100ms after the first tone in a control participant.

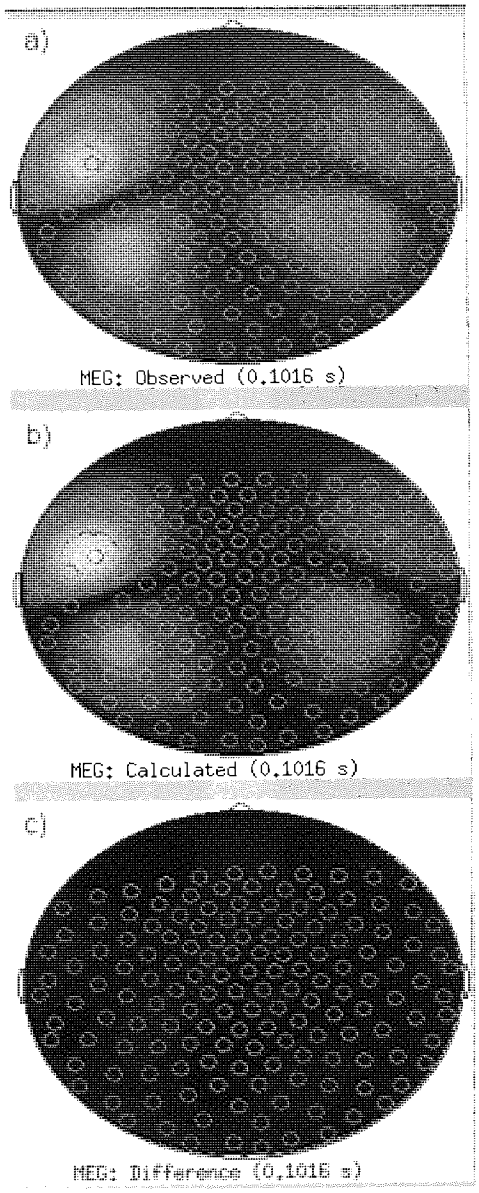

Figure 5-5 N1m Measured and Modelled Field Maps
a) Measured magnetic field approximately 100ms after tone onset in a control participant. b) Magnetic field of the dipole model derived by a least squares fit from the field shown in (a). c) The difference between the fields shown in (a) and (b).

N1m ECDs were superimposed onto the individual MRIs of two of the dyslexics and five of the control participants. The results confirmed that the dipoles were reliably located within the left and right auditory cortices (Figure 5-6 and 5-7).

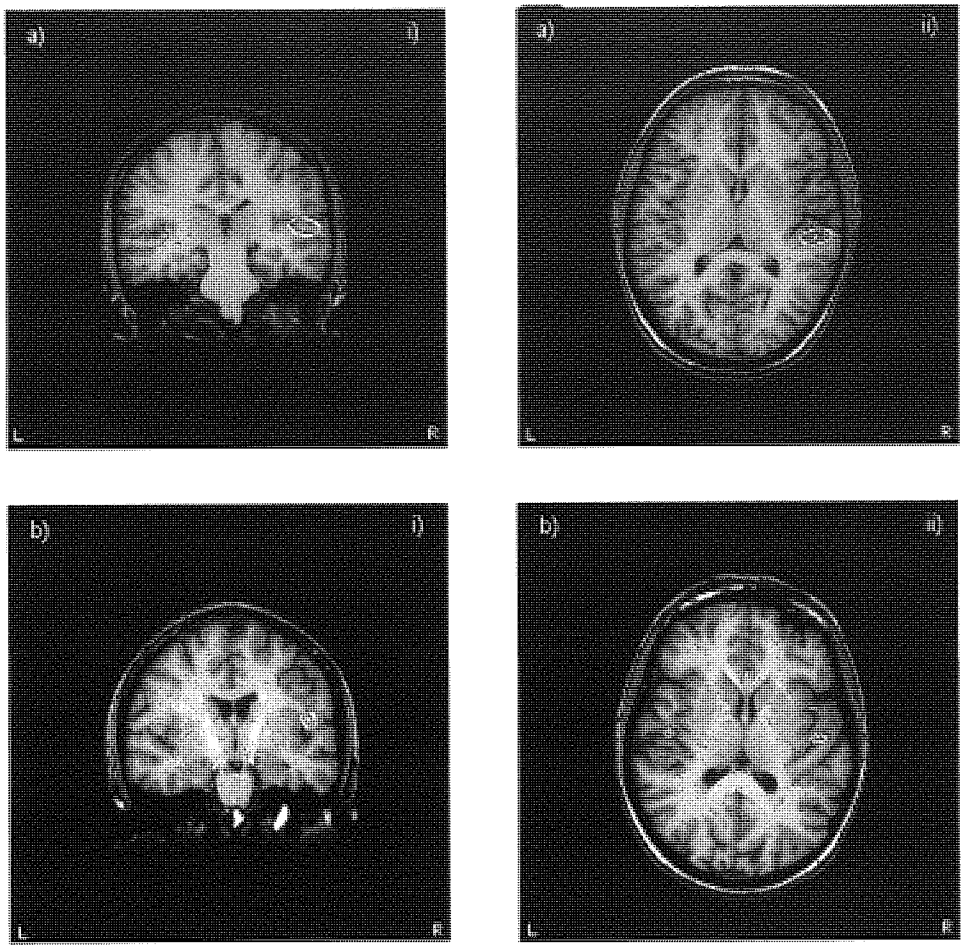

Figure 5-6 N1m Dipoles Superimposed on MRI Slices
The dipoles modelled to explain the N1m peak in the evoked response and superimposed onto coronal (i) and axial (ii) MRI slices in a control (a) and dyslexic (b) participant. Small dots indicate dipole location while spheres represent the 95% Confidence Volume calculated from Monte Carlo analysis.

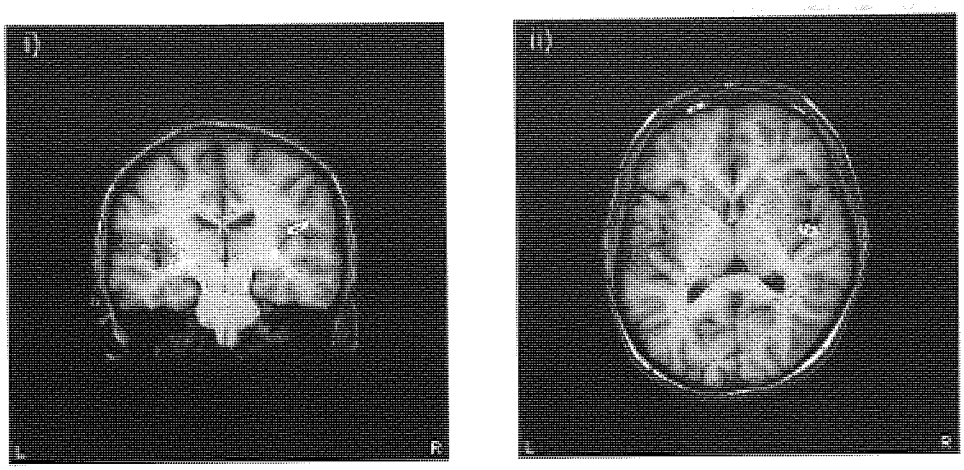

Figure 5-7 N1m Dipoles Across Conditions
Dipoles independently modelled to explain the N1m peak in the evoked response across the four stimulus conditions in a representative control participant. Dipoles are each superimposed onto a coronal (i) and axial (ii) MRI slice to demonstrate the repeatability of the N1m dipoles obtained.

5.2.7 Statistical Analyses

The study was initially designed as a 2 x (2 x 2) factorial experiment, each level of ISI being compared with each level of FS. However, due to the small sample size this design was retrospectively considered to be over complicated for statistical analyses (see Appendix 1, Table A-1). Therefore, the experimental manipulation of ISI and FS were considered separately: To examine the effect of shortening the ISI, data from the 500ms ISI – 400Hz FS condition were statistically compared to data from the 200ms ISI – 400Hz FS condition. To examine the effect of reducing the FS, data from the 500ms ISI – 400Hz FS condition were statistically compared to data from the 500ms – 100Hz FS condition.

Due to the small participant numbers, in addition to unequal variance between participant groups in many measures, non-parametric statistical tests were used.

For behavioural data, dependent variables were the mean percentage of correct behavioural responses and the mean latency of behavioural responses. In section 5.3.3 the dependent variables for the physiological data are the latency and amplitude of the modelled dipoles. In section 5.3.4, the difference in latency/amplitude between the dipole response to first and second tones (Tone2

minus Tone 1) was taken as the dependent variable. Analyses considering dipole modelled N1m responses report results for the right hemisphere (in line with Loveless & Koivikko, 2000). However, equivalent analyses were conducted for left hemisphere N1m responses and differences in hemispheric responses were considered (see section 5.3.6). It should be noted that dipole modelled N1m latencies were corrected for a 2.5ms delay in stimulus presentation resulting from delivery via plastic tubes (section 4.3.1). This correction is not made in the field maps presented in section 5.3.2.

5.3 Results

5.3.1 Behavioural Data

Performance accuracy (percentage of correct discrimination responses) and response times (latency of discrimination responses) were considered across the four tone pair conditions.

The dyslexic group's accuracy scores were lower than those of the control group across all tone pair conditions (Table 5-1). However, the group difference was only significant in the 400Hz FS conditions (500ms ISI – 400Hz FS condition, U = 4.5, $p=0.015_{(1\ tailed\ test)}$; 200ms ISI – 400Hz FS condition, U = 6.0, $p=0.027_{(1\ tailed\ test)}$). Considering the effect of manipulating the stimulus conditions, a Wilcoxon Signed Ranks analysis revealed that the control group's accuracy scores were significantly poorer as the FS narrowed (500ms ISI – 400Hz FS compared to 500ms ISI – 100Hz FS, t = 0.0, $p=0.014_{(1\ tailed\ test)}$), while reducing the ISI did not have a significant effect. Neither narrowing the FS nor reducing the ISI had a significant effect of the dyslexic group's accuracy scores.

Table 5-1 Percentage of Correct Behavioural Responses

	Control		Dyslexic	
Condition	Median	Range	Median	Range
500ms-400Hz	97.25	4.00	92.50	17.00
200ms-400Hz	96.50	6.00	91.00	21.00
500ms-100Hz	91.75	27.50	85.75	35.50
200ms-100Hz	89.75	27.50	82.25	44.00

Individual data were examined to explore the large degrees of variance in the data. Figure 5-8 reveals that reducing the FS between tones may have actually had a detrimental effect on two of the dyslexic participants (D4+D6). These individuals' scores are markedly worse in the narrower RS conditions. However, the same can also be said for C3 when considering this participants accuracy scores along with the rest of the control groups. Therefore, any disadvantage with narrowing FS cannot be interpreted as a group effect.

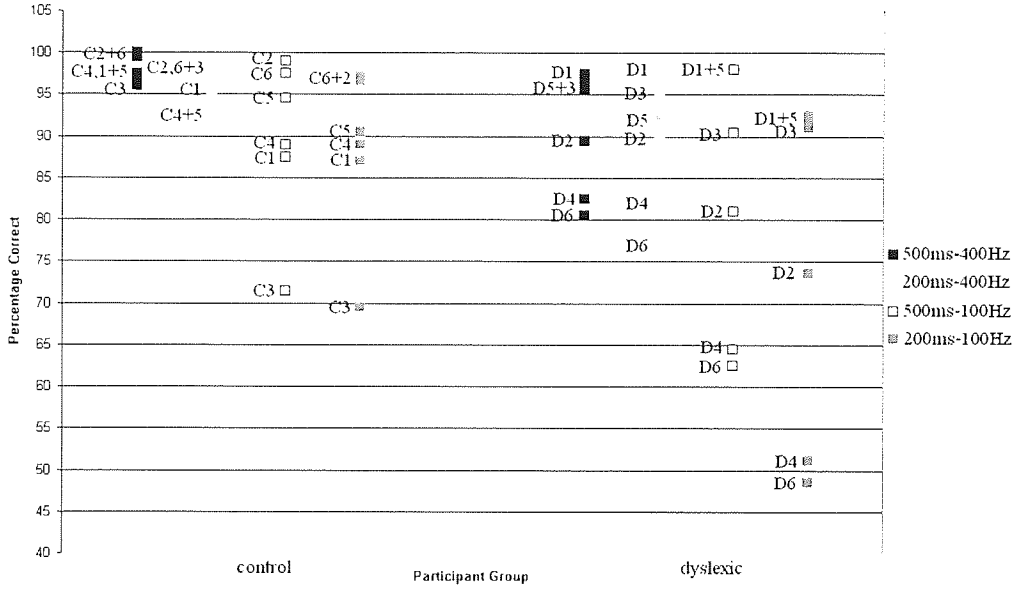

Figure 5-8 Percentage of Correct Behavioural Responses (Individual Data)
Graph illustrating the percentage of correct discrimination responses for the 12 participants. Data point markers identify each of the individual subjects.

Table 5-2 Latency of Behavioural Response

	Control		Dyslexic	
Condition	Median	Range	Median	Range
500ms-400Hz	0.605	0.336	0.683	0.312
200ms-400Hz	0.660	0.438	0.697	0.270
500ms-100Hz	0.693	0.396	0.746	0.251
200ms-100Hz	0.654	0.296	0.763	0.368

The dyslexic group's response times were typically slower than those of the control group across all tone pair conditions (Table 5-2). However, the group difference was only significant in the 500ms ISI - 400Hz FS condition ($U = 6.0$, $p=0.0275_{(1\text{ tailed test})}$). A Wilcoxon Signed Ranks analysis revealed that response

times in the control group were significantly slower as the ISI was reduced (500ms ISI – 400Hz FS compared to 200ms ISI – 400Hz FS, t = 1.0, $p=0.023_{(1\ tailed\ test)}$), while manipulating the FS had no significant effect. In contrast, the dyslexic group's responses were significantly slower as the FS was narrowed (500ms ISI – 400Hz FS compared to 500ms ISI – 100Hz FS, t = 1.0, $p=0.023_{(1\ tailed\ test)}$), while reducing the ISI had no significant effect.

Individual data are plotted in Figure 5-9. Interestingly, the two dyslexic individuals identified above (D4 and D6) as being detrimentally effected by reducing the FS were slower to make behavioural responses in all of the tone pair conditions, possibly reflecting a difficulty with the frequency discrimination task.

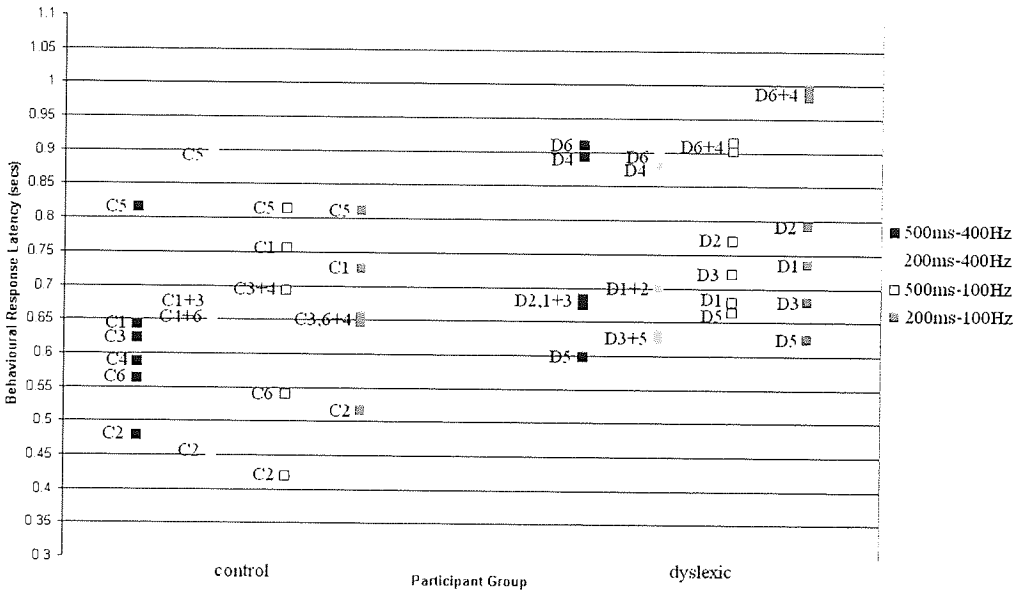

Figure 5-9 Latency of Behavioural Responses (Individual Data)
Graph illustrating the percentage of correct discrimination responses for the 12 participants. Data point markers identify each of the individual subjects.

5.3.2 Averaged MEG Data

Individual participants' averaged MEG data are visualised in butterfly plots and field maps in Figure 5-10 through Figure 5-25. Red markers on butterfly plots indicate 100ms after the onset of each tone, the predicted latency of the N1m response. Field maps are plotted at the peak of each of the N1m responses, based on Global Field Power calculations. The peak latency is reported below each of the field maps.

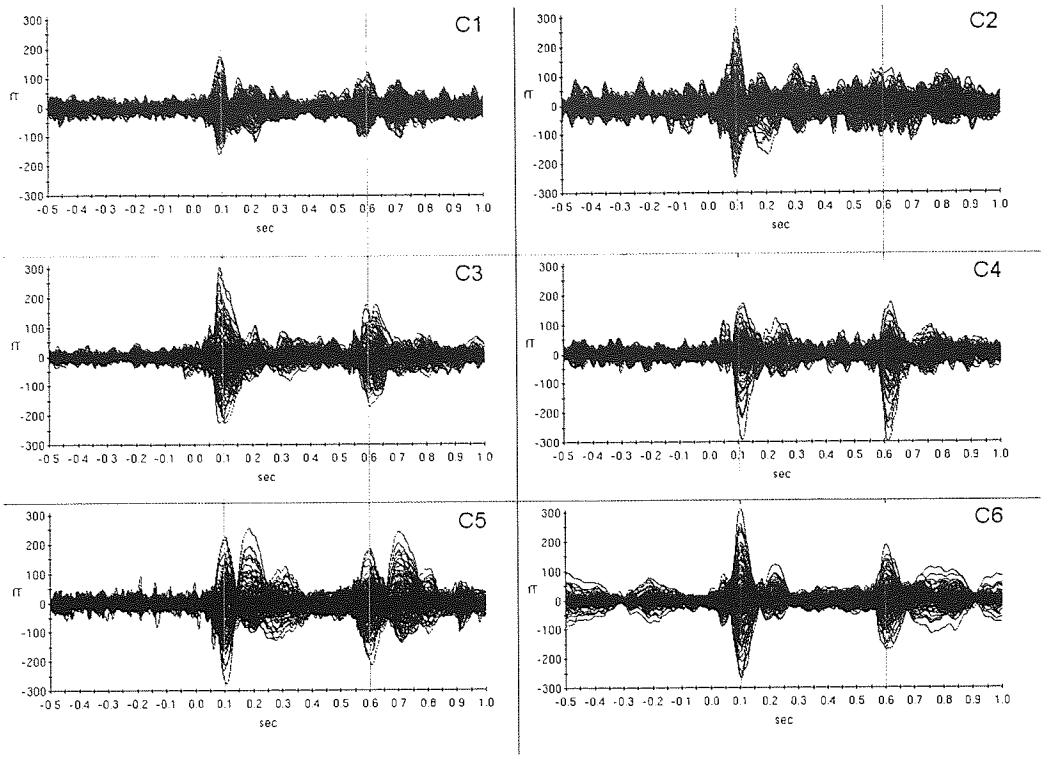

Figure 5-10 Butterfly Plot: 500ms ISI - 400Hz FS condition, Control Participants
A plot of the overlay data from all 151 MEG Channels for each control participant. Tone presentations occur at 0secs and 0.5secs, red data markers indicate 100ms after each tone onset.

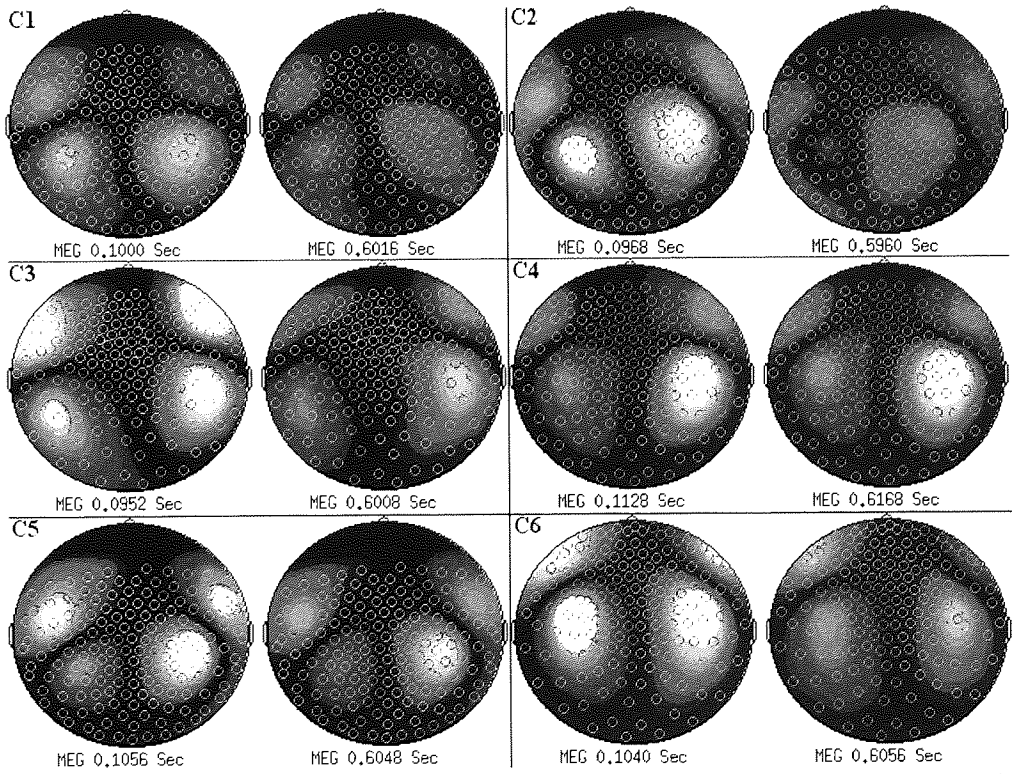

Figure 5-11 Field Map at the N1m Peak in Response to Each Tone: 500ms ISI - 400Hz FS condition, Control Participants
Maps representing the observed field at the peak of the N1m response (based on GFP calculations) for each control participant. Left hand plots relate to initial tones while right hand plots relate to second tones. The peak GFP latency is reported below each field map.

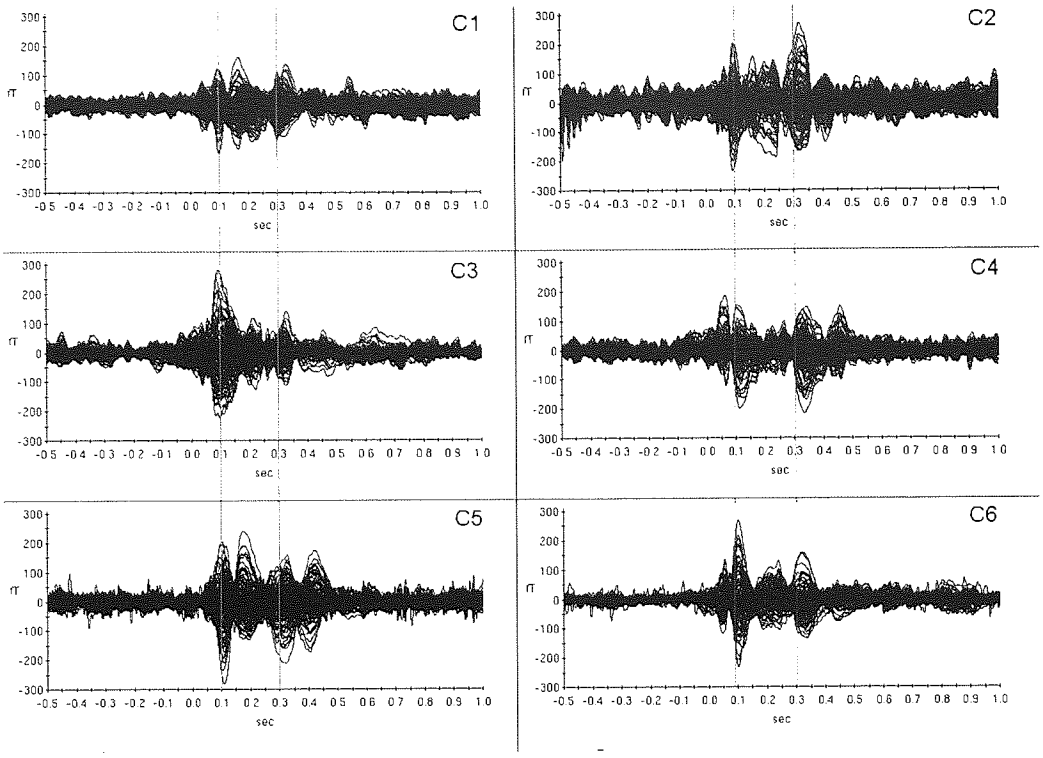

Figure 5-12 Butterfly Plot: 200ms ISI - 400Hz FS condition, Control Participants
A plot of the overlay data from all 151 MEG Channels for each control participant. Tone presentations occur at 0secs and 0.2secs, red data markers indicate 100ms after each tone onset.

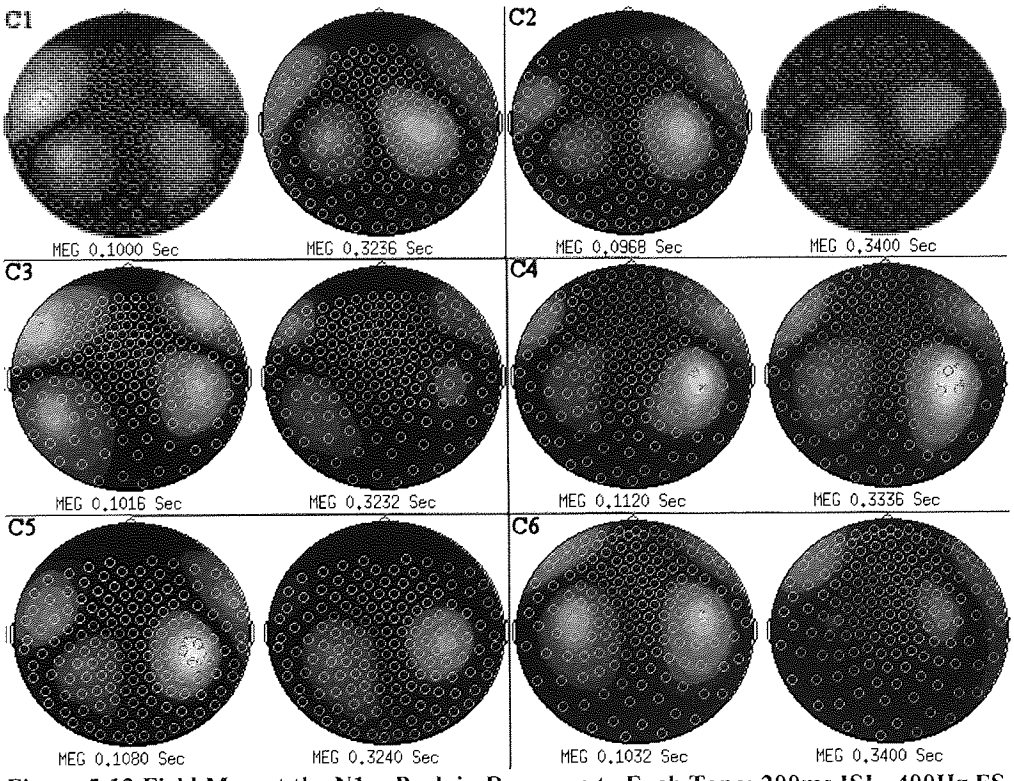

Figure 5-13 Field Map at the N1m Peak in Response to Each Tone: 200ms ISI - 400Hz FS condition, Control Participants
Maps representing the observed field at the peak of the N1m response (based on GFP calculations) for each control participant. Left hand plots relate to initial tones while right hand plots relate to second tones. The peak GFP latency is reported below each field map.

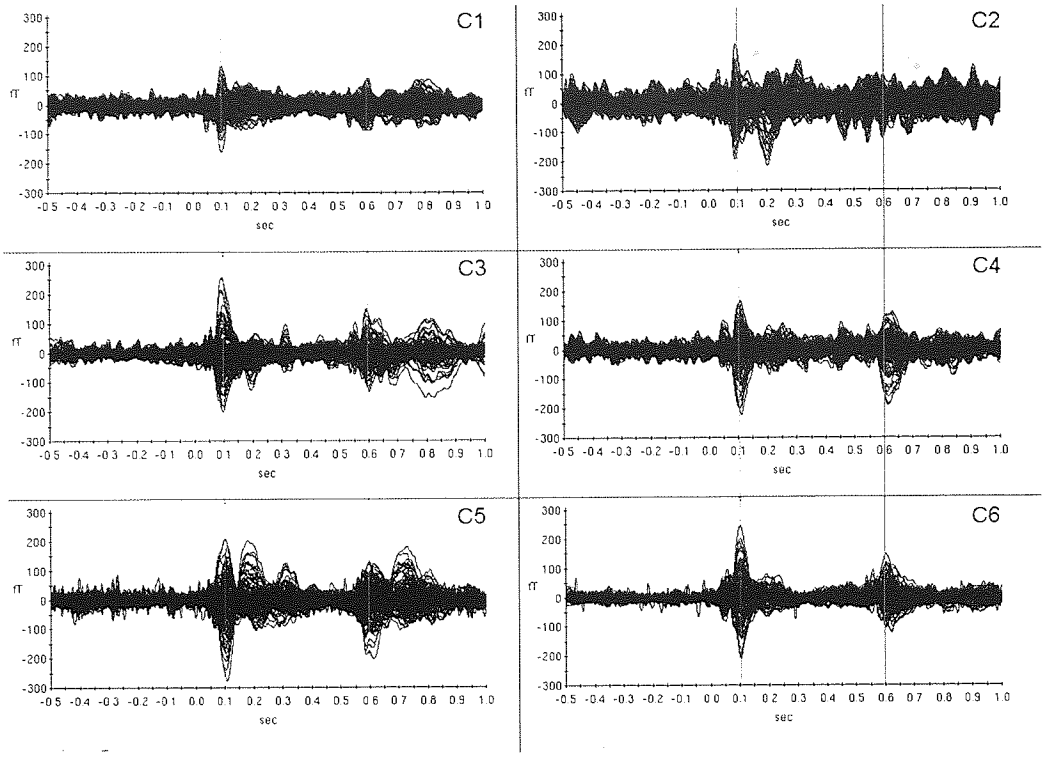

Figure 5-14 Butterfly Plot: 500ms ISI - 100Hz FS condition, Control Participants
A plot of the overlay data from all 151 MEG Channels for each control participant. Tone presentations occur at 0secs and 0.5secs, red data markers indicate 100ms after each tone onset.

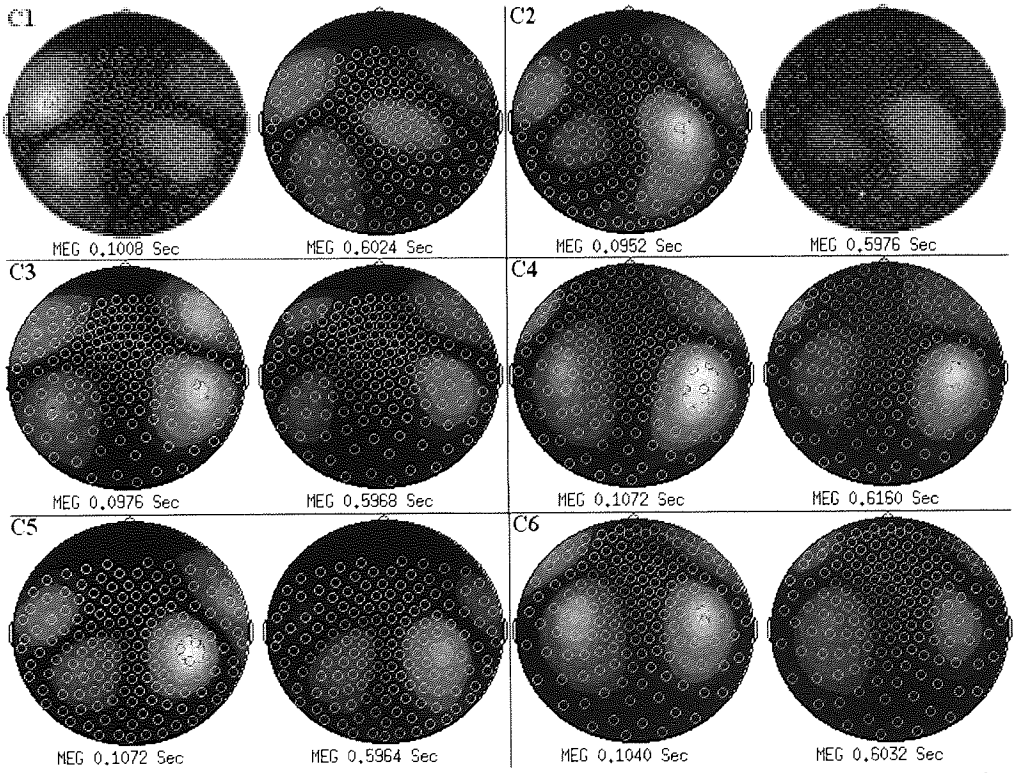

Figure 5-15 Field Map at the N1m Peak in Response to Each Tone: 500ms ISI - 100Hz FS condition, Control Participants
Maps representing the observed field at the peak of the N1m response (based on GFP calculations) for each control participant. Left hand plots relate to initial tones while right hand plots relate to second tones. The peak GFP latency is reported below each field map.

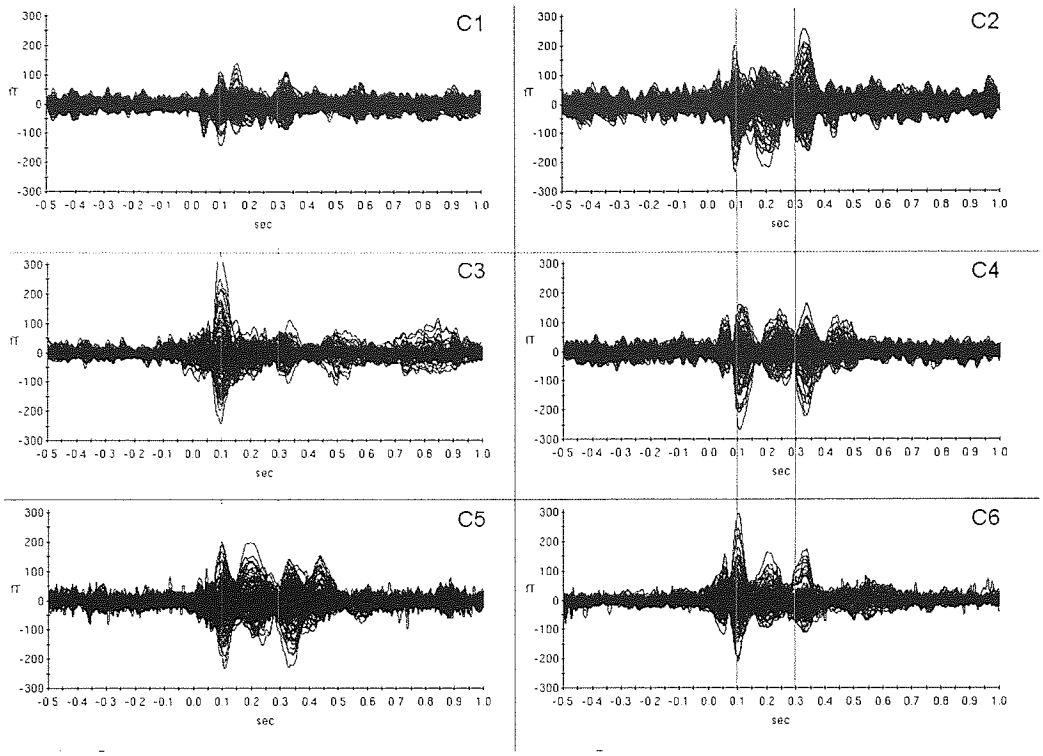

Figure 5-16 Butterfly Plot: 200ms ISI - 100Hz FS condition, Control Participants
A plot of the overlay data from all 151 MEG Channels for each control participant. Tone presentations occur at 0secs and 0.2secs, red data markers indicate 100ms after each tone onset.

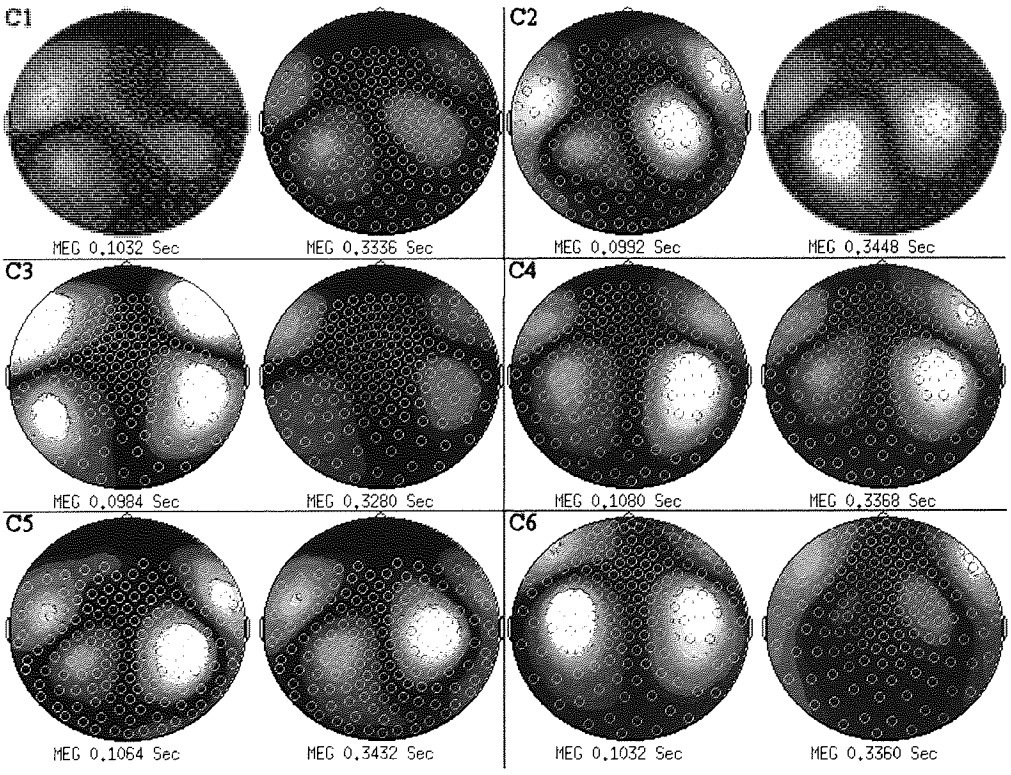

Figure 5-17 Field Map at the N1m Peak in Response to Each Tone: 200ms ISI - 100Hz FS condition, Control Participants
Maps representing the observed field at the peak of the N1m response (based on GFP calculations) for each control participant. Left hand plots relate to initial tones while right hand plots relate to second tones. The peak GFP latency is reported below each field map.

Examining butterfly plots for each control participant, clear deflections peaking at around 100ms after the onset of the first tone in the pair are evident. The peak latency of the response falls between 95ms and 108ms after the onset of the first tone in five of the six control participants' data. In the case of C4, the N1m peal latency to initial tones appears slightly delayed, falling at around 112ms after onset in the 400Hz FS conditions. The field patterns generated at the peak of these deflections reveal bilateral dipolar activation over each of the temporal lobes, in accordance with that predicted for the N1m response.

In the 500ms ISI conditions, N1m deflections are evident in response to the second tone at around 100ms after tone onset. These deflections are typically smaller than responses to first tones, particularly in the case of C2 (this is also reflected in the weaker field pattern). The latency of this response typically lies between 595ms and 608ms (95ms and 108ms after the onset of the second tone). However, reflecting that reported above, in the case of C4 the latency is slightly delayed at around 116ms after tone onset.

A delay in the N1m deflection in response to second tones in the 200ms ISI conditions is evident in each of the control participants' data. In each dataset this deflection peaks between 323ms and 344ms (123ms – 144ms after tone onset). In addition, the deflection does not appear as attenuated as second tone responses in the 500ms ISI conditions although, as noted above, direct comparisons of amplitude cannot be made between conditions.

It is worth noting that the morphology of responses evoked by the tone pair stimuli display notable variability between individual control participants, although the morphology of the averaged responses does appear to be comparable within participants across the four tone pair conditions. Additional peaks, not attributable to the N1m response, can be seen in the control participants' data. For example, in the case of C5 N1m responses are followed by large deflections at approximately 200ms after tone onset. The field maps generated at the peak of these deflections are similar to those generated for the N1m response though with a reversal of the influx outflux pattern. Considering the latency and the mirror of dipolar orientation it is likely that these deflections relate to the P2m response.

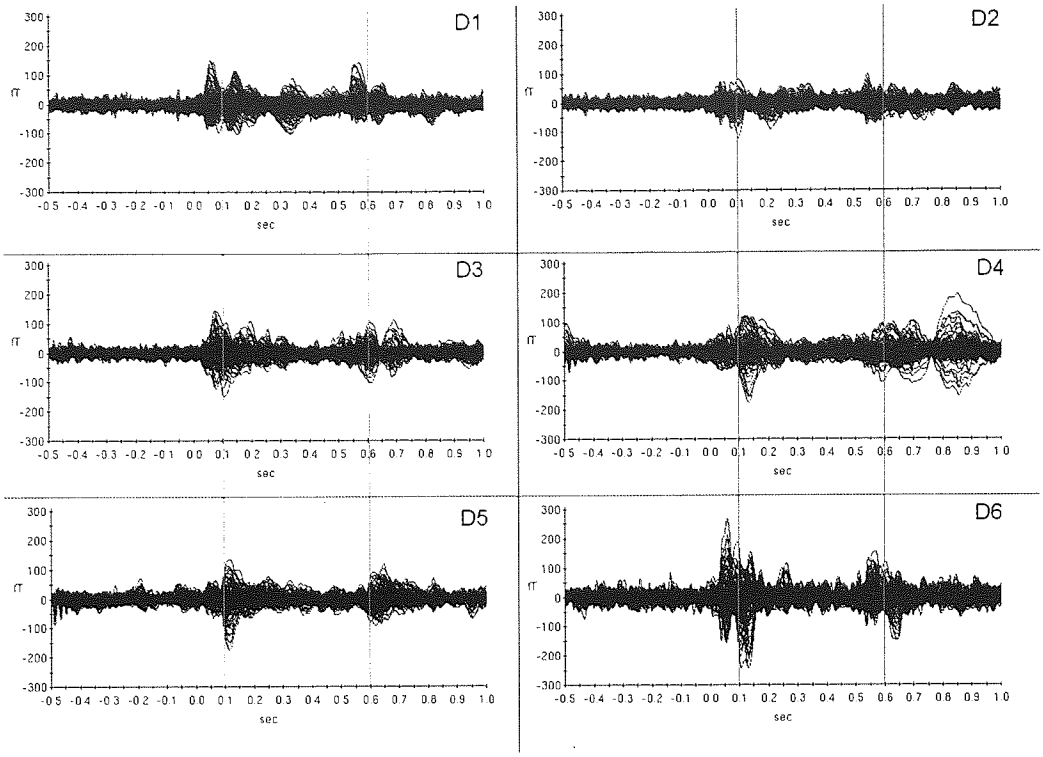

Figure 5-18 Butterfly Plot: 500ms ISI - 400Hz FS condition, Dyslexic Participants
A plot of the overlay data from all 151 MEG Channels for each dyslexic participant. Tone presentations occur at 0secs and 0.5secs, red data markers indicate 100ms after each tone onset.

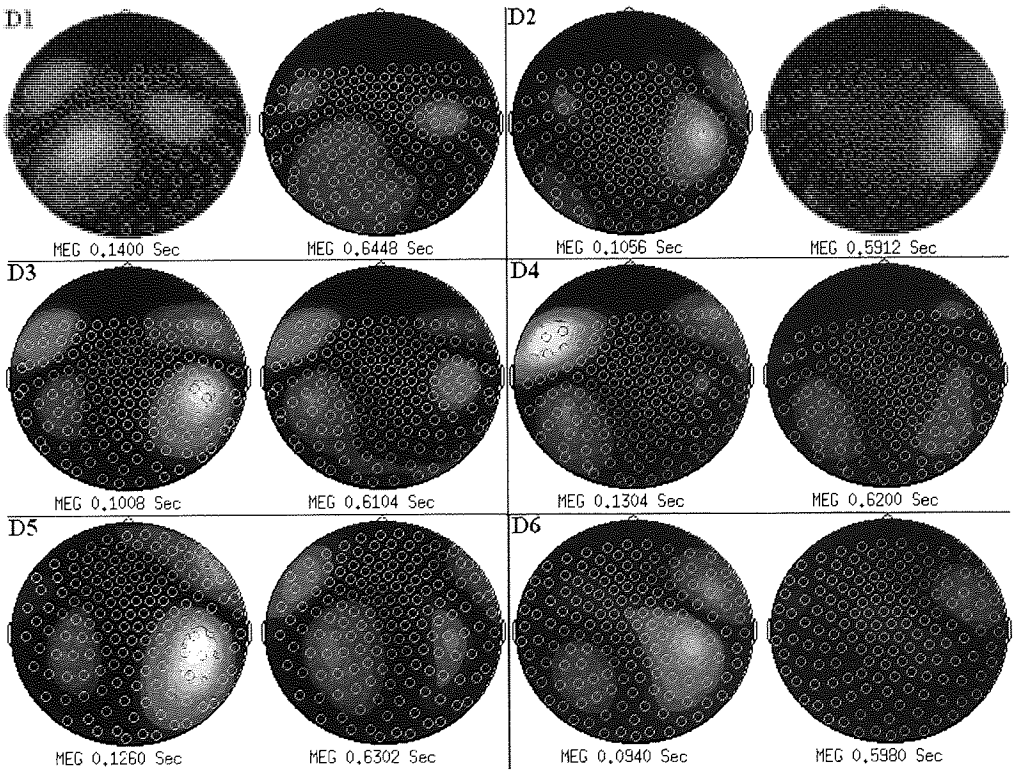

Figure 5-19 Field Map at the N1m Peak in Response to Each Tone: 500ms ISI - 400Hz FS condition, Dyslexic Participants
Maps representing the observed field at the peak of the N1m response (based on GFP calculations) for each dyslexic participant. Left hand plots relate to initial tones while right hand plots relate to second tones. The peak GFP latency is reported below each field map.

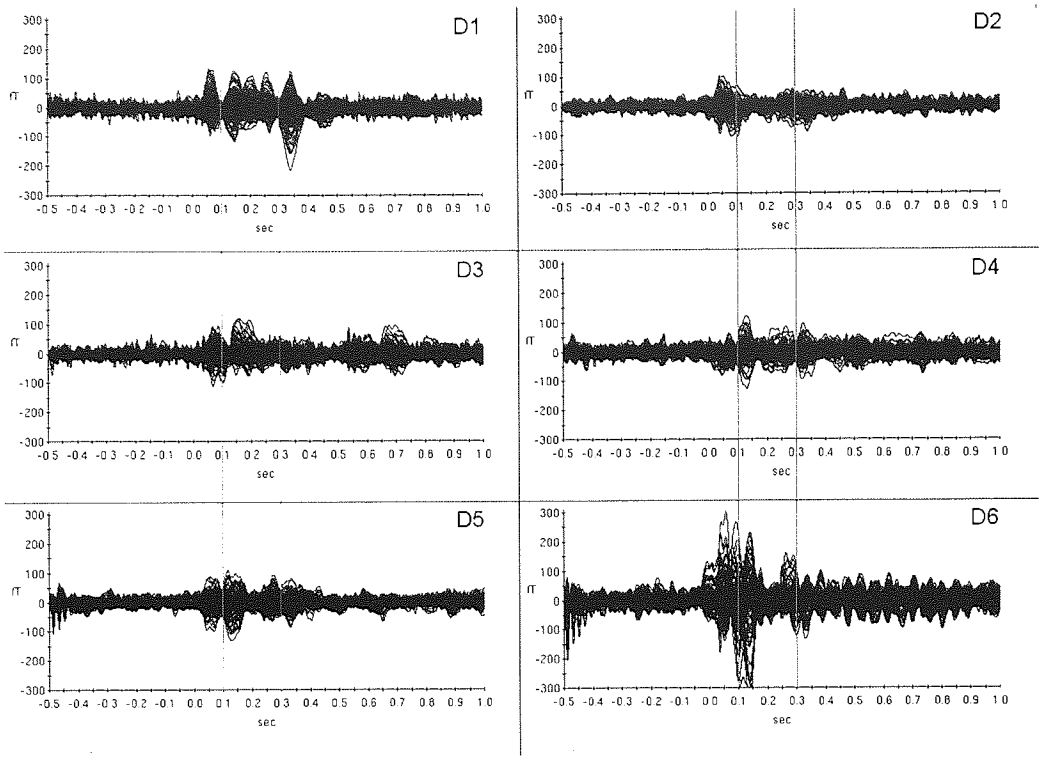

Figure 5-20 Butterfly Plot: 200ms ISI - 400Hz FS condition, Dyslexic Participants
A plot of the overlay data from all 151 MEG Channels for each dyslexic participant. Tone presentations occur at 0secs and 0.2secs, red data markers indicate 100ms after each tone onset.

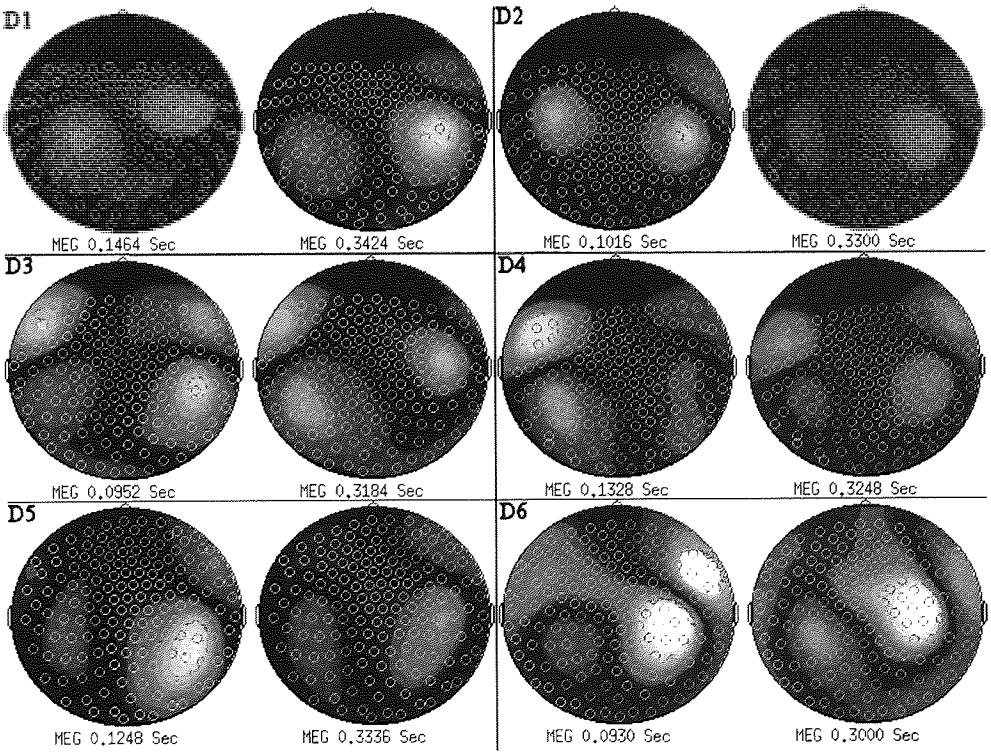

Figure 5-21 Field Map at the N1m Peak in Response to Each Tone: 200ms ISI - 400Hz FS condition, Dyslexic Participants
Maps representing the observed field at the peak of the N1m response (based on GFP calculations) for each dyslexic participant. Left hand plots relate to initial tones while right hand plots relate to second tones. The peak GFP latency is reported below each field map.

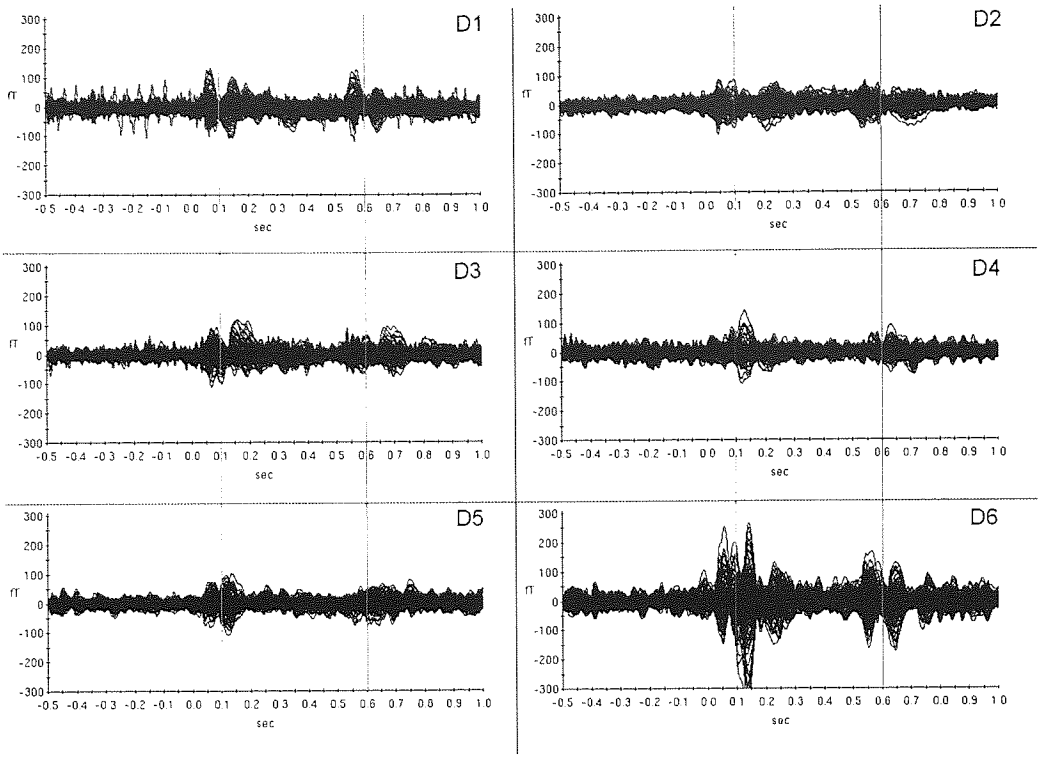

Figure 5-22 Butterfly Plot: 500ms ISI - 100Hz FS condition, Dyslexic Participants
A plot of the overlay data from all 151 MEG Channels for each dyslexic participant. Tone presentations occur at 0secs and 0.5secs, red data markers indicate 100ms after each tone onset.

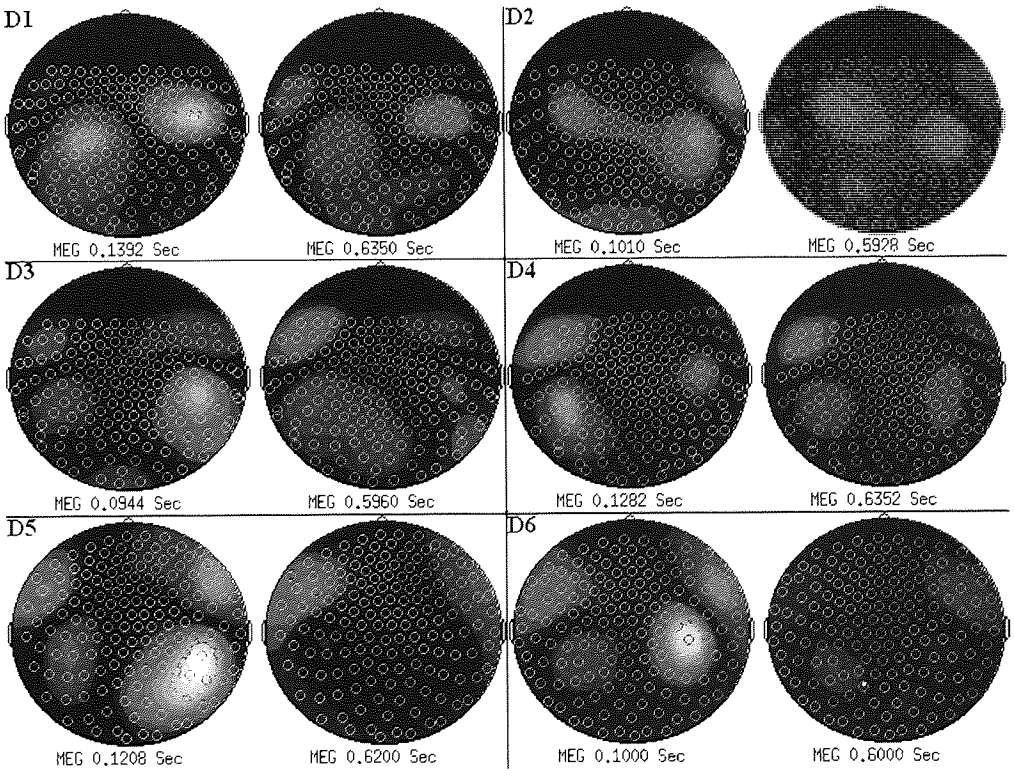

Figure 5-23 Field Map at the N1m Peak in Response to Each Tone: 500ms ISI - 100Hz FS condition, Dyslexic Participants
Maps representing the observed field at the peak of the N1m response (based on GFP calculations) for each dyslexic participant. Left hand plots relate to initial tones while right hand plots relate to second tones. The peak GFP latency is reported below each field map.

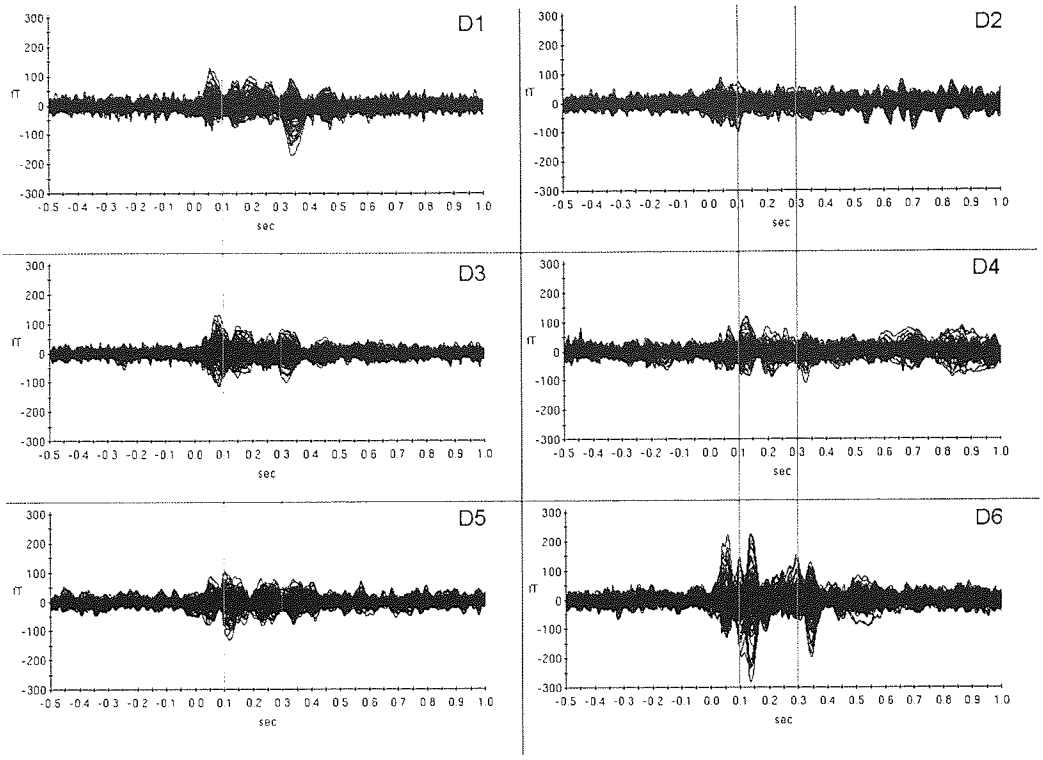

Figure 5-24 Butterfly Plot: 200ms ISI - 100Hz FS condition, Dyslexic Participants
A plot of the overlay data from all 151 MEG Channels for each dyslexic participant. Tone presentations occur at 0secs and 0.2secs, red data markers indicate 100ms after each tone onset.

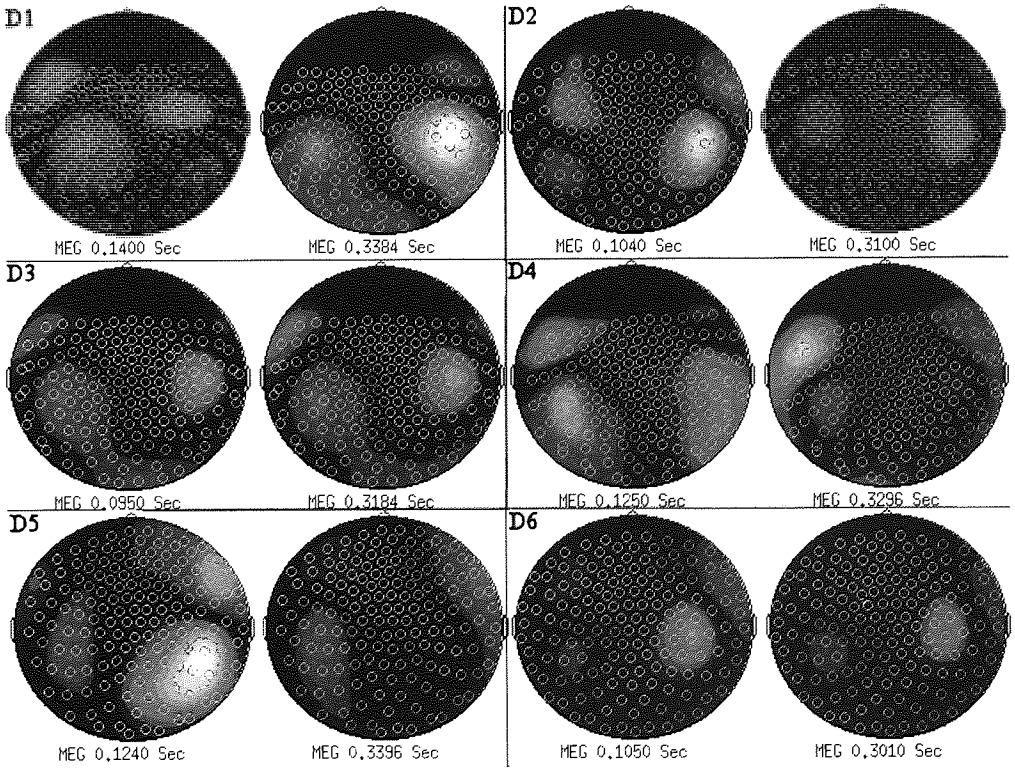

Figure 5-25 Field Map at the N1m Peak in Response to Each Tone: 200ms ISI - 100Hz FS condition, Dyslexic Participants
Maps representing the observed field at the peak of the N1m response (based on GFP calculations) for each dyslexic participant. Left hand plots relate to initial tones while right hand plots relate to second tones. The peak GFP latency is reported below each field map.

The first group difference evident when looking at the dyslexic participants' data is that N1m deflections are not as easy to distinguish from the averaged traces. Again, it should be stressed that no absolute amplitude values can be discerned without a source model. However, at a glance it appears that the dyslexic participants' responses to the tone pair stimuli are more complicated.

Considering the dyslexics' responses to first tones, deflections peaking at around 100ms after tone onset are seen in three of the dyslexic participants; D2, D3 and D6. In the case of these three participants, the Global Field Power peak signal occurs between 93 and 105ms after tone onset and field maps plotted at the peak latency indicate bilateral dipolar sources within temporal lobes. Deflections around 100ms in the butterfly plots of D2 are particularly weak but do have a field pattern of activation indicating an N1m response. Earlier deflections peaking at around 45ms after tone onset demonstrate a mirrored field pattern (Figure 5-26). Thus, it seems likely that these deflections reflect a P50m response. Deflections are seen in the data of D6 peaking slightly before and slightly after the 100ms deflection. The earlier deflection has a bilateral dipolar source field with a field pattern reversal from the N1m response, again suggesting that this deflection reflects the P50m. The later deflection indicates a single dipolar source originating from a deep structure, possibly due to eye movements (Figure 5-27).

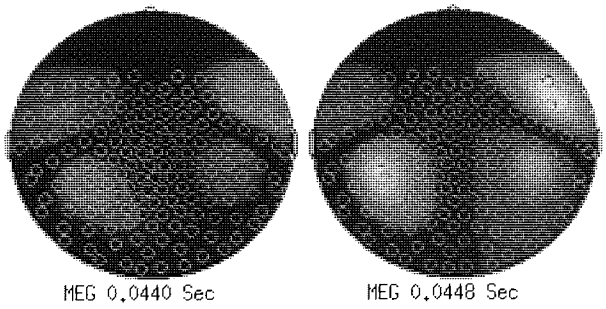

Figure 5-26 D2: Field Map at the Peak of the Deflection Prior to 100ms
Maps representing the observed field at the peak of the deflection occurring around 45ms after tone onset in participant D2. Plots are shown for the 500ms ISI – 400Hz FS condition (left) and the 500ms ISI – 100Hz FS (right) condition. The peak GFP latency is reported below each field map.

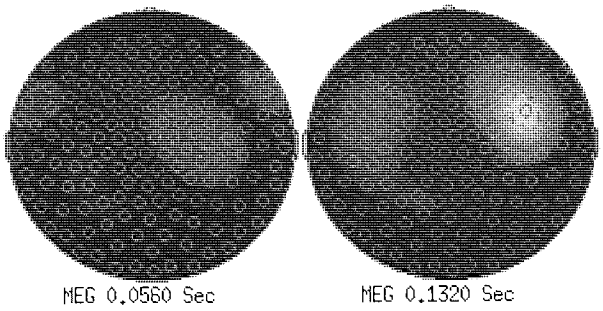

Figure 5-27 D6: Field Map at the Peak of the Deflection Prior to and After 100ms
Maps representing the observed field at the peak of the deflection occurring around 56ms (left) and 132ms (right) after tone onset in participant D2. Plots are shown for the 500ms ISI – 400Hz FS condition. The peak GFP latency is reported below each field map.

Looking at the butterfly plots for D4 and D5, the largest deflections occur slightly later than 100ms after tone onset; at around 130ms for D4 and 124ms for D5. These peaks generate the typical N1m field pattern and so it seems that the response is delayed in these participants. In the case of D1, peaks occur immediately prior to 100ms (around 64ms) and immediately after 100ms (around 140ms). While the later deflections generate an N1m pattern of activation, according to field maps, the earlier deflections suggest temporal sources with a different orientation, perhaps P50m (Figure 5-28). Thus, the N1m response also appears to be delayed in this participant's response to initial tones.

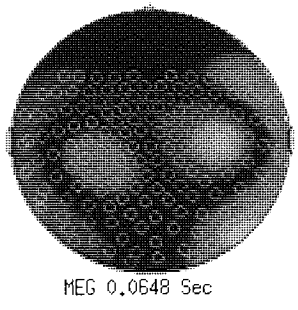

Figure 5-28 D1: Field Map at the Peak of the Deflection Prior to 100ms
Map representing the observed field at the peak of the deflection occurring around 64ms after tone onset in participant D1. The plot is shown for the 500ms ISI – 400Hz FS condition. The peak GFP latency is reported below the field map.

In the 500ms ISI conditions, N1m deflections in response to second tones peak between 91-110ms after tone onset in the data of participants D2, D3 and D6. For D1, D4 and D5, N1m deflections are again delayed, peaking between 120-144ms after tone onset. These latencies reflect those reported for initial tone responses

in each case. In all cases, deflections in response to second tones are typically smaller than responses to first tones.

Examining responses to second tones in the 200ms ISI conditions is complicated in the dyslexic group's data. For D2 deflections 100ms after the second tone are not easily visible. According to GFP measurements peak amplitude occurs at 130ms in the 200ms ISI – 400Hz FS condition and at 110ms in the 200ms ISI – 100Hz FS condition. In each case a bilateral field distribution is seen in the field map plots at these latencies. Thus, in the 200ms ISI – 400Hz FS but not the 200ms ISI – 100Hz FS condition there is evidence of a delay in the response to the second tone, relative to the first. A clear deflection in not visible in the 200ms ISI – 400Hz condition in the case of D3. However, GFP values indicate peak amplitude at 118ms after second tone onset in this and the 200ms ISI – 100Hz FS condition. Field map distributions indicate an N1m response at these latencies, suggesting that responses to the second tones presented after a 200ms ISI are slightly delayed, relative to responses to initial tones. For D6 no such evidence is found; while deflections in the data peaking around 100ms are more visible, their latency is not delayed relative to first tone responses.

Looking at data for D1 in the 200ms ISI conditions, deflections are evident at around 140ms after tone onset. While these latencies are later than the predicted 100ms response latency, they are comparable with response latencies for initial tones. Likewise for D4 there is no evidence of a relative delay in responses to second tones, with responses peaking around 125ms after second tone onset. There is evidence of a slight relative delay in responses to second tones in the data of D5; deflections peaking 133ms and 139ms after second tone onset are more delayed than responses to first tones (124ms).

5.3.3 N1m Response to Tone 1 (Dipoles)

Table 5-3 demonstrates that the peak latency of the N1m response to initial tones was typically later in the dyslexic group. However, this result was not significant in any of the tone pair conditions and examining the individual data (Figure 5-29) a large degree of overlap is apparent between groups. Indeed, it appears that the N1m latency is consistently delayed in the case of only three of the dyslexic

participants; D1, D4 and D5. Identifying these specific participants as outliers when considering the latency of their dipole modelled N1m response latencies agrees with the averaged data displayed in section 5.3.2. Peak latencies amongst control participants demonstrate less intra-group variance. In the 400Hz FS conditions, the data of C4 does appear to be slightly more separated from the rest of the control group. Examination of averaged data in the butterfly plots also suggested a slight N1m latency delay in this control participant in the larger FS conditions.

Table 5-3 Right Dipole N1m Response to Tone 1: Latency

	Control		Dyslexic	
Condition	Median	Range	Median	Range
500ms-400Hz	92.25	25.80	102.80	33.60
200ms-400Hz	95.90	20.00	105.20	37.60
500ms-100Hz	94.40	12.60	102.40	30.40
200ms-100Hz	94.30	11.20	102.80	42.40

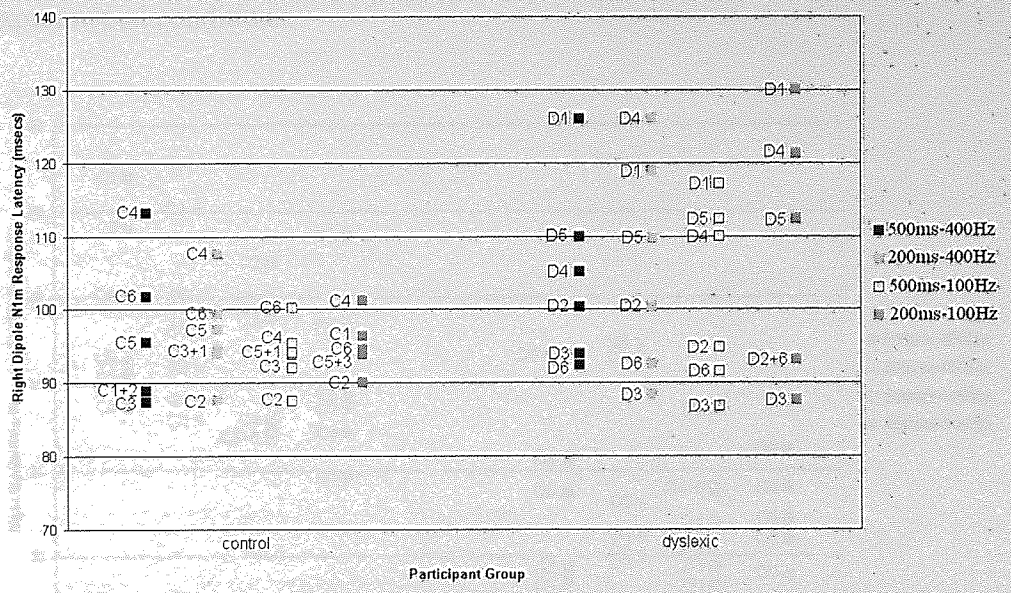

Figure 5-29 Right Dipole N1m Response to Tone 1: Latency (Individual Data)
Graph illustrating the peak latency of the right hemisphere dipole N1m response to initial tones for all 12 participants. The data key indicates the experimental condition and data point markers identify each of the individual subjects.

Data considering the amplitude of the N1m response to initial tones is reported in Table 5-4. Mann-Whitney tests revealed that the amplitude of the N1m dipole in

response to initial tones was significantly weaker in the dyslexic group in each of the tone pair conditions (500ms ISI – 400Hz FS, U = 6.0, $p=0.028_{(1\text{ tailed test})}$; 200ms ISI – 400Hz FS condition, U = 6.0, $p=0.028_{(1\text{ tailed test})}$; 500ms ISI – 100Hz FS, U = 3.0, $p=0.008_{(1\text{ tailed test})}$; 200ms ISI – 100Hz FS condition, U = 1.0, $p=0.003_{(1\text{ tailed test})}$).

Table 5-4 Right Dipole N1m Response to Tone 1: Amplitude

	Control		Dyslexic	
Condition	Median	Range	Median	Range
500ms-400Hz	36.47	26.52	19.33	26.28
200ms-400Hz	33.93	24.57	14.33	24.76
500ms-100Hz	31.64	20.53	15.74	20.34
200ms-100Hz	28.07	27.80	13.10	19.19

Figure 5-30 shows individual data points for the amplitude of the N1m response to the first tone. The group difference is clear and the amplitude of the N1m response in participants D1 and D2, in particular, is reduced across all experimental conditions.

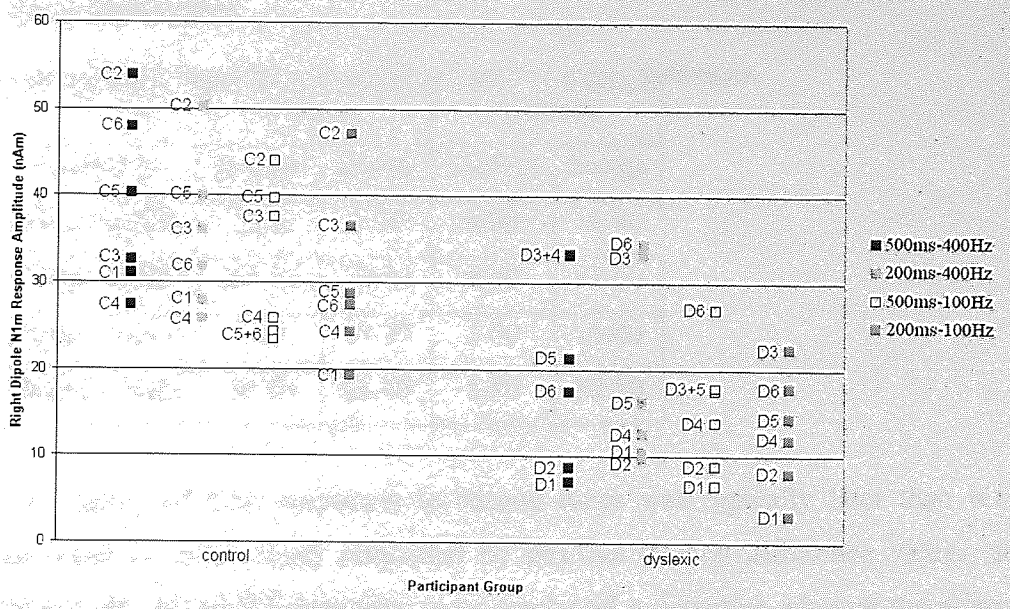

Figure 5-30 Right Dipole N1m Response to Tone 1: Amplitude (Individual Data)
Graph illustrating the peak amplitude of the right hemisphere dipole N1m response to initial tones for all 12 participants. The data key indicates the experimental condition and data point markers identify each of the individual subjects.

Theoretically, the durations of the silent interval between tones should not affect the latency or amplitude of the response to the first tone. This was confirmed exploring these measures with use of Wilcoxon Signed Ranks tests for each participant group (500ms ISI – 400Hz FS vs. 200ms ISI – 400Hz FS). When considering the effect of reducing the FS between tones within pairs a trend is evident in the data; N1m amplitudes appear to be smaller in the 100Hz FS conditions than the 400Hz FS conditions, particularly in the dyslexic group. However, this result was not significant and no consistent effect was evident when considering the effect of manipulating FS on the latency of the N1m responses.

5.3.4 N1m Response to Tone 2 (Dipoles)

When examining the N1m response to second tones, the effect of manipulating the experimental conditions (ISI and FS) was of principle interest. As group differences were evident in first tone responses it was unrepresentative to consider the absolute latency and amplitude values of the N1m response to the second tone. Rather, the difference in each of these measures (Tone 2 minus Tone 1) was considered as the dependent variable.

Group Differences

Table 5-5 Right Dipole N1m Response to Tone 2: Latency Difference

	Control		Dyslexic	
Condition	Median	Range	Median	Range
500ms-400Hz	2.55	5.60	6.80	16.80
200ms-400Hz	27.10	32.80	8.00	41.60
500ms-100Hz	1.20	19.20	3.90	16.80
200ms-100Hz	36.00	26.40	8.80	32.80

The latency of N1m responses to second tones was typically later than N1m responses to initial tones (indicated by positive latency difference values, see Table 5-5). Mann-Whitney tests were employed to examine whether the relative latency delay was significantly different between participant groups. No significant group differences were found when data from the 500ms ISI conditions were examined. However, in the 200ms ISI – 100Hz FS condition (U

= 3.0, $p=0.008_{(1\ tailed\ test)}$) and the 200ms ISI – 400Hz FS condition (U = 6.0, $p=0.027_{(1\ tailed\ test)}$) the relative delay in latency to second tones was significantly larger in the control group.

Considering individual participants' data (Figure 5-31) the group difference in relative latency delay with shortening ISI is evident although, as reported throughout, a larger variance is notable in the dyslexic group. In the case of each control participant, an increase in the relative delay is notable. Looking at the dyslexic group's data, an increase in the relative latency delay is evident across 400Hz FS conditions but not 100Hz FS conditions in the case of D2. Interestingly the same trend was evident when examining the averaged traces. In section 5.3.2 evidence suggested that D5 demonstrated consistent N1m delays as ISI reduced. Indeed, the same trend is apparent viewing dipole modelled data. However, while examination of raw data suggested latency delays in D3, analysis of the dipole modelled N1m responses suggest that this trend is only apparent in the 100Hz FS data. Indeed, it was reported in section 5.3.2 that the N1m deflection could not be easily discerned for this participant in the 400Hz FS data.

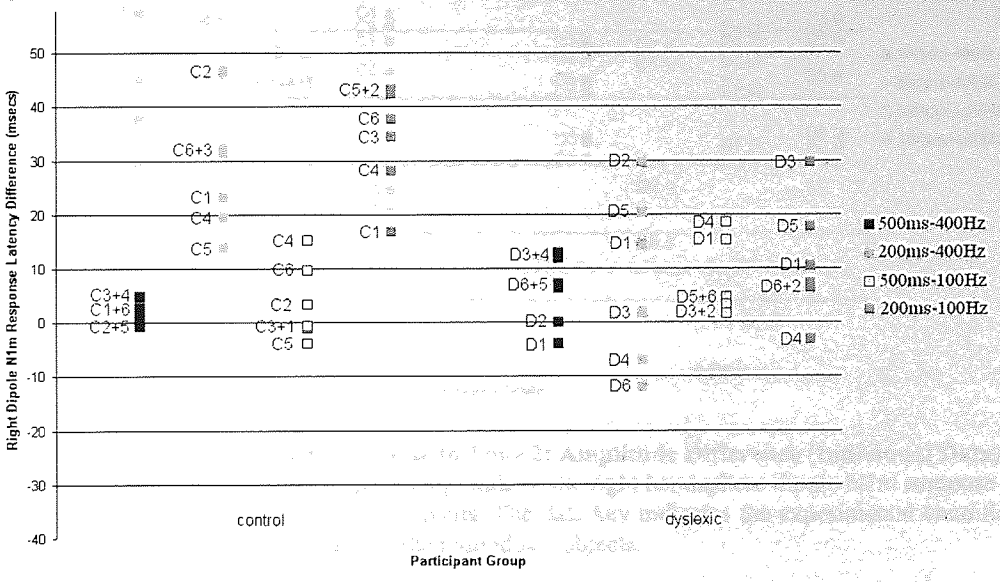

Figure 5-31 Right Dipole N1m Response to Tone 2: Latency Difference (Individual Data)
Graph illustrating the difference in peak latency of the right hemisphere dipole N1m response to initial and second tones, for all 12 participants. The data key indicates the experimental condition and data point markers identify each of the individual subjects.

The amplitude of N1m responses to second tones was typically smaller than N1m responses to initial tones (indicated by the negative amplitude difference values,

see Table 5-6). Again, Mann-Whitney tests were employed to examine whether the relative amplitude reduction was significantly different between participant groups. No significant group differences were found in any of the tone pair conditions. The individual data (Figure 5-32) confirm the result while again highlighting the intra-group variability.

Table 5-6 Right Dipole N1m Response to Tone 2: Amplitude Difference

	Control		Dyslexic	
Condition	Median	Range	Median	Range
500ms-400Hz	-12.86	25.99	-8.44	17.62
200ms-400Hz	-13.66	38.67	-3.88	48.30
500ms-100Hz	-11.35	15.86	-6.53	17.10
200ms-100Hz	-3.83	29.35	-4.16	32.96

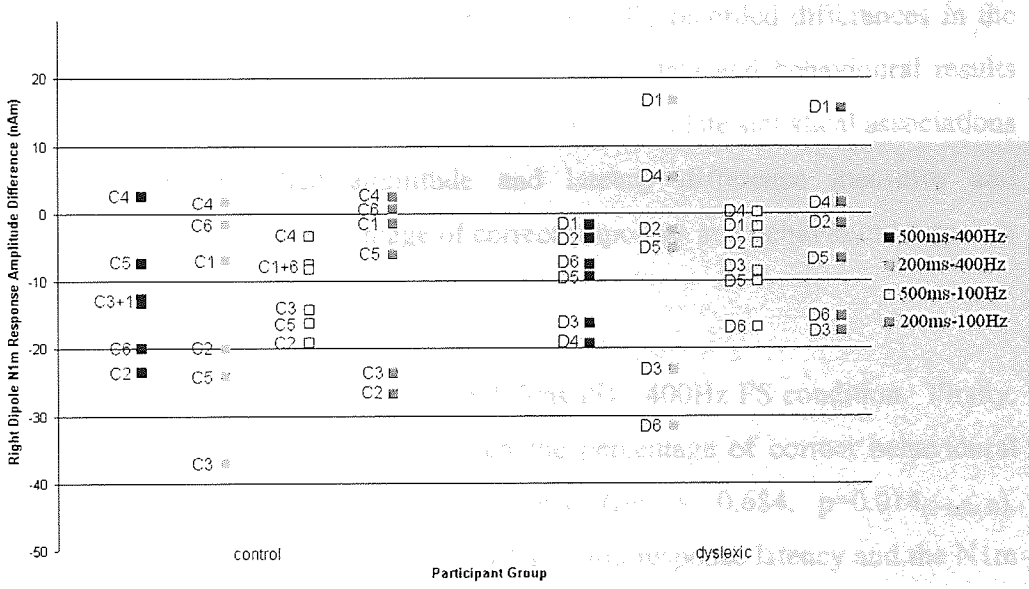

Figure 5-32 Right Dipole N1m Response to Tone 2: Amplitude Difference (Individual Data)
Graph illustrating the difference in peak amplitude of the right hemisphere dipole N1m response to initial and second tones, for all 12 participants. The data key indicates the experimental condition and data point markers identify each of the individual subjects.

Effect of ISI

Wilcoxon Signed Ranks tests, run separately for each participant group, were used to examine the effect of manipulating the ISI on the latency of second tones (500ms ISI – 400Hz FS vs. 200ms ISI – 400Hz FS). In the control group, reducing the ISI significantly increased the relative latency delay (t = 0.0,

$p=0.014_{(1\ tailed\ test)}$). The equivalent comparison was not significant when considering the data of the dyslexic group ($t = 8.0$, $p=0.45_{(1\ tailed\ test)}$). This confirms the group finding reported above: in shortening the silent interval between tones, the latency of the N1m response to second tones is further delayed in control participants but not in dyslexic participants.

Considering the effect of varying the ISI on the amplitude of the N1m response to the second tone, no significant effects were revealed for either participant group.

Effect of FS

Considering the effect of reducing the FS between tones on the N1m response to second tones, no significant results were obtained for either group in terms of latency or amplitude difference.

5.3.5 Correlations Between Behavioural and Physiological Measures

In order to consider the relevance of physiologically recorded differences in the participant groups, the relationships between these data and behavioural results were measured. Spearman's rho was employed to calculate statistical associations between dipole modelled amplitude and latency difference measures and behavioural measures of percentage of correct responses and behavioural response latency.

Significant results were revealed in the 200ms ISI - 400Hz FS condition. Firstly, there was a positive correlation between the percentage of correct behavioural responses and the N1m latency difference ($rho = 0.684$, $p=0.014_{(2\text{-tailed})}$). Secondly, the relationship between the behavioural response latency and the N1m latency difference was negatively correlated ($rho = -0.622$, $p=0.031_{(2\text{-tailed})}$). These results suggest that performance accuracy improves and behavioural response times reduce as the N1m response to second tones is further delayed.

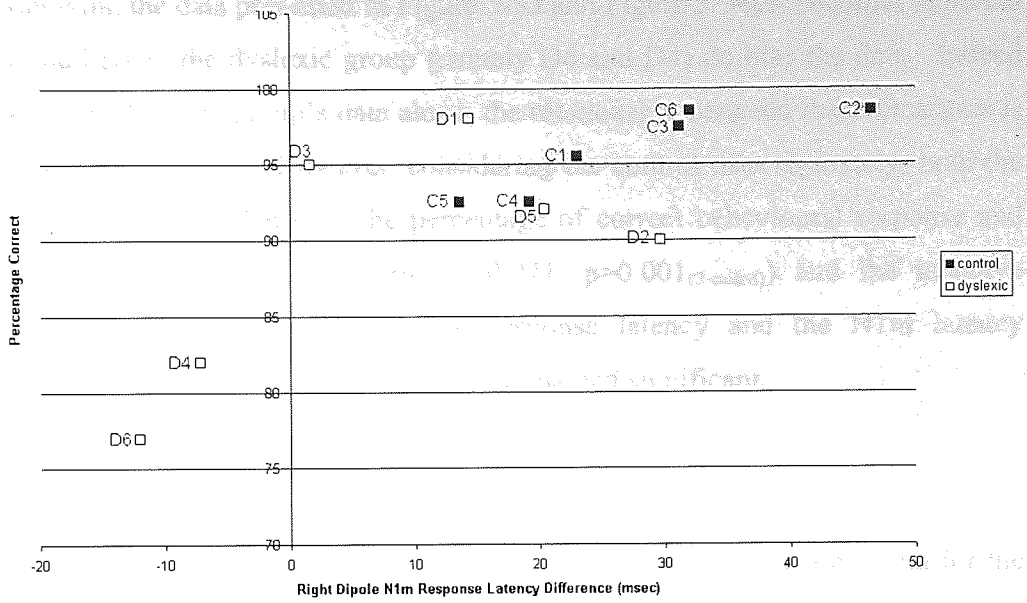

Figure 5-33 Association Between Percentage of Correct Behavioural Responses and N1m Latency Difference in the 200ms ISI – 400Hz FS Condition

Graph illustrating the relationship between percentage of correct discrimination responses and difference in latency of the right hemisphere dipole N1m response to initial and second tones. The data key indicates the participant group and data point markers identify each of the individual subjects.

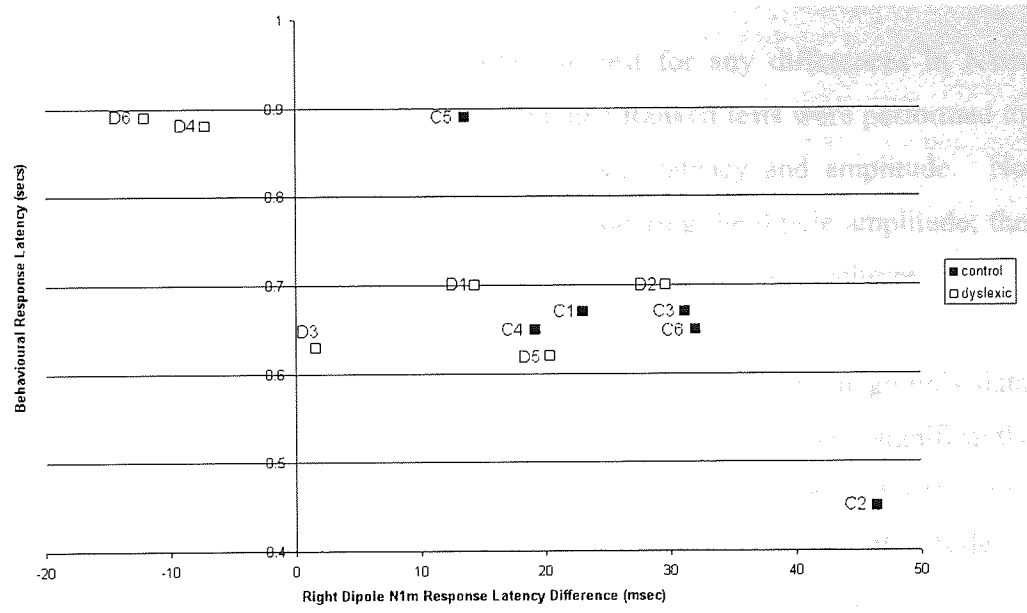

Figure 5-34 Association Between Behavioural Response Latency and N1m Latency Difference in the 200ms ISI – 400Hz FS Condition

Graph illustrating the relationship between behavioural response latency and difference in latency of the right hemisphere dipole N1m response to initial and second tones. The data key indicates the participant group and data point markers identify each of the individual subjects.

Examining the data presented in Figure 5-33 and Figure 5-34, it becomes apparent that outliers in the dyslexic group (namely D6 and D4) do bias the data. Indeed taking the dyslexic group's data alone, the relationship between these measures is no longer significant. However, considering the control data separately, both the positive correlation between the percentage of correct behavioural response and the N1m latency difference (rho = 0.971, $p=0.001_{(2\text{-tailed})}$) and the negative correlation between the behavioural response latency and the N1m latency difference (rho = -0.829, $p=0.042_{(2\text{-tailed})}$) remained significant.

5.3.6 Right Versus Left Hemisphere Responses

Results reported above (sections 5.3.3, 5.3.4 and 5.3.5) consider only data for the right hemisphere modelled dipoles (in line with Loveless & Koivikko, 2000). However, when analyses were repeated with data from the left hemisphere dipole, the pattern of significant and non-significant results remained unchanged. This suggests that the participant groups were not differentiated by the responses of any specific hemisphere.

Nevertheless, it was considered important to test for any differences in N1m responses across hemispheres. Wilcoxon Signed Ranked tests were performed to investigate any hemispheric differences in dipole latency and amplitude. No significant differences were obtained when considering the dipole amplitude; the strength of the N1m response appears to be consistent across hemispheres.

In terms of latency of the N1m response, analysis of the control group's data revealed that the right hemisphere response to initial tones peaked significantly earlier than the left hemisphere response in the 500ms ISI – 100Hz FS (t = 3.0, $p=0.026_{(2\text{ tailed test})}$) condition. This result was non-significant for the dyslexic group. It seems unlikely that the N1m response to initial tones should peak earlier in the right hemisphere in response to this stimulus condition alone. The failure to repeat this finding in any other comparison suggests that it does not reflect a general trend; indeed the significant result may simply reflect statistical chance resulting from multiple comparisons.

5.4 Discussion

5.4.1 Summary of Results

N1m amplitudes in response to tone pair stimuli were significantly reduced in the dyslexic group. N1m latencies were significantly more delayed in response to tones presented after a short as opposed to a long silent interval in the control group, but this result was not replicated in the dyslexic group. There is no evidence that manipulating rates of stimulus presentation or the coarseness of FS has a detrimental effect on the performance of the dyslexic group specifically.

5.4.2 Task Performance

The dyslexic group's accuracy scores on the tone pair discrimination tasks were typically lower than the control groups. However, group differences were only significant in the two 400Hz FS conditions. Likewise, the dyslexic group were typically slower at behaviourally responding in these tasks, though the group difference was only significant in the 500ms ISI – 400Hz FS condition. Slow responses were observed across the four conditions in the case of D6 and D4.

In terms of performance accuracy, reducing the ISI did not have a significant impact on the data of either participant group. In the control group, reducing the ISI resulted in significantly slower behavioural responses, a result not replicated in the dyslexic group. This result is contrary to the prediction that reducing the ISI would have a greater detrimental effect on dyslexic participants than control participants (section 5.1.2). Indeed, the ceiling level performance of controls across all conditions in Nagarajan's (1999) study makes it impossible to conclude that rate effects were specific to their dyslexic group.

Narrowing the FS between tones significantly reduced performance accuracy in the control group but not the dyslexic group. This, in addition to the fact that group differences in performance accuracy were only significant in the larger FS conditions, contradicts the prediction that the dyslexic group would find the tone pair task more difficult as the FS narrowed. Such a result fails to replicate the findings of previous researchers who report that dyslexic groups demonstrate impairments on frequency discrimination tasks (see section 3.3.4). Examining the individual data (Figure 5-8) it becomes apparent that the accuracy of two of the

dyslexic participants was notably reduced in the smaller FS conditions (D4 and D6). Although a similar trend is apparent in the case of C3 suggesting that any difficulties do not reflect a group effect but rather one specific to individuals.

Considering the failure to find a group difference in the contribution of FS, it should be noted that the frequency discriminations required were crude in each of the FS conditions. The majority of studies reporting behaviourally observable frequency discrimination impairments employ threshold measures, which are more sensitive to subtle difficulties. Indeed, McAnally & Stein (1996), examining just-noticeable-difference thresholds for frequency changes around 1000Hz, report thresholds of around 1% in controls (i.e. 10Hz difference) and approximately 2% in dyslexics (i.e. 20Hz difference). Therefore, the present dyslexic group may or may not demonstrate frequency discrimination impairments when tested with more sensitive measures. Importantly, reducing the FS did result in significantly slower behavioural responses in the dyslexic but not the control group. Moreover, the two dyslexic participants identified as having relatively more difficulties as the FS narrowed (D4 and D6) were also the participants who obtained slower behavioural response times over all conditions. Perhaps the slower response times reflect the dyslexic group's underlying difficulties with this task.

5.4.3 N1m Responses to Initial Tones

N1m amplitudes in response to initial tones were significantly reduced in the dyslexic group compared to the control group. This finding is mirrored by the results of previous researchers (Byring and Javilento, 1985, cited in Leppanen & Lyytinen, 1997; Pinkerton et al, 1989, cited in Leppanen & Lyytinen, 1997; Renvall & Hari, 2002). While Nagarajan et al. (1999) report no significant group differences in N1m amplitudes to initial tones, examination of the data presented appears to suggest that the dyslexics' N1m amplitudes to initial tones were somewhat reduced compared to controls (see section 5.1.5). Loveless and Koivikko (2000) do not report amplitude data for first tone responses.

One possible explanation for the significant group result could be that the ECD model was less able to explain the dyslexic participants' data. For example, a

poorer signal to noise ratio in the dyslexics' data would result in a less accurate model. However, reduced chi-square values were below five (and never below 1) for each of the dipoles, suggesting that the model was well able to account for the data in each participant's case. Furthermore, visual inspection of averaged data traces (section 5.3.2) also indicated that N1m responses were less evident in the dyslexic participants' data.

Decreased N1m amplitudes in the dyslexic group could reflect insufficient synchrony in generating neurons. However, Renvall & Hari (2002) noted that reduced amplitudes were not accompanied by significantly delayed latencies and are as such were unlikely to reflect reduced neural synchrony. In the present study there were no significant group differences in the latency of the N1m response to initial tones. However, data presented in section 5.3.2 and Figure 5-29 do reveal delayed N1m latencies in the case of D1, D4 and D5. While these participants do have among the lowest N1m amplitudes in the dyslexic group, they are not markedly separate from the rest of the group. D2 also has notably low N1m amplitude values without the corresponding latency delay. Alternatively the N1m latency may have been less stable in the dyslexic group. As amplitude was measured at a single time point (peak amplitude), it is possible that reduced amplitude reflected more latency jitter in the dyslexics' response.

The properties of the N1 response are reviewed in section 3.4.1. The recovery cycle of this component is estimated to be approximately 9s (see section 3.4.1). Complex inhibitory processes mediate attenuation in N1 amplitudes at faster rates of presentation. The response is highly stimulus specific (i.e. its amplitude is less attenuated when intervening stimuli consisting of different frequencies are presented). This specificity is related to the frequency of intervening tones as opposed to the perceived pitch of intervening tones. Therefore, any stimulus specific amplitude decrement is related to actual frequency tuning as opposed to perceptual thresholds.

The inter-trial intervals (ITIs) of 2s employed in the current study would not allow full recovery of the N1m response. Thus, the reduced N1m amplitude of the dyslexic group may indicate less specificity of auditory neurons to particular

frequencies, i.e. more overlap between the neural populations responding to each stimulus. As noted in section 5.1.5 there is an indication of N1m amplitude reduction to initial tones in the Nagarajan et al. (1999) study, which also employed two different frequency tones. Moreover, data presented in Figure 5-30 does reveal the trend that the N1m amplitude reduces in dyslexic individuals as the FS narrows. However, this result was very subtle and non-significant.

A further possibility is that the N1m amplitude difference observed between the groups reflects differences in attentional or motivational factors. N1 amplitude is modulated by attention, it is increased as task demands are increased and reduced when stimuli are ignored. These effects are due to increased excitability of neuronal populations contributing to the N1 wave (Näätänen & Picton, 1987). While both groups were instructed to perform the frequency discrimination task while physiological data were recorded, no measure of task performance was taken at this time. Thus, the reduced N1m amplitudes in the dyslexic group could simply reflect that these participants were paying less attention to the task. Further studies could assess the morphology of the N1m wave at different points throughout the data collection period in order to identify any attention/motivation driven changes between the groups. In later studies (chapters 6 and 7) attention free measures of auditory processing are considered.

Attention can be focused by stimulus driven processes in addition to top-down executive processes (Näätänen's, 1990). Renvall & Hari (2002) suggested that reduced N1m amplitudes to initial stimuli could indicate that these stimuli were less effective at capturing covert attention in dyslexic individuals. According to Näätänen's (1990) model, the supratemporal N1 generator reflects an attentional triggering mechanism. Thus, the reduced N1m amplitude in dyslexics found in the present study could reflect reduced attentional capture by auditory stimuli.

5.4.4 N1m Responses to Second Stimuli

N1m peak amplitudes to second tones were typically smaller than N1m peak amplitudes to initial tones (Figure 5-32). However, there was no evidence to suggest that N1m amplitudes to second stimuli were more reduced in dyslexics than controls at shorter ISIs, as reported by Nagarajan et al. (1999). Had analyses

been conducted comparing actual second tone N1m amplitudes, a significant group difference would have been obtained (as reported by Nagarajan et al, 1999). However, this would have simply reflected the fact that N1m amplitudes to all tones (first and second) were significantly reduced in the dyslexic group.

As discussed in section 5.1.5, it is possible that the amplitude reduction to second tones in rapidly presented pairs reported by Nagarajan et al, may simply reflect a similar trend, as the data presented appears to reveal a group difference (though not significant) to initial tones in their participants' data. The measures of amplitude and latency difference employed in the present study allow for a true measure of the effect of varying the ISI. Furthermore, the amplitude measure (RMS) used by Nagarajan et al. was not based on a source model approach. As discussed in section 4.2.5, interpretation of raw MEG data (particularly amplitude) across participants is flawed, as source depth from sensor is not accounted for.

Narrowing the FS did not differentiate between the participant groups; neither the relative N1m amplitude nor latency difference was significantly different between the FS conditions. However, as noted in 5.4.2, the frequency discriminations were rather crude. Nevertheless, this failure to find a significant result does not support the argument that N1m amplitudes are generally reduced in the dyslexic group as a result of less specific frequency tuning. Responses to second tones occur after a notably shorter silent interval than responses to initial tones. As such, any amplitude reduction resulting from reduced firing in a 'tired' neural pool would be more marked in the response to second tones. While D1 and D2 had the lowest amplitude values for the initial N1m response, relative amplitude reductions to second tones were not any greater in these participants than in the rest of the dyslexic group.

The FSs employed were chosen to establish whether group differences reported in the Nagarajan et al. (1999) study actually reflected subtle frequency discrimination impairments in the dyslexic group (section 5.1.5). This interpretation relies on the assumption that subtle deficits, not measurable with behavioural data, are measurable in physiological data. If group differences exist

at 400Hz FS they should be amplified at 100Hz FS. Retrospectively, the inclusion of a narrower FS condition, closer to the dyslexic populations reported threshold, would have been more informative.

Reducing the ISI resulted in significantly greater relative latency delays to second tones in the control but not the dyslexic group. This effect was also evident when examining the averaged data traces presented in section 5.3.2. Increases in the latency of the N1m response to second tones, relative to initial tones, were evident in each of the control participants' data. The effect was marginally seen in the case of D5 (both FS conditions), D2 (only for the 400Hz FS condition) and D3 (only for the 100Hz FS condition).

As noted in section 3.4.1, the supratemporal N1m response may actually be generated by two subcomponents ($N1m^P$ and $N1m^A$). The $N1m^P$ subcomponent peaks at a latency of around 90ms after stimulus presentation, while the $N1m^A$ component peaks at a latency of around 140ms after stimulus presentation. While the contribution of $N1m^A$ is typically very small (meaning that N1m responses are typically well modelled by single ECDs), it is enhanced in response to stimuli that are presented within approximately 300ms of preceding stimuli. Thus, McEvoy et al. (1997) have suggested that enhancement of the $N1m^A$ component may reflect persistence due to temporal integration.

Perhaps the larger relative latency delay to second stimuli at short ISIs found in the data of control participants reflects a larger contribution of the later $N1m^A$ component. While ECD models were based on single bilateral dipoles fitted to the first tone responses, an ECD model simply reflects the centre of gravity of excitation in a large neuronal population (McEvoy et al., 1997). Thus, components that are spatially close (as are the $N1m^P$ and $N1m^A$) can each contribute to the strength of the modelled response.

Examining the averaged data traces presented in section 5.3.2, delays in control participants' N1m responses to second tones in the shorter ISI conditions are clearly observable. However, such visual inspection cannot provide information about the relative contribution of distinct component processes. The present study

was principally designed to establish the contribution of the intervening period on N1m responses to second tones. In order to achieve this, measures of N1m responses to second tones were made relative to first tone measures; the dipole model fitted to initial responses was used to explain second responses. In addition, the spatial location of neural sources was not a focus (essentially limited by the fact that neuroanatomical data was not available for the majority of participants). Future studies could be better designed to examine contributions of separable components on the N1m response to stimuli occurring after short intervals in dyslexic and control groups, by placing more emphasis on the results of source modelling of these responses.

If the increased relative latency delay observed in the control but not the dyslexic data does reflect an increased contribution of the $N1m^{A}$ component, the present study's results appear to indicate that temporal integration processes are disrupted in the dyslexic group. This possibility is examined in more detail in Chapter 9.

Evidence of disrupted temporal integration processes in the dyslexic group supports the findings of Loveless & Koivikko (2000) who found that N1m enhancements fell away at shorter ISIs in their dyslexic group. The authors argue that initial stimuli within tone pairs exert an influence on the second tones at short SOAs by means of increased sensitivity. They propose that the group difference at longer SOAs may reflect weakened enhancement of auditory inputs by prior stimulation in the dyslexic group. In conclusion, they suggest that the brief stimuli capture attention less effectively for dyslexic than control listeners. Such an account can explain the absent relative N1m delays in the dyslexic group with 200ms ISIs in addition to the reduced N1m amplitudes overall.

5.4.5 Participant Profiles

Considering the results presented it is apparent that the dyslexic data is marked by intra-group variability. It is therefore useful to consider the profiles of individual dyslexic participants. Obviously, with small participant numbers only tentative conclusions can be drawn.

Behavioural data suggested that participants D4 and D6 specifically had difficulties with the tone pair discrimination task (longer response times), especially as the FS was reduced (lower accuracy scores). In contrast, participants D1 and D5 performed well in comparison with the rest of the dyslexic group and at a level equivalent to the control group's performance. Reducing the FS also appeared to have a detrimental effect on the performance of the control participant C3.

N1m responses to initial tones were somewhat delayed in the case of D4. However, the N1m latency was normal in the case of D6. Moreover, noticeably delayed N1m responses to initial tones were reported for the two dyslexic participants who performed well on the behavioural discrimination tasks (D1 and D5). Likewise, in the case of D1, despite good behavioural results, this participant's N1m response was the weakest in the dyslexic group in four of the stimulus conditions (Figure 5-30). Therefore, it seems unlikely that the dyslexic group's performance on the task is reflected in the physiological responses to initial tones.

Considering N1m responses to second tones, dyslexic participants D4 and D6 demonstrated no evidence of the greater relative latency delay as ISI reduced. Indeed there was a significant relationship between the relative latency delay in the 200ms ISI – 400Hz FS condition and behavioural performance (accuracy and latency of behavioural responses) in the control group (section 5.3.5). This result suggests that the temporal integration process, which led to the increased relative latency delay, resulted in improved performance on the task. While the correlation was not significant in the dyslexic group, examination of individual data (Figure 5-31) reveals that latency delays were observed in the data of the dyslexic participants with more accurate and faster performance on the behavioural task (D1 and D5).

5.4.6 Retrospective Power Analyses

As acknowledged in section 5.2.7, the originally planned 2x(2x2) mixed factorial design was over complicated with the small participant numbers in the present

study. The results of retrospective power analyses for such a design, based on effect sizes obtained, are documented in Appendix 1, Table A-1.

For some main effects a sample size of six was sufficient; power of 90% was obtained for the main effect of group on N1m amplitude to the initial tone, confirming that this effect was significant. In addition, the significantly greater relative N1m latency delay to second tones in the control group had power close to 80%. However, in order to find a significant group difference on behavioural measures, the sample size would need to be increased to 24 participants.

Nagarajan et al. (1999) reported a significant interaction between participant group and ISI in the N1m amplitude to second tones. This interaction has a power of only 14% in the present study, where relative amplitude decrement (as opposed to absolute amplitude) was measured as the dependent variable. With such low power, the failure to find a significant group effect is more likely to reflect that no group difference was present as opposed to reflecting a lack of participants. As noted above, the relative measure used here is more reliable.

Retrospective power calculations for the FS*Group interaction reveal extremely low power for each of the dependent variables. While this reflects the fact that the sample size was very low, it is primarily likely to result from the crude FS contrast used.

5.4.7 Conclusions

There was no evidence that either increasing rates of stimulus presentation or narrowing the FS between tones had a greater detrimental effect on the performance of dyslexic as opposed to control groups in tone pair discrimination tasks (although the point is made that FSs in the current study may have been too crude to reveal frequency discrimination impairments in the dyslexic group). N1m responses were significantly weaker in the dyslexic group, and delayed in the case of three participants, when compared to the control group. However, neither reducing the silent interval nor reducing the FS between tones resulted in a greater relative amplitude reduction to second stimuli in the dyslexic group. There was some evidence that tone pairs presented at short intervals were integrated in

control but not dyslexic participants. Physiological differences between the groups may reflect the fact that stimuli were less effective at capturing covert attention in the dyslexic group.

6 FREQUENCY DEVIANT MISMATCH RESPONSE

6.1 Introduction

6.1.1 Aim

The aim of the present study is to examine the processing of frequency deviations in dyslexic and control groups. While the study presented in Chapter 5 required attentive processing of auditory stimuli, here pre-attentive physiological processing of frequency changes is assessed. By examining the mismatch negativity (MMN), a component of the auditory evoked response, the products of Sensory Memory can be directly assessed. The latency and amplitude of this component, in response to stimuli with deviant frequencies will be measured in order to index the fine-tuned discrimination abilities of the participant groups.

6.1.2 Frequency Discrimination

The issue of impaired frequency discrimination abilities in dyslexia has already been raised (section 3.3.4). A number of researchers have reported that dyslexic groups have higher frequency discrimination thresholds than control groups (Ahissar et al., 2000; Cacace et al., 2000; France et al., 1997; McAnally & Stein, 1996), while others have noted that this group are less able to exploit phase locked cues (Dougherty et al., 1998; McAnally & Stein, 1996), which are thought to encode the spectral properties of stimuli.

Results presented in Chapter 5 did not demonstrate that reducing the frequency separation (FS) in a tone pair discrimination task had a greater detrimental effect on the performance of the dyslexic compared to the control group. While accuracy scores were poorer in the dyslexic compared to the control group, the group result was only significant in the larger FS condition. However, as discussed in section 5.4.2, the frequency separations employed were much larger than just-noticeable-difference threshold frequencies recorded for dyslexics by McAnally & Stein (1996).

6.1.3 Physiological Results

Considering the results presented in Chapter 5, it was argued that some aspects of low-level auditory processing are disrupted in the dyslexic group. N1m amplitudes in response to simple tonal stimuli of differing frequencies were significantly smaller in the dyslexic than the control group. The results were interpreted as reflecting impairment at a stimulus driven level of processing. However, task demands and the arousal levels of participants modulate the amplitude of the N1 response (Näätänen & Tecler, 1991). While during the recording of physiological data, all participants were instructed to attend to the auditory stimuli and actively discriminate them, no online measures of compliance or performance were taken. Thus, the contribution of top down executive processing deficits cannot be firmly ruled out.

6.1.4 The MMN Response

The mismatch negativity (MMN) is a component of the auditory evoked response, elicited by a change in an auditory stimulus sequence (see section 3.4.1). Typically, MMN paradigms involve presentation of rare 'deviant' stimuli within sequences of high probability 'standard' stimuli. Change in any of a number of stimulus features can elicit the response, for example frequency, duration, spatial location, intensity and even more complex and abstract temporal properties. Importantly, the response is thought to be independent of selective attention. The MMN can be used to index the degree of stimulus deviance as the response is earlier and larger when the physical difference between standards and deviants is increased. Indeed, there is a strong association between MMN amplitude and perceptual discrimination.

The MMN response has been taken as evidence for the existence of a pre-conscious representation of physical stimulus features, this representation forming the neurophysiological basis of Sensory Memory. Specifically, a trace of standard stimuli must exist to allow for comparison with incoming deviant stimuli; the MMN response indexes the detection of a mismatch.

The neural generators of this response are primarily located in the auditory cortices. However, an additional frontal generator exists. Rinne et al. (2000)

have reported evidence to suggest that the temporal generators reflect a change detection mechanism, which in turn instigate the frontal MMN component, which underlies the process of attentional switch to the deviant stimulus. However, employing simultaneous EEG and MEG recordings this group found that the frontal component was not detected in the MEG measured response. They suggest that this may be due to the fact that the source of this component is either radially oriented or located deeper (see section 4.2.7). Furthermore, they note that this component is not easily identifiable with dipole source analysis as it is far smaller in amplitude than the supratemporal component and the two temporally overlap.

A number of groups have employed MMN paradigms in order to assess low-level auditory processing in dyslexic individuals (a comprehensive review is provided in sections 3.4.3 and 3.4.6). The present chapter is concerned with studies that have employed MMN paradigms to examine the processing of simple non-linguistic stimuli, specifically those relating to frequency discrimination abilities in dyslexic individuals (section 3.4.3).

Baldeweg et al. (1999) recorded the MMN response across a range of frequency deviants in a group of dyslexic adults and matched controls. As expected, with smaller degrees of deviance, MMN responses were reduced and delayed. In addition, a significant group effect was reported; the MMN responses of the dyslexic group were significantly delayed and the area under the MMN wave was significantly reduced (although peak amplitude measures did not significantly differ between groups). Furthermore, behavioural results followed the same pattern; dyslexic individuals' performance in a task requiring detection of the target deviant tones was significantly worse than that of the controls. Correlations between measures of MMN morphology, behavioural performance and even degree of impairment on phonological tasks were all highly significant.

Interestingly, these group effects were not significant when the same participants were presented with duration deviants, in the case of either MMN morphology or behavioural accuracy. In addition, N1 waves to standard stimuli did not differ between participant groups. As such, Baldeweg et al. (1999) related their results

to the model of attention and automaticity in auditory processing developed by Näätänen (1992). An overview of this model is provided in section 3.4.1. According to this model, a Transient Feature-Detector System is sensitive only to stimulus onset and offset, as indexed by the N1 response. Qualitative aspects of stimuli (physical characteristics) are, on the other hand, encoded into a Permanent Feature-Detector System, which feeds information directly to Sensory Memory. Applying this model Baldeweg et al proposed that the normal N1 and duration deviant MMN responses indicated normal functioning of the Transient Feature-Detector System, while abnormal pitch deviant MMN responses reflected selective impairment of the Permanent Feature-Detector System for pitch.

In partial agreement with these results, Hugdahl et al. (1998) reported significant delays in MMN peak latency in a group of dyslexic children in response to pitch deviants. However, peak amplitude measures in the dyslexic group were significantly higher than for the control group. In addition, this group also reported finding comparable MMN latency delays in response to stimuli containing gaps of variable lengths. This result contradicts the hypothesis forwarded by Baldeweg et al. (1999) that the Permanent Feature-Detector System was selectively impaired for pitch in dyslexics.

Schulte-Korne et al. (1998a) failed to identify a reduction of the MMN response to frequency deviant pure tone stimuli in their sample of spelling disabled children, contradicting the results of Baldeweg et al. (1999) and Hugdahl et al. (1998). However, they did find that in a speech stimuli condition employing synthetic phonemes the mean area under the MMN curve, between 300-620msec, was significantly reduced in their spelling disabled group. The group argued that this provided evidence for speech-specific processing deficits in dyslexia.

6.1.5 Unresolved Issues

While Baldeweg et al. (1999) and Hugdahl et al. (1998) have reported finding abnormal MMN responses to frequency deviant stimuli in their dyslexic groups, the findings are contradicted by the results of Schulte-Korne et al. (1998b). Reconciling the inconsistencies in findings across the studies is difficult due to the differing methodologies employed.

Schulte-Korne et al. (1998b) employed frequency deviant stimuli that were separated from standard stimuli by 50Hz, while in the Baldeweg et al study the smallest frequency deviants were separated by only 15Hz. Nevertheless, Baldeweg and colleagues also report finding a significant reduction and delay in MMN waves between groups with deviants separated by as much as 60Hz (though not for 90Hz). Also, Hugdahl et al recorded significantly delayed MMN peak latencies with deviants of 50Hz.

Here, frequency deviant stimuli have been selected to span the range where findings are contradictory. In the large frequency deviant condition, standard and deviant stimuli are separated by 80Hz. Should significant differences in MMN responses between groups be found in this condition, the present results would appear to directly contradict the results of Schulte-Korne et al. Considering the possibility that significant group differences are not identified with this degree of frequency deviance, a smaller frequency deviant condition is included, with a separation of 20Hz between standard and deviant stimuli. This frequency separation is smaller than that employed by Schulte-Korne et al. and may uncover group differences not elicited in the larger frequency deviant condition.

All three research groups recorded physiological data with EEG. Baldeweg et al's. recordings were made over 28 scalp electrodes, although amplitude and latency measurements considered only responses at the central frontal electrode (Fz), where the MMN response shows its maximal amplitude. Schulte-Korne et al. recorded responses over 19 scalp electrodes and assessed MMN values with reference to waveforms averaged over eight sites, Fz being given double weight. Hugdahl et al. recorded data at 13 sites, although they only report data obtained at three mid-leads (Fz, Cz and Pz).

MMN responses were also assessed differently across the three studies. Baldeweg et al. used a point-to-point t-test across the group average ERP waveforms to standard and deviant tones in order to identify the time range containing a significant MMN response, for each group separately. Amplitude and latency values were calculated with reference to difference waveforms, obtained by

subtracting averaged waves to standard stimuli form those to deviant stimuli. MMN amplitude was recorded at the peak, referenced to baseline, and area under the MMN difference curve was calculated in fixed time windows between 90-250msec. Schulte-Korne et al. also constructed difference waveforms in order to assess MMN morphology. This group distinguished two time windows in order to assess the MMN response to tonal stimuli (100-300ms and 300-700msec). This first time window corresponds with Baldeweg et al's. time frame of analysis. Schulte-Korne and colleagues then calculated the mean area under the difference curve within each time window. Importantly, no latency measures were reported. Hugdahl et al. analysed MMN data from difference waveforms between 108-284msec. In this study peak latency and amplitude measures were made; although no details on reference for amplitude values are provided, it is assumed that they were referenced to baseline.

Clearly, these varying methods of analysis make comparisons across the three studies difficult. While both Baldeweg et al. and Hugdahl et al. report latency delays in the MMN response to pitch deviants, latency values are not reported by Schulte-Korne et al. as analyses were conducted in pre-defined time windows. Considering the amplitude of the MMN response, Baldeweg et al. found no difference in peak amplitude values although there was significant reduction in a more sensitive measure: mean area under the MMN difference wave (the duration of which was defined for each participant). Schulte-Korne and colleagues failed to find differences between groups in area under the difference curve, although this measure was calculated for a fixed time window in all participants making it less sensitive to the duration of the MMN response. Surprisingly, Hugdahl et al. actually found an increase in MMN peak amplitude.

In the present study, physiological data are recorded with MEG; the advantages of this technique over EEG are reviewed in section 4.2.10. Thus, the magnetic counterpart (MMNm) of the MMN response is considered. MMNm morphology is assessed using the data recorded over all 151 channels, as opposed to at the site of a single or few electrodes as in the above reviewed studies. The presence of an MMN response is assessed in each participant, independently, before any analyses of response morphology are considered. Fields evoked in response to standard

and deviant stimuli are examined for significant differences, with use of GLM analysis (see section 4.5.2). An MMNm response is only considered to be present if the two waveforms differ significantly in the 90-290ms post stimulus latency range. If they do not differ significantly, there is no evidence that the deviant stimuli are evoking a mismatch response. In cases where a significant MMNm response is identified, difference waveforms are constructed by point-to-point subtraction of the standard response from the deviant response and this waveform is analysed with two separate but related measures. Firstly, Global Field Power (GFP) waveforms are constructed; the GFP represents the squared sum of signal strength at each time point across all channels. Secondly, the MMNm component is modelled with Equivalent Current Dipoles (ECDs), providing a noise independent model of the source activity. For each of these representations of the data, peak latency and amplitude values are recorded for each participant and subjected to group and individual analyses.

In using EEG to record physiological responses and in analysing the data from a limited number of scalp sites, the results of the above studies can conclude little about the lateralisation of the MMN response in the dyslexic and control groups. Hugdahl et al. did consider the strength of response over two temporal electrodes but found no hemispheric effect. One of the main advantages of the MEG over EEG is its superior spatial resolution. Thus, hemispheric effects can be considered in more detail.

As noted previously, the significant finding, reported in Chapter 5, of reduced N1m amplitudes in the dyslexic group may have simply reflected reduced attentive processing by dyslexics in the discrimination task. Employing a MMN paradigm allows for an attention independent analysis of auditory processing, as MMN responses are not thought to be modulated by attention. Indeed, participants are instructed to ignore the auditory stimuli and view a silent video. Therefore, group differences in MMN responses may suggest evidence of genuine low-level auditory processing impairments in dyslexia, not accounted for by attentional or motivational differences between experimental groups.

6.2 Methods

6.2.1 Participants

Six dyslexic (D1, D2, D3, D4, D5, D7) and six control (C1, C2, C3, C4, C5, C6) individuals, as described in Chapter 4, completed the study. One of the dyslexic participants from the original pool of seven withdrew their participation before all data for this study were collected. Also, some data files from one of the control participants became corrupted and their data were not analysed any further. The remaining participants were all students from Aston University and groups were matched for age, sex and IQ. The dyslexic group's performance on tests of auditory short-term memory, phonological skills and literacy measures were significantly worse than the control group's performance on the same measures (see section 4.1.5).

6.2.2 Stimuli

Auditory stimuli (Figure 6-1) were tone bursts of 50ms duration (5ms Hanning Window) presented binaurally at 65dBSPL. Standard tones were pure tones with a frequency of 1000Hz. In the 20Hz-Deviant condition deviant tones were pure tones with a frequency of 1020Hz, while in the 80Hz-Deviant condition deviant tones were pure tones with a frequency of 1080Hz. The two conditions were presented in separate blocks, with the order of presentation randomised across subjects. For each condition, 1000 tones were presented; standard tones with a probability of .9 and deviant tones with a probability of .1. Tones within each condition were presented randomly, with the constraint that at least three standard tones were presented between deviants. The interstimulus interval (ISI) (offset to onset) between individual tones was 500ms.

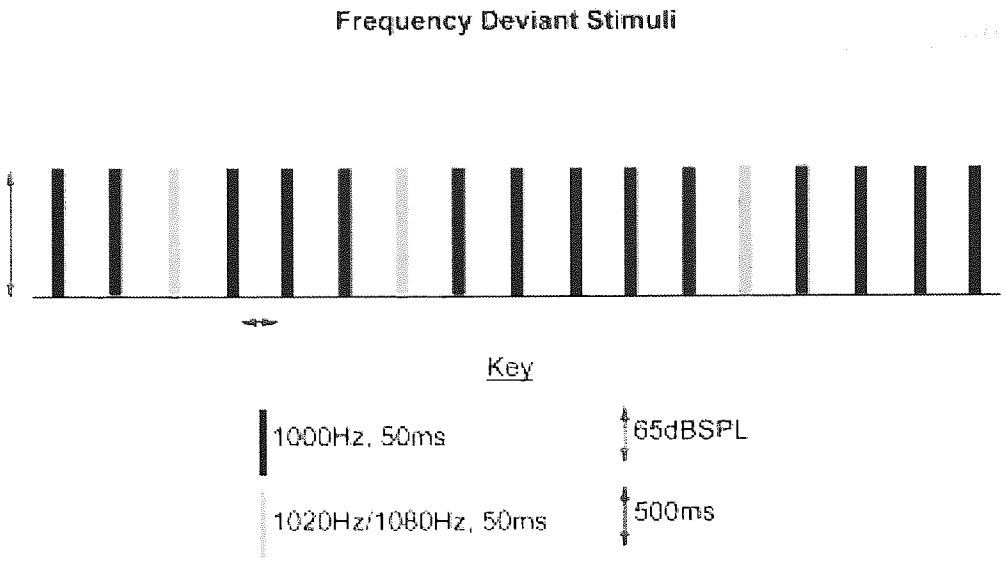

Figure 6-1 Frequency Deviant Stimuli
Graphical representation of the auditory stimuli.

6.2.3 Data Acquisition

Physiological data were collected with the CTF 151-channel whole-head MEG system outlined in Chapter 4. Participants were instructed to ignore the auditory stimuli and watch a cartoon video, which was viewed via mirrors from a television screen placed outside the magnetically shielded room, at a fixed distance. Data were recorded at a sampling rate of 625Hz, with a low pass filter of 200Hz. Epochs were triggered by each of the tones (standard and deviant); the analysis period was 500ms including a pre-stimulus period of 100ms. Five minutes resting time was provided on completion of each of the condition blocks.

6.2.4 Data Processing

Standard tone trials immediately following deviant tone trials were removed from datasets, resulting in 799 standard tone trials and 100 deviant tone trials for each frequency deviant condition. The raw physiological data were DC corrected using the pre-stimulus baseline and carefully inspected for eye-blink artefacts, epochs with large deflections were rejected; for all 12 subjects, no more than 25 trials were rejected from any one dataset (this total includes no more than 10 deviant tone trials).

Raw data were then analysed with the GLM programme, described in section 4.5.2. Standard tone trials were compared to deviant tone trials over the 1-30Hz range. The analysis period extended from 90ms after stimulus presentation to 290ms after stimulus presentation. For each analysis, chi-square values were obtained for 20 degrees of freedom. The resulting p values were recorded and a significant difference between the standard and deviant tone trials was assumed if p was less than 0.01. In cases where the tone trial conditions were significantly different, the resulting canonical mode plots were examined and an MMNm component was considered present if a deflection was visible at a peak latency of between 150-230ms with patterns of activation over the temporal lobes. The canonical modes can be seen plotted along the analysis period in the 80Hz-deviant condition (Figure 6-2) along with the field map generated at the peak signal latency. The field map reveals activation over temporal regions.

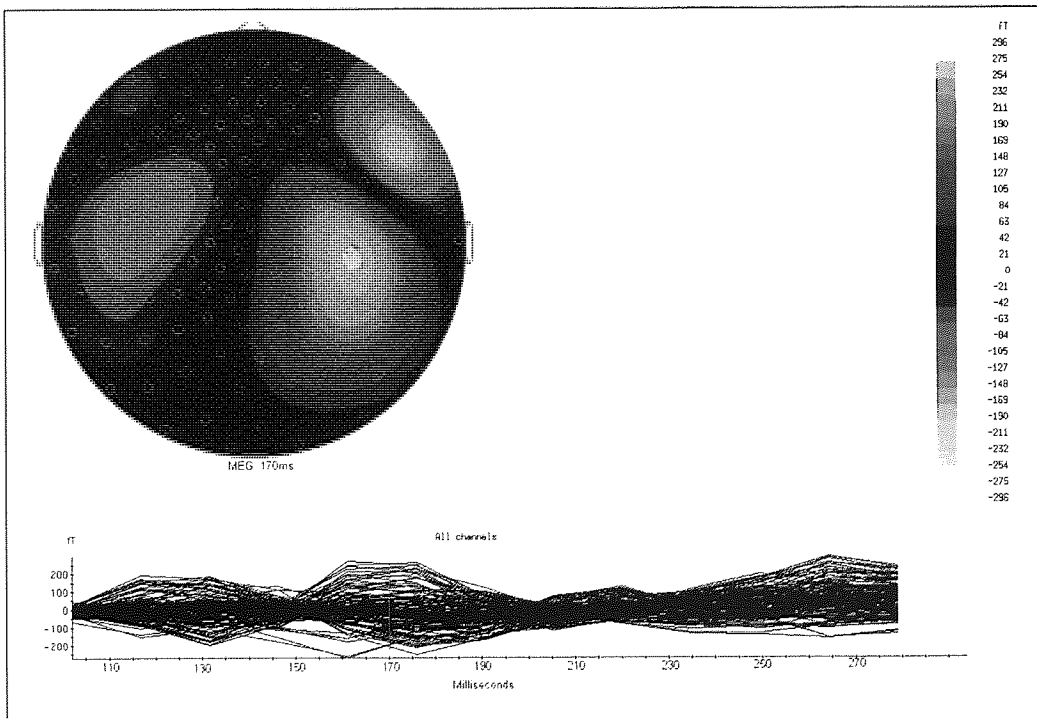

Figure 6-2 Canonical Modes and Resulting Field Map in the 80Hz-Deviant Condition
The canonical modes resulting from the GLM analysis comparing standard tone trials with deviant tone trials in the 80Hz-deviant condition for one control participant (df=20). A distinct deflection can be seen peaking at around 170ms. The isocontour field map demonstrates that this deflection results in patterns of activation over the left and right temporal lobes. The map is shown on a schematic head.

Average datasets were then created for the two condition blocks; standard tone trials and deviant tone trials. In addition, the average of the standard tone trials was subtracted from the average of the deviant tone trials to create the 'subtraction' averaged dataset. The data were bandpass filtered from 0.626-40Hz and comb filtered to remove the 50Hz powerline and its harmonics.

For each averaged and filtered data set created, the time course and strength of the signal was plotted as the Global Field Power (GFP), which takes the signals from all 151 channels into account. Peak latency and peak amplitude values from the resulting plots were recorded as well as the latencies at 50% of the peak amplitude.

6.2.5 Source Modelling

The averaged standard tone response of a representative control participant in the 80Hz deviant condition can be seen in Figure 6-3. The standard tone evokes a response at a latency of about 100ms, identifiable as the N1m response. The peak amplitude of this response is largest over the temporal lobes and the field map reveals dipolar patterns over the left and right temporal regions, as two influx and outflux magnetic field peaks.

The N1m component was identified as the first major peak in the measured signal to standard and deviant tones, occurring >80ms after stimulus onset, with a field pattern of activation equivalent to that seen in Figure 6-3. Where possible, bilateral equivalent current dipoles (ECDs) in a spherical head model were employed to explain the 151-channel field data during the N1m peak (see section 4.5.3 for details on the ECD model used). A spatiotemporal algorithm was used and ECDs were fitted, using a least-squares search, over a time period containing 50% of the peak N1m response (as calculated from the GFP plot). Firstly a single ECD was fitted and fixed and then a second dipole was introduced and fitted in the opposite hemisphere. Each dipole was then fitted and fixed a further time.

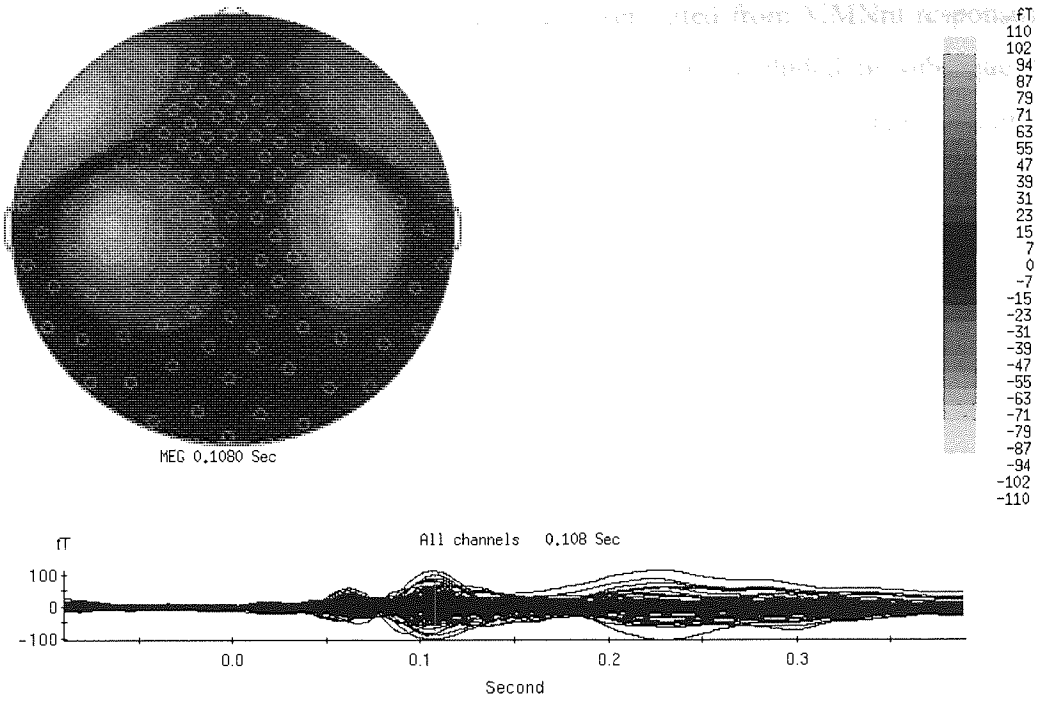

Figure 6-3 Response to Standard Tones and Resulting Field Map in the 80Hz-Deviant Condition

The averaged response to the standard tones in the 80Hz-deviant condition for one control participant, measured over all 151 channels. A distinct deflection can be seen peaking at around 100ms after the tone onset. The isocontour field map demonstrates that this deflection results in dipolar activation over the left and right temporal lobes. The map is shown on a schematic head; red colours represent ingoing field values, while blue colours represent outgoing field values.

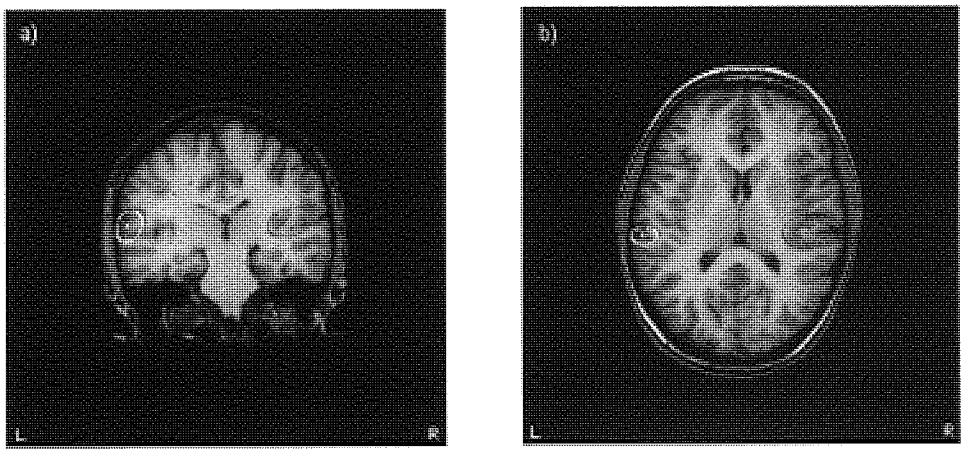

Figure 6-4 N1m Dipoles Superimposed on MRI Slices

The dipoles modelled to explain the N1m field response in the 80Hz-deviant condition, superimposed onto axial (i) and coronal (ii) MRI slices in a control participant. Small dots indicate dipole location while spheres represent the 95% Confidence Volume calculated from Monte Carlo analysis.

Unfortunately, N1m responses to standard tones were not successfully modelled for either frequency deviant condition in three of the six control participants and in four of the dyslexic participants (Monte Carlo Volume greater than $5cm^3$). In

addition, N1m responses could not be reliably separated from MMNm responses in deviant averages. As such, N1m values were not included in subsequent analyses, though the location of these dipoles can be seen in a representative control participant in Figure 6-4.

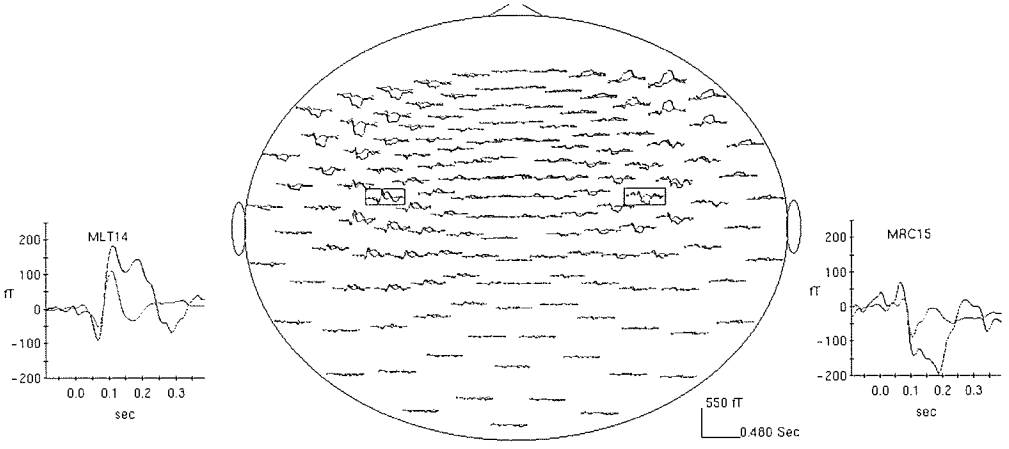

Figure 6-5 151-Channel Averaged Response to Standards and Deviants in the 80Hz-Deviant Condition

The averaged response to standard (red) and deviant (black) tones in the 80Hz-deviant condition for a representative control participant. Differences between responses to standard and deviant tones can be seen peaking at around 170ms after the onset of each tone. The channel showing the largest response over each hemisphere is shown enlarged in the insets at the bottom of the figure.

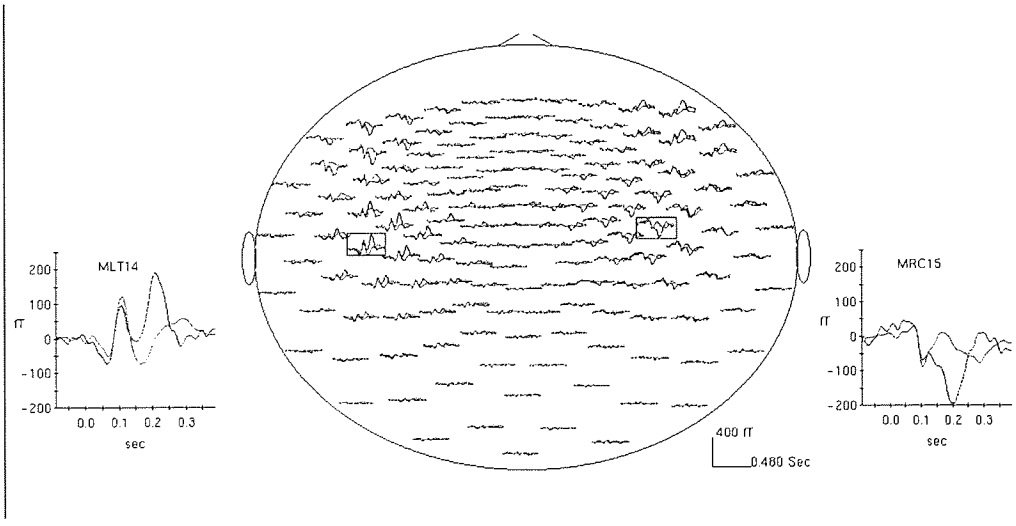

Figure 6-6 151-Channel Averaged Response to Standards and Deviants in the 20Hz-Deviant Condition

The averaged response to standard (red) and deviant (black) tones in the 20Hz-deviant condition for a representative control participant. Differences between responses to standard and deviant tones can be seen peaking at around 200ms after the onset of each tone. The channel showing the largest response over each hemisphere is shown enlarged in the insets at the bottom of the figure.

The difference between responses to standard and deviant tones was defined as the 'subtraction' response. Such differences are seen across all 151-channels in the 80Hz-deviant condition (Figure 6-5) and the 20Hz-deviant condition (Figure 6-6).

As noted above, the averaged response to standard tones was subtracted from the averaged response to deviant tones. The resulting averaged responses are defined as 'subtraction' responses and can be seen for a control participant in the 80Hz-deviant condition (Figure 6-7) and the 20Hz-deviant condition (Figure 6-8). The field maps generated at the peak of the signal demonstrate bilateral dipolar activation pattern over left and right temporal lobes.

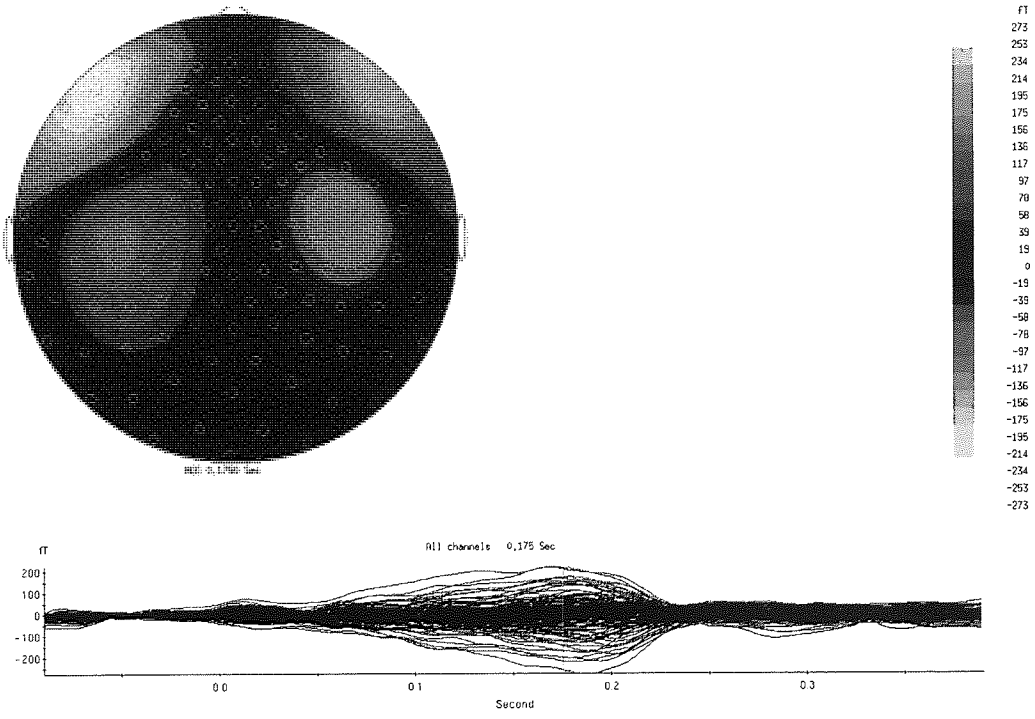

Figure 6-7 Response to Subtraction Averages and Resulting Field Map in the 80Hz-Deviant Condition
The subtraction averaged response in the 80Hz-deviant condition for one control participant, measured over all 151 channels. A distinct deflection can be seen peaking at around 175ms after the tone onset. The isocontour field map demonstrates that this deflection results in dipolar activation over the left and right temporal lobes. The map is shown on a schematic head; red colours represent ingoing field values, while blue colours represent outgoing field values.

The MMNm component was considered to be present where GLM values were significant (standard tone response vs. deviant tone response, $p<0.01$) and the resulting canonical modes revealed activation at a latency of between 150-230ms over the temporal lobes. In addition, the field map at the peak of the response in

the 'subtraction' average had to reveal dipolar activation over auditory cortex, similar to that seen in Figure 6-7/Figure 6-8.

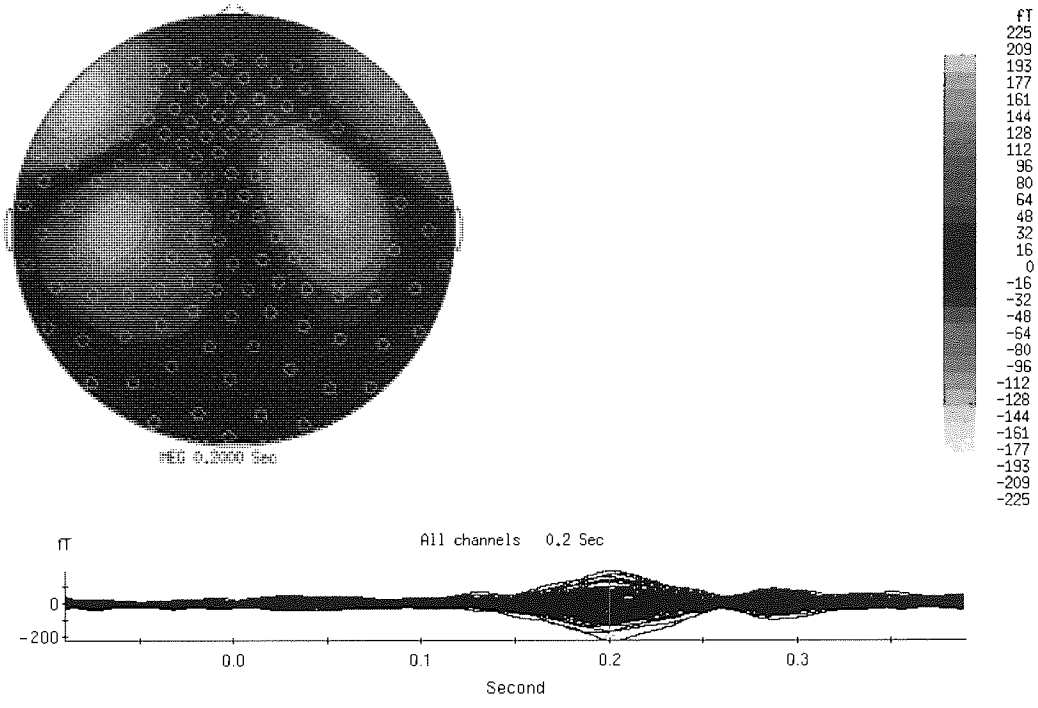

Figure 6-8 Response to Subtraction Averages and Resulting Field Map in the 20Hz-Deviant Condition
The subtraction averaged response in the 20Hz-deviant condition for one control participant, measured over all 151 channels. A distinct deflection can be seen peaking at around 200ms after the tone onset. The isocontour field map demonstrates that this deflection results in dipolar activation over the left and right temporal lobes. The map is shown on a schematic head; red colours represent ingoing field values, while blue colours represent outgoing field values.

The MMNm component was modelled from the data in the 'subtraction' average. Data from all 151-channels were used and a spatiotemporal algorithm was adopted. ECDs in a spherical head model were fitted, using a least-squares search, over the time period containing 50% of the peak MMNm response. As with modelling of the N1m response, a single ECD was fitted and fixed and then a second dipole was introduced and fitted in the opposite hemisphere. Each dipole was then fitted and fixed a further time. In one control participant's case (C4), a single dipole modelled the MMNm response in the 20Hz-deviant condition. In all other cases where the GLM analysis was significant, two bilateral dipoles were required to model the response. All modelled dipoles had a Monte Carlo Volume of less than 5.5cm^3.

Where a significant MMNm response was present, dipole waveforms were analysed and peak latency and amplitude values were noted (Figure 6-9). For all analysed datasets, chi-square error values at the peak latency of the MMNm response were five or below. Figure 6-10 demonstrates the accuracy of the model for explaining the field pattern 170ms after the tone onset in the 80Hz deviant condition for a control participant.

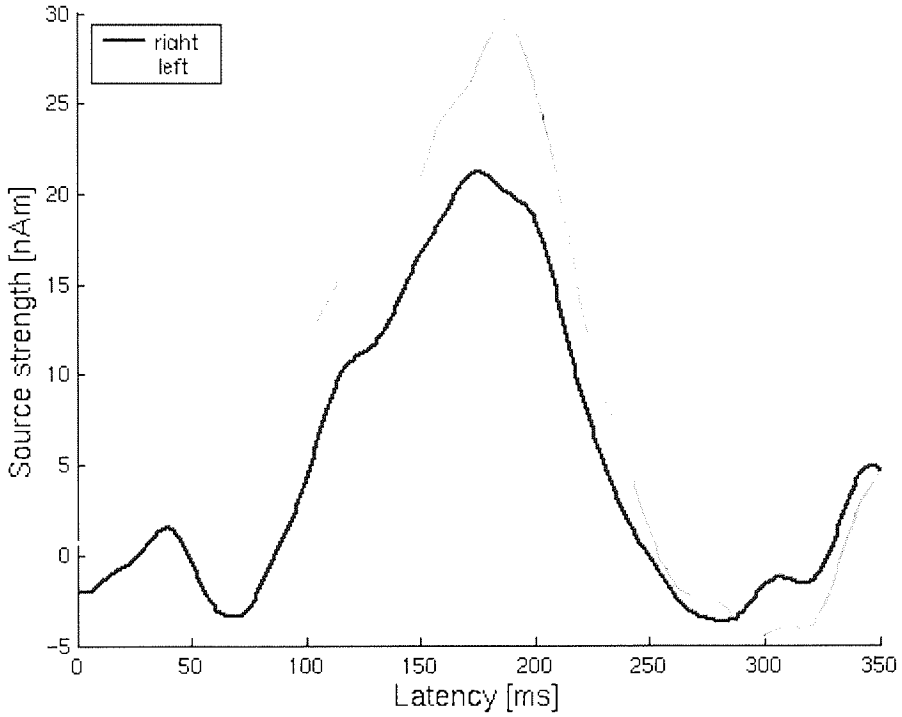

Figure 6-9 Time Course of MMNm Dipoles in the 80Hz-Deviant Condition
A plot of the time course of left and right hemisphere dipoles fitted in a representative control participant in the 80Hz-deviant condition. The amplitude peaks of the dipoles occur approximately 170ms after the tone.

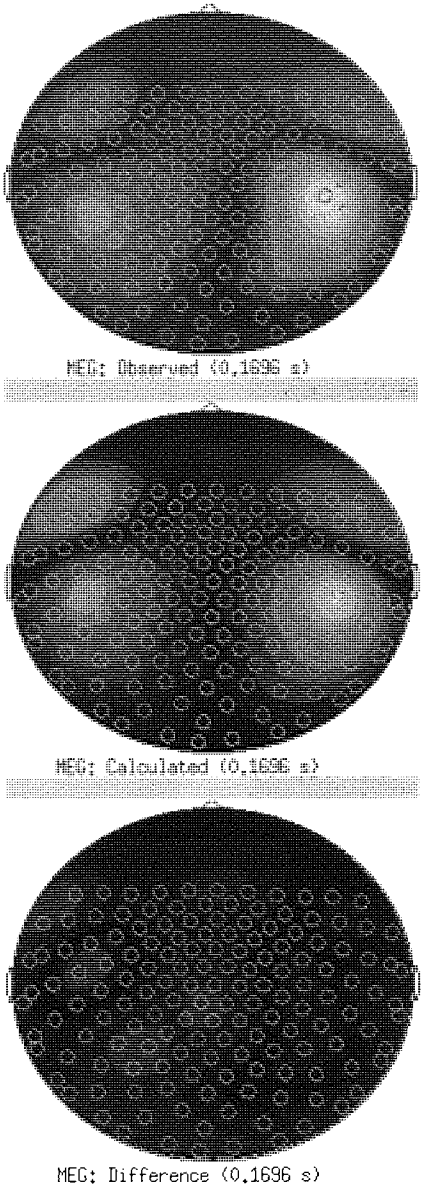

Figure 6-10 Measured and Modelled Field Maps in the 80Hz-Deviant Condition
a) Measured magnetic field at around 170ms after tone onset in a representative control participant in the 80Hz-deviant condition. b) Magnetic field of the dipole model derived by a least squares fit from the field shown in (a). c) Difference between the fields shown in (a) and (b).

MMNm ECDs were superimposed onto the individual MRIs of two of the dyslexic and five of the control participants. The results confirmed that the dipoles were located within the left and right auditory cortices (Figure 6-11).

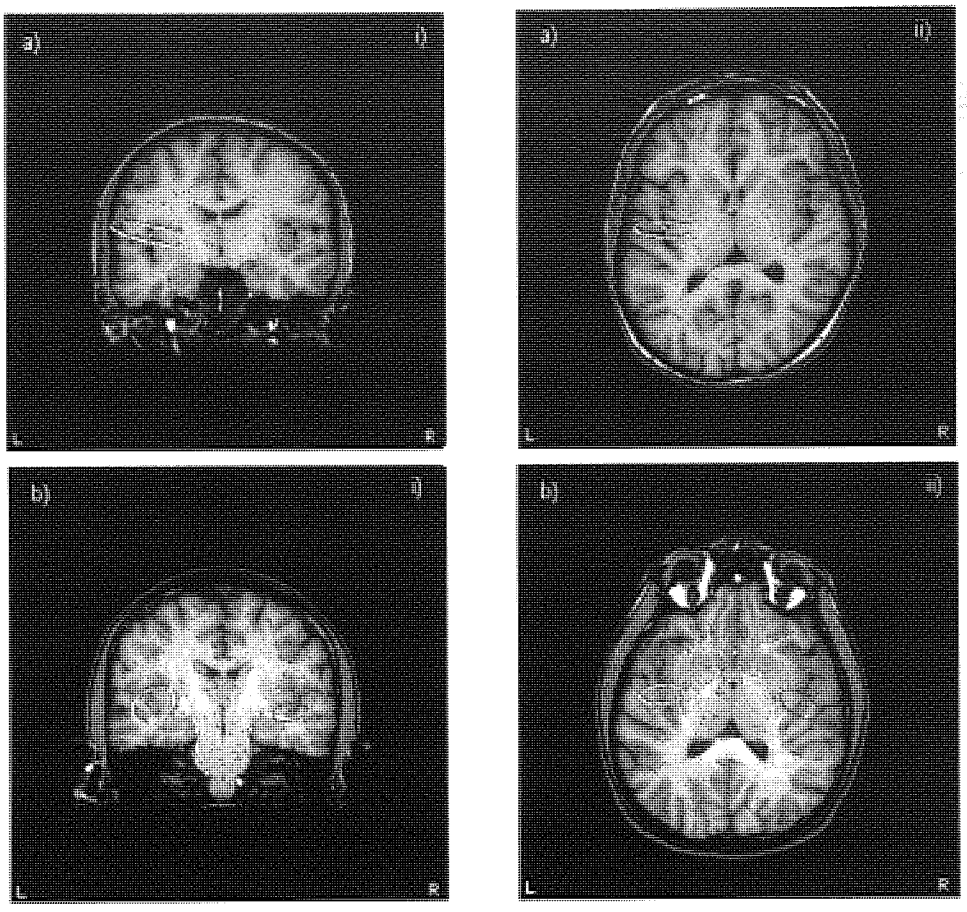

Figure 6-11 MMNm Dipoles Superimposed on MRI Slices
The dipoles modelled to explain the MMNm field response in the 80Hz-deviant condition, superimposed onto coronal (i) and axial (ii) MRI slices in a control (a) and dyslexic (b) participant. Small dots indicate dipole location while spheres represent the 95% Confidence Volume calculated from Monte Carlo analysis.

In order to reliably differentiate the MMNm response from the N1m response, both N1m and MMNm dipoles were modelled in one control participant using data from the deviant response average in the 20Hz deviant condition. Bilateral ECDs were modelled over the peak of the N1m response as outlined above. These dipoles were fixed and the analysis period was extended to contain the peak of the MMNm response. Two further ECDs were introduced and fitted to explain the data. Monte Carlo Volume estimates for each of the four dipoles was less than $1cm^3$, and chi-square error values at the peak latencies of each dipole were below two. Figure 6-12 shows these four dipoles on a schematic head, alongside the

N1m and MMNm dipoles modelled independently using the standard and subtraction averages, respectively.

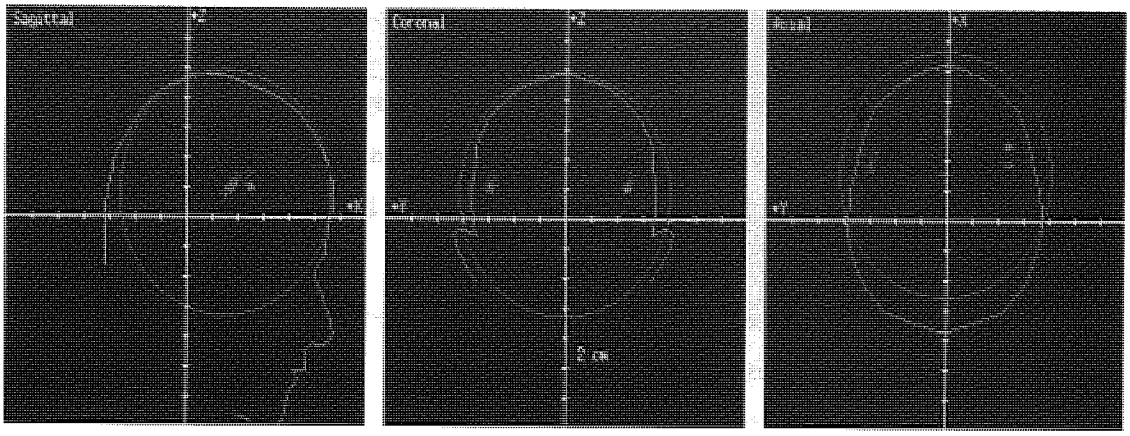

Figure 6-12 Overlay of N1m and MMNm Dipoles Independently Modelled
The dipoles modelled to explain the N1m and MMNm responses in the 20Hz-deviant condition for one control participant. Blue dipoles represent the N1m response to standard tones; red dipoles represent the N1m response to deviant tones. Green dipoles represent the MMNm response modelled from the subtraction average; purple dipoles represent the MMNm response modelled from the deviant average. Dipoles are shown on a schematic head viewed from sagittal, coronal and axial views.

The locations of the independently modelled N1m dipoles are very closely related, as are those for MMNm responses. In addition, a spatial separation can be seen, with MMNm dipoles assuming a source that is slightly more anteriorly located, in agreement with the estimated generator sources of these two components (Sams, Kaukoranta, Hamalainen, & Näätänen, 1991).

6.2.6 Criterion for Assessing the Presence of an MMNm Response

The GLM analyses conducted for each participant in the two separate frequency deviant conditions determined whether MEG traces to standard and deviant stimuli were significantly different. As noted in chapter 4, GLM analyses do not directly assess the presence or absence of an MMN response. Where GLM analyses revealed a significant difference between the responses to the different tone types, the presence of an MMNm component was confirmed by visual inspection of the canonical modes dataset generated by the GLM programme; in each case a peak was visible at a latency of between 150-230ms and this deflection resulted in bilateral activation over the temporal lobes. Furthermore, the subtraction averages revealed dipolar activation over the left and right

auditory cortices within the same latency range, as demonstrated by field patterns of activation similar to those seen in Figure 6-7/Figure 6-8.

6.2.7 Statistical Analyses

In cases where an MMNm response was present, two measures of peak latency and amplitude were analysed; those resulting from GFP plots and also the modelled dipole latencies and amplitudes.

Retrospective power analyses (Appendix 1, Table A-3) revealed that 9 participants would be required to obtain 80% power in group comparisons for each of the dependent variables. Due to the small participant numbers, in addition to unequal variance across participant groups, non-parametric analyses were chosen.

6.3 Results

6.3.1 Small Frequency Deviant Condition

In the 20Hz deviant condition, GLM analyses revealed significant differences between the signals evoked in response to standard and deviant tones ($p<0.01$) in only four of the six control participants (C1, C4, C5, C6) but in none of the dyslexic participants. Figure 6-13 and Figure 6-14 show the waveforms to standard and deviant stimuli in the 20Hz-deviant condition, at the channel with the largest response to deviants, for each of the participants.

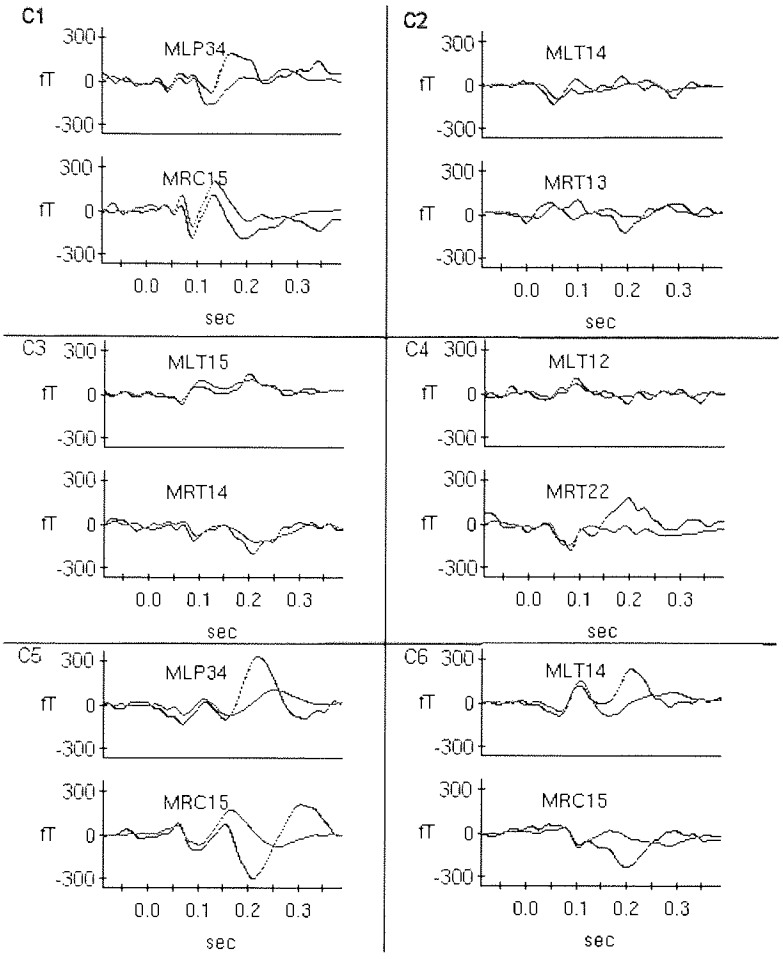

Figure 6-13 20Hz-Deviant Condition, Control Group: Responses to Standard and Deviant Tones

Waveforms to frequency deviants (black traces) and standards (red traces) in the 20Hz-deviant condition for all control participants. Responses are shown in the channels with the largest response to deviants over each hemisphere (top traces correspond to left hemisphere channels, bottom traces correspond to right hemisphere channels).

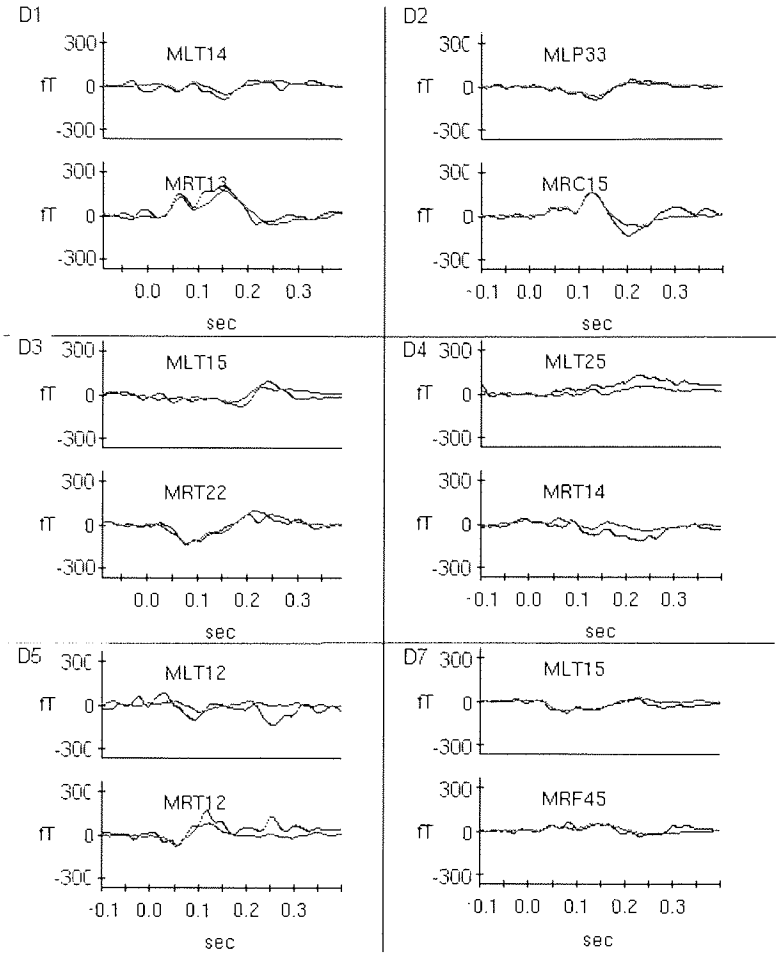

Figure 6-14 20Hz-Deviant Condition, Dyslexic Group: Responses to Standard and Deviant Tones

Waveforms to frequency deviants (black traces) and standards (red traces) in the 20Hz-deviant condition for all dyslexic participants. Responses are shown in the channels with the largest response to deviants over each hemisphere (top traces correspond to left hemisphere channels, bottom traces correspond to right hemisphere channels).

Due to the fact that none of the dyslexic participants demonstrated a significant MMNm response to the small frequency deviant, no statistical analyses were performed to further differentiate the two groups. Descriptive data relating to the control group in the small frequency deviant condition are displayed in Table 6-1. However, it should be noted that this data relates only to those four control participants who obtained significant MMNm responses in the 20Hz-deviant condition. Furthermore, in the case of one of these participants (C4), a single MMNm dipole in the right hemisphere explained all of the data and a left hemisphere dipole could not be modelled.

Table 6-1 20Hz-Deviant Condition: GFP Peak Latency and Peak Amplitude and Modelled MMNm Dipole Peak Latency and Peak Amplitude (Control data only)

Measure	Control	
	Median	Range
GFP Peak Latency (ms)	197.40	22.40
GFP Peak Amplitude (fT^2)	377514.95	2.23E+11
Right Dipole Modelled Latency (ms)	197.40	16.00
Left Dipole Modelled Latency (ms)	207.36	28.80
Right Dipole Modelled Amplitude (nAm)	21.50	15.61
Left Dipole Modelled Amplitude (nAm)	22.34	12.08

6.3.2 Large Frequency Deviant

In the 80Hz deviant condition, there was a significant difference between the signals evoked in response to standard and deviant tones ($p<0.01$) in all participants, suggesting the presence of an MMNm response to deviant tones.

Figure 6-15 and Figure 6-16 show the waveforms to standard and deviant stimuli in the 80Hz-deviant condition for each of the participants. Responses are shown in the channels with the largest response to deviants, over each hemisphere.

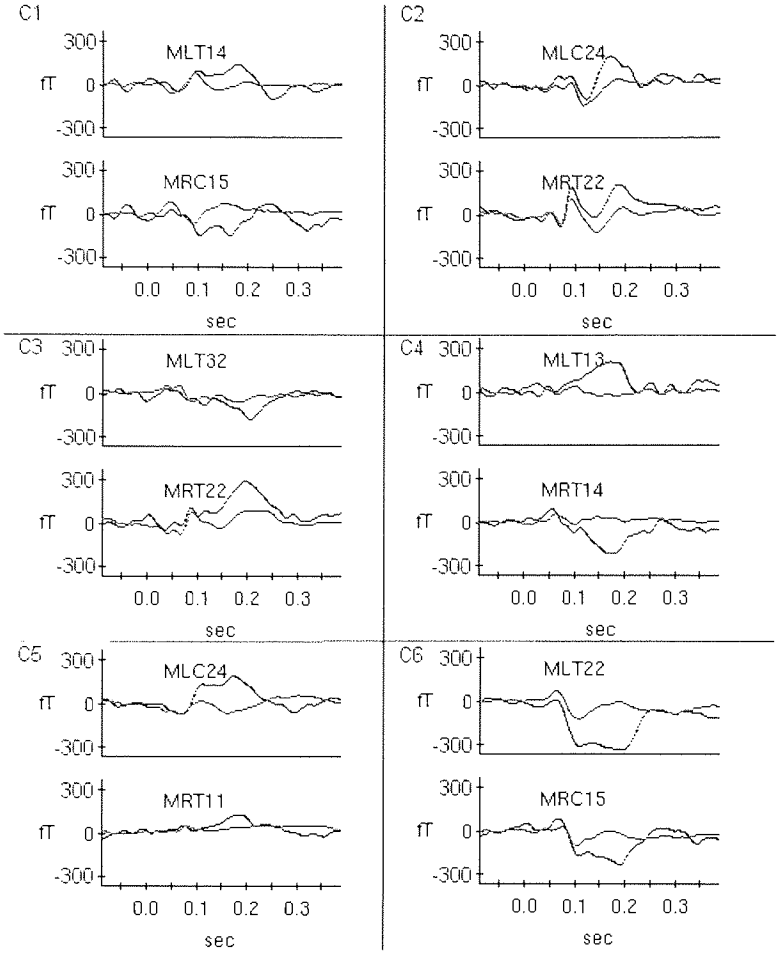

Figure 6-15 80Hz-Deviant Condition, Control Group: Responses to Standard and Deviant Tones

Waveforms to frequency deviants (black traces) and standards (red traces) in the 80Hz-deviant condition for all control participants. Responses are shown in the channels with the largest response to deviants over each hemisphere (top traces correspond to left hemisphere channels, bottom traces correspond to right hemisphere channels).

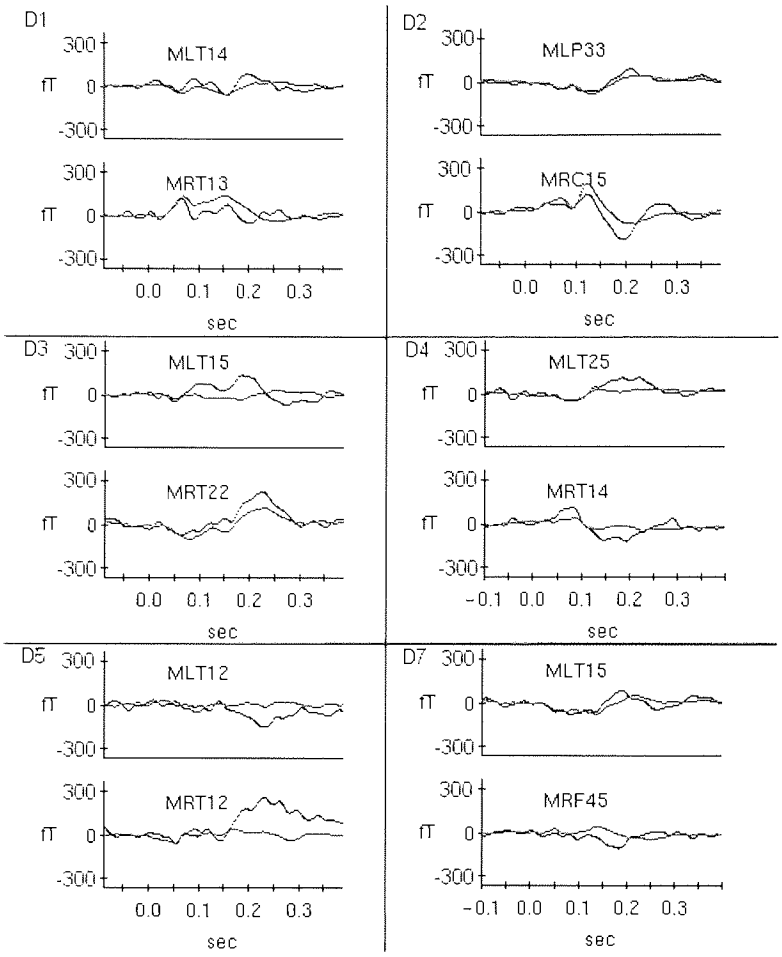

Figure 6-16 80Hz-Deviant Condition, Dyslexic Group: Responses to Standard and Deviant Tones

Waveforms to frequency deviants (black traces) and standards (red traces) in the 80Hz-deviant condition for all dyslexic participants. Responses are shown in the channels with the largest response to deviants over each hemisphere (top traces correspond to left hemisphere channels, bottom traces correspond to right hemisphere channels).

Two tailed Mann Whitney tests were conducted to compare the GFP peak latencies and amplitudes between the participant groups. The results demonstrate that the peak latency of the MMNm response was significantly later in the dyslexic group ($U = 5.0$, $p=0.036$) and that the peak amplitude of the MMNm response was significantly smaller in the dyslexic group ($U = 1.0$, $p=0.006$), demonstrated in Table 6-2. In order to address the issue of individual variability, latency and amplitude values for each participant are plotted in Figure 6-17 and Figure 6-18, respectively. While there is variability within groups, clear group differences are evident in each case.

Table 6-2 80Hz-Deviant Condition: GFP Peak Latency and Peak Amplitude

Measure	Control		Dyslexic	
	Median	Range	Median	Range
GFP Peak Latency (ms)	168.6	27.20	183.00	52.80
GFP Peak Amplitude (fT^2)	377839.37	328227.49	103055.58	190343.309

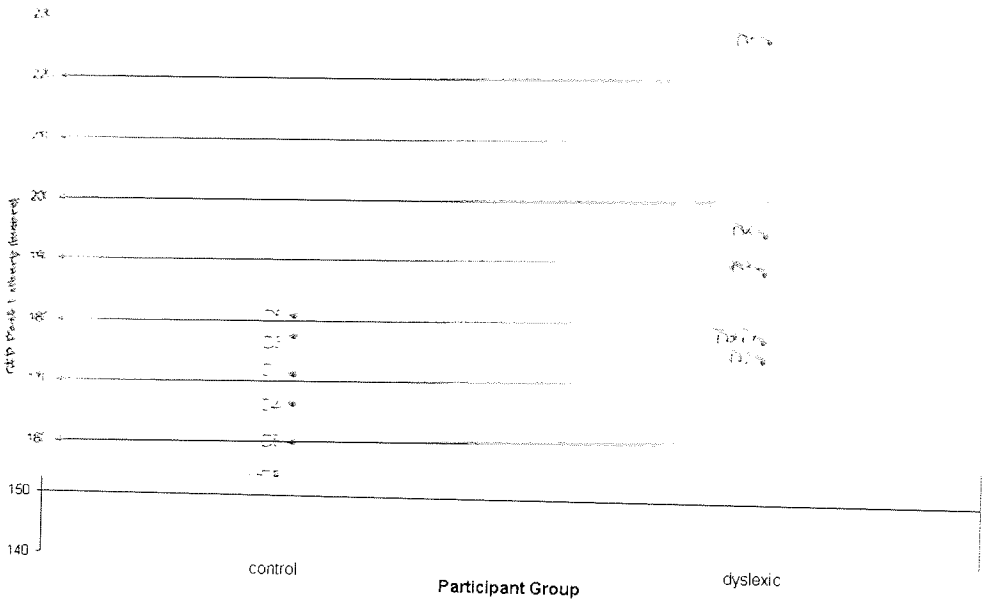

Figure 6-17 80Hz-Deviant Condition: MMNm GFP Latency (Individual Data)
Graph illustrating the GFP peak latency for the 12 participants. Data point markers identify each of the individual participants.

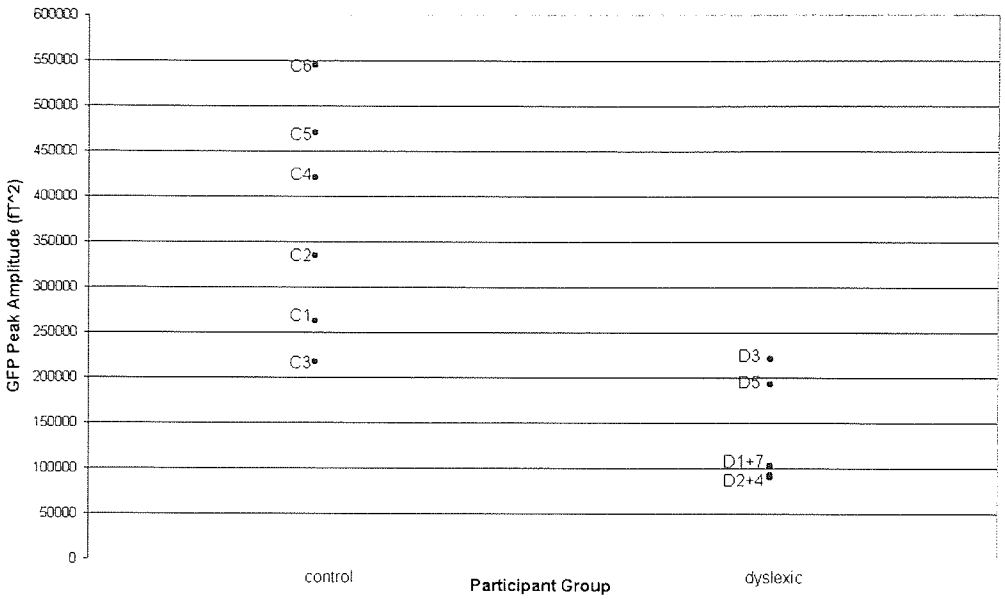

Figure 6-18 80Hz-Deviant Condition :MMNm GFP Amplitude (Individual Data)
Graph illustrating the GFP peak amplitude for the 12 participants. Data point markers identify each of the individual participants.

Two tailed Mann Whitney tests were conducted to compare participant groups in terms of the latency and amplitude of the modelled dipoles in the 80Hz-deviant condition. Mirroring the results found when considering the GFP values, the group effect was significant for latency (right hemisphere; U = 0.5, p=0.005, left hemisphere; U = 6.0, p=0.050) and amplitude (right hemisphere; U = 2.0, p=0.010, left hemisphere; U = 1.0, p=0.006) measures. Table 6-3 demonstrates that the peak dipole latency was significantly later in the dyslexic group, and that the peak dipole amplitude was significantly reduced in the dyslexic group.

Table 6-3 80Hz-Deviant Condition: Modelled MMNm Dipole Peak Latency and Peak Amplitude

Measure	Control		Dyslexic	
	Median	Range	Median	Range
Right Dipole Modelled Latency (ms)	171.00	28.80	187.00	36.80
Left Dipole Modelled Latency (ms)	167.80	54.40	194.20	24.00
Right Dipole Modelled Amplitude (nAm)	27.17	9.93	12.84	16.27
Left Dipole Modelled Amplitude (nAm)	23.87	12.08	14.01	13.48

Considering the dipole latencies and amplitudes, no significant differences were obtained when comparing right and left hemisphere dipole values. Individual data can be seen in Figure 6-19 and Figure 6-20.

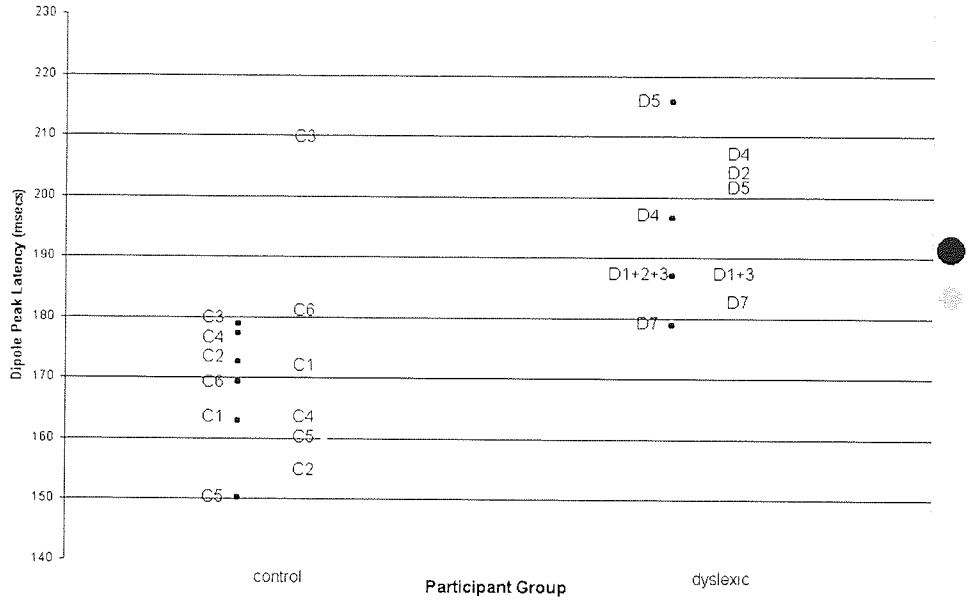

Figure 6-19 80Hz-Deviant Condition: MMNm Modelled Dipole Latency (Individual Data)
Graph illustrating the dipole peak latency for the 12 participants. Black data points indicate the right hemisphere dipole response; grey data points indicate the left hemisphere dipole response. Data point markers identify each of the individual participants.

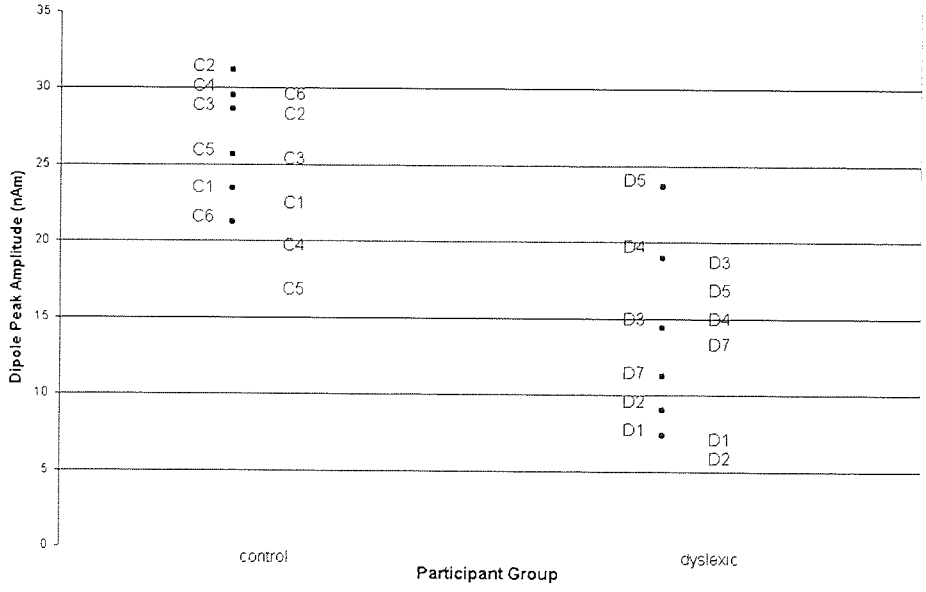

Figure 6-20 80Hz-Deviant Condition: MMNm Modelled Dipole Amplitude (Individual Data)
Graph illustrating the dipole peak amplitude for the 12 participants. Black data points indicate the right hemisphere dipole response; grey data points indicate the left hemisphere dipole response. Data point markers identify each of the individual participants.

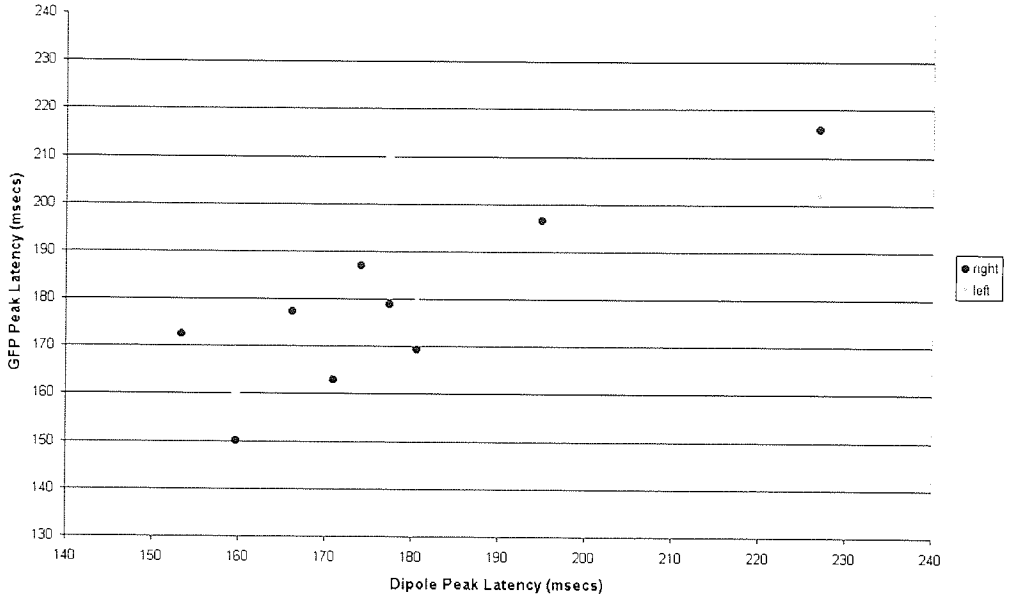

Figure 6-21 Association Between GFP and Dipole Latency Values
Scatter plots illustrating the relationship between GFP and right dipole latency values (black) and GFP and left dipole latency values (grey).

The correlations between the GFP and modelled dipole values were measured using Spearman's rho (2-tailed). There were significant relationships between GFP latency and right dipole latency (rho = .732, p=0.007), and GFP latency and left dipole latency (rho = .709, p=0.010) (see Figure 6-21). Likewise, amplitude values for GFP and right dipole (rho = .615, p=0.033) and GFP and left dipole (rho = .776, p=0.003) were significantly correlated (Figure 6-22).

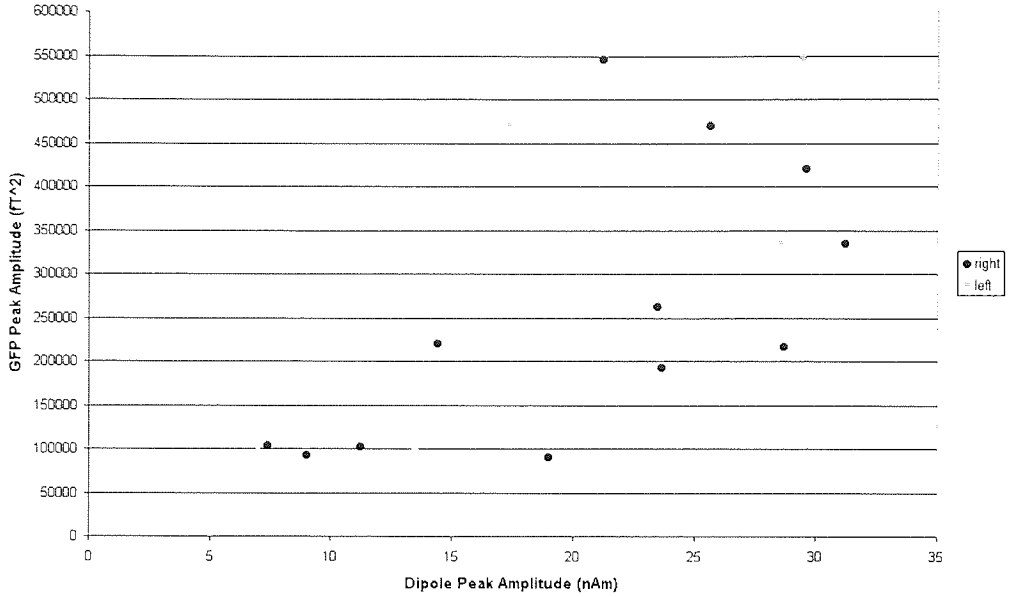

Figure 6-22 Association Between GFP and Dipole Amplitude Values
Scatter plots illustrating the relationship between GFP and right dipole latency values (black) and GFP and left dipole latency values (grey).

6.3.3 Responses of Control Participants Across the Frequency Deviant Conditions

Where control participants obtained significant MMNm responses to both the large and small frequency deviants, the differences in responses across the two conditions were analysed. However, it should be noted that significant MMNm responses in the 20Hz-deviant condition were obtained for only four of the control participants. Furthermore, in the case of one of these participants (C4), a single MMNm dipole in the right hemisphere explained all of the data and a left hemisphere dipole could not be modelled. Thus, a small, and unequal in the case of left dipole values, sample size means that the data should be interpreted with caution.

Peak GFP latency (individual data) in these four cases is plotted in Figure 6-23. Wilcoxon Signed Ranked tests revealed a significant delay in MMNm peak latency in the smaller frequency deviant condition ($t = 0.00$, $p = 0.034_{(1\text{-tailed test})}$).

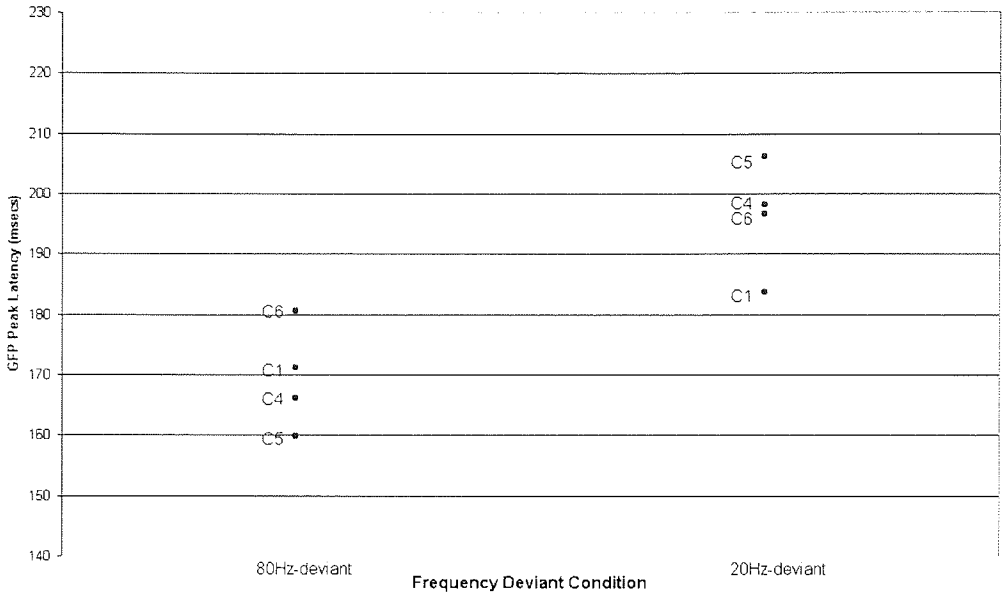

Figure 6-23 MMNm GFP Values Across Conditions: Latency of Response (Individual Data) Graph illustrating the GFP peak latency for the four control participants in the two frequency deviant conditions, where deviant tone responses were significantly different from standard tone responses. Data point markers identify each of the individual participants.

Considering the GFP peak amplitude values, there was no significant difference across the two conditions (Figure 6-24). Examining the individual data it is apparent that the GFP peak amplitude is typically smaller in the smaller frequency deviant condition, in the case of C5 the peak amplitude in the smaller frequency deviant condition is larger.

Wilcoxon Signed Ranks tests were also conducted to examine the effect of varying the degree of deviance on the amplitude and latency values of modelled dipoles. The peak latency of modelled dipoles was significantly delayed in the smaller frequency deviant condition (right hemisphere; $t = 0.0$, $p=0.038_{(1\text{-tailed})}$, left hemisphere; $U = 0.0$, $p=0.050_{(1\text{-tailed})}$), individual dipole latency values can be seen in Figure 6-25.

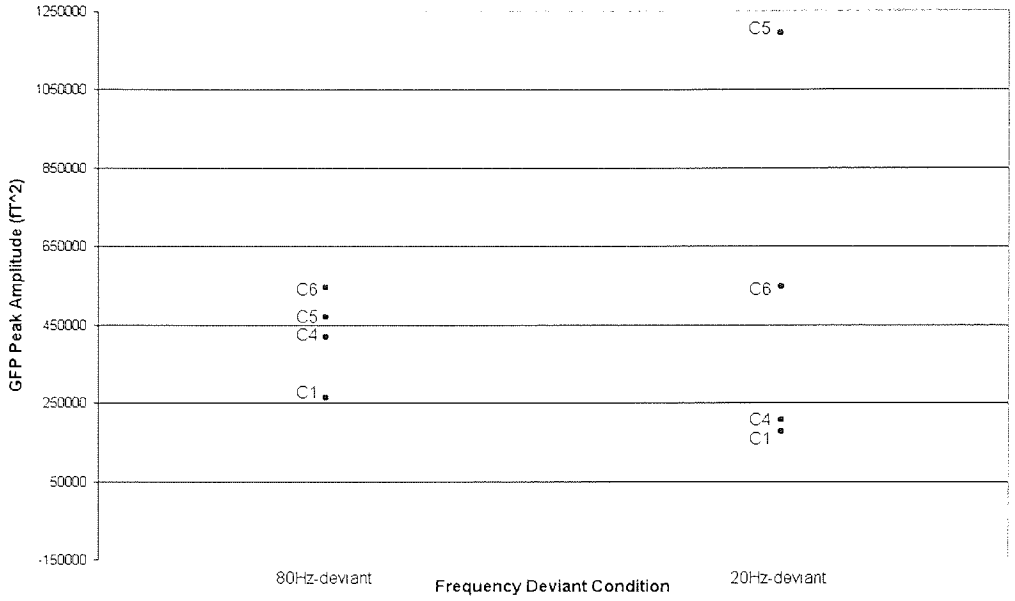

Figure 6-24 MMNm GFP Values Across Conditions: Amplitude of Response (Individual Data)

Graph illustrating the GFP peak amplitude for the four control participants in the two frequency deviant conditions, where deviant tone responses were significantly different from standard tone responses. Data point markers identify each of the individual participants.

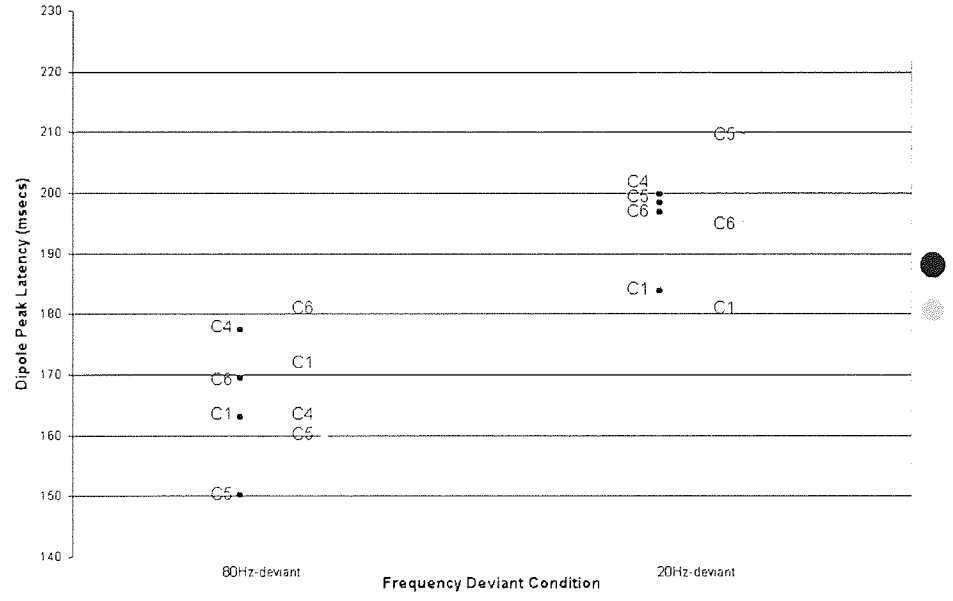

Figure 6-25 MMNm Modelled Dipole Values Across Conditions: Latency of Response (Individual Data)

Graph illustrating the dipole peak latencies for the four control participants in the two frequency deviant conditions, where deviant tone responses were significantly different from standard tone responses. Black data points represent the right dipole response; grey data points represent the left dipole response. Data point markers identify each of the individual participants.

The right hemisphere modelled dipole was significantly smaller in amplitude in the smaller frequency deviant condition than the larger frequency deviant condition (U = 0.0, p=0.034(1-tailed)), while this comparison was not significant when considering the left hemisphere modelled dipole (Figure 7-26).

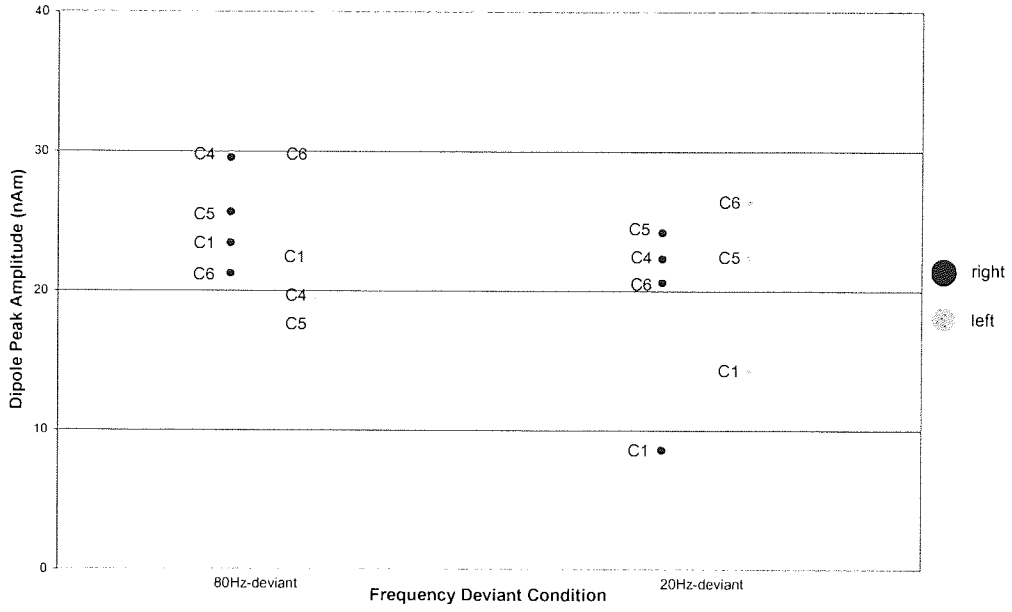

Figure 6-26 MMNm Modelled Dipole Values Across Conditions: Amplitude of Response (Individual Data)
Graph illustrating the dipole peak amplitudes for the four control participants in the two frequency deviant conditions, where deviant tone responses were significantly different from standard tone responses. Black data points represent the right dipole response; grey data points represent the left dipole response. Data point markers identify each of the individual participants.

6.4 Discussion

6.4.1 Summary of Results

The results of this study have demonstrated an impairment of pre-attentive frequency discrimination processes in dyslexic individuals. Physiological responses indexing change detection have shown graded abnormality in the dyslexic group. Significant MMNm in response to frequency deviant stimuli with small degrees of deviance were absent in all dyslexics and present in four of the six controls. In response to larger frequency deviants, MMNm responses were delayed and attenuated in the dyslexic group.

6.4.2 Small Frequency Deviant Condition

In the small frequency deviant condition, significant MMNm responses were elicited in only four of the control individuals and in none of the dyslexic

participants. The absence of this component in dyslexic individuals in response to stimuli with 20Hz deviance corresponds with the findings of Baldeweg et al. (1999). This group reported that, with a deviance of 15Hz, MMN responses were only visible in the group-average data of their control participants. Considering the group mean average waveforms to standard and deviant stimuli in this condition, point-to-point t-tests revealed a significant difference between waveforms in the control but not the dyslexic group. In the present study, analyses of individual participants' data confirm this finding. The waveforms in response to standard and deviant stimuli in the 20Hz deviant condition, at the channel with the largest response to deviants over each hemisphere, are shown in Figure 6-13 and Figure 6-14. Clear differences are observed over left and right hemispheres in the case of participants C1, C5 and C6 and in the right hemisphere channel in C4. This corresponds with the results of GLM analyses, which identified that responses to standard and deviant stimuli were significantly different in these individuals. In contrast, no clear differences are observed in a visual inspection of the dyslexics' data (Figure 6-14).

Where mismatch responses were present in control participants, the latency at the peak of this response was approximately 200ms after tone onset. This is approximately equivalent to the peak latency reported by Baldeweg et al. (1999) for controls in their 30Hz deviant condition.

6.4.3 Large Frequency Deviant Condition

In the 80Hz deviant condition, significant mismatch responses were evoked in all participants. Single channel waveforms in response to standard and deviant stimuli in this condition are shown in Figure 6-15 and Figure 6-16. Differences between waveforms in each hemisphere are visible in the case of all control participants, and while such differences are clearly reduced in the case of the dyslexic participants, they are still visible.

The peak of the MMNm response in the 80Hz deviant condition was significantly later and significantly smaller in the dyslexic group. The latency delay observed in the dyslexic group corresponds to the findings of Hugdahl et al. (1998) and Baldeweg et al. (1999) who also reported significantly delayed MMN latencies in

their dyslexic participants to frequency deviants at 50Hz and 60Hz, respectively. Furthermore, this significant group result is demonstrated in two separate but related measurements of peak latency (GFP and dipole modelled). In addition, the values obtained by the two measures were found to be significantly correlated.

While Baldeweg et al. (1999) found that the peak amplitude of MMN response was not significantly different between groups, the authors do report that the mean area under the MMN curve (onset and offset latency defined as the maximal positivity immediately before and after MMN peak), a more sensitive measure, was significantly reduced in the dyslexic group. The significant group difference in peak amplitude measures reported here, therefore, validates and extends the results of Baldeweg et al.. Again, the fact that the result was obtained independently with two amplitude measures (GFP and dipole modelled), in addition to the significant correlation between these measures, further substantiates the results. In contrast, the finding of significantly reduced MMNm amplitudes contradicts the results of Hugdahl et al. (1998) and Schulte-Korne et al. (1998a). Schulte-Korne et al. found no difference in area under the MMN curve in their dyslexic group. However, this measure was calculated from a fixed time window, not allowing for latency differences between groups, or even individuals. Hugdahl et al. actually report significantly larger MMN peak amplitude in their dyslexic group, in direct contrast to the present results. No adequate account for this difference in results can be provided, although it is worth noting that, according to the MMN literature (see section 3.4.1), a delay in latency along with an increase in amplitude is an unexpected finding. Hugdahl et al. themselves comment in their discussion of results that this effect may have been due to larger variability in the results of their dyslexic sample.

Paavilainen, Alho, Reinikainen, Sams, & Näätänen (1991) found that the MMN response to frequency deviants is typically larger over the right hemisphere. While this trend was apparent (Figure 6-20), the effect of hemisphere was non-significant. Furthermore, no significant differences were noted in responses across hemispheres between the participant groups.

6.4.4 Control Participants' MMNm Responses Across Conditions

Significant MMNm responses were evoked in both frequency deviant conditions in only four of the control participants. Examining changes in the latency and amplitude of the MMNm response across the two conditions allow for confirmation that the morphology of this response is related to the degree of stimulus deviance.

With a larger degree of deviance the peak latency of the MMNm component was significantly earlier (approximately 170ms compared to approximately 200ms in the smaller frequency deviant condition). This corresponds to MMNm literature, which reports that as the degree of deviance increases, the component peaks earlier. In fact, with very large degrees of deviance, the MMN component overlaps with the N1 response (Näätänen, Simpson, & Loveless, 1982).

No significant effect of deviant condition was found when considering the GFP measured amplitude of the MMNm response. Examining the individual data (Figure 6-24) it is noted that peak amplitude actually increased in one control participant (C5) in response to a smaller degree of deviance. Data for all other participants reveals a slight decrease in peak amplitude with smaller deviance. Considering the amplitude values obtained with the dipole modelling, data for the right hemisphere dipole revealed a significant decrease in amplitude in the 20Hz deviant condition. The result was non significant when considering the left hemisphere dipole. Näätänen et al. (1982) note that while the MMN peak latency occurs earlier with larger deviations, MMN amplitude remains relatively stable once the deviance has become recognisable.

6.4.5 The Nature of the Impairment

The results of this study confirm the existence of low-level auditory processing deficits in dyslexia, not accounted for by attentional or motivational differences between groups. Specifically, dyslexic individuals demonstrate impairment of a pre-attentive change detection mechanism for frequency changes. The presence of such an impairment would seem to account for the difficulties this population have shown in active frequency discrimination tasks (Ahissar et al., 2000; Cacace et al., 2000; France et al., 1997; McAnally & Stein, 1996). Data presented in

Chapter 5 found no evidence that this dyslexic sample were selectively impaired in a discrimination task with reducing frequency separations. However, the required discriminations were relatively crude and may have been insensitive to subtle deficits.

Considering the nature of the reported impairment, it is important to consider what the mismatch response actually reflects. In reviewing a large number of studies, Näätänen (1992) argues that a process that registers stimulus change generates the MMN. The biological significance of such a change detection mechanism would be to alert the individual to changes in the environment.

According to Näätänen's model (see section 3.4.1), the permanent feature detector system encodes physical features of the standard stimuli. The outcome of this sensory analysis then enters Sensory Memory. The presentation of a deviant stimulus (also encoded by the permanent feature detector system) is compared to the representation in Sensory Memory and a change detection mechanism registers a mismatch. This in turn triggers frontal processes, which directs attention to the stimulus change.

The alerting mechanism is reflected in the frontal MMN component (Rinne et al., 2000). While both the temporal and frontal generators of MMN are thought to contribute to the electrically recorded MMN response, Rinne et al. have argued that due to its likely radial orientation and deep location, the frontal generator component is not reflected in the magnetically recorded MMNm. The two dipoles modelled to account for the data in the present study were found to lie in the auditory cortex and they resulted in chi-square values of less than five, suggesting that no further sources accounted for the data. Therefore, MMNm responses recorded in the present study are likely to be generated by the supratemporal component.

A number of failed processes could result in a reduced MMNm response: Perhaps stimuli were not encoded as appropriately in dyslexic individuals. The traces held in Sensory Memory may have deteriorated in the dyslexic group. Alternatively,

the comparative mechanism may have failed to register the change in dyslexic listeners.

The presence of any MMN suggests that the change detection mechanism is able to register change in dyslexic individuals. Baldeweg et al. (1999) report finding no group differences in MMN latency or amplitude in response to duration deviants. Furthermore, the results of both the present and Baldeweg et al's. study reflect graded abnormality of change detection processes in the dyslexic groups. Indeed, Baldeweg's group found no significant group differences in MMN response to stimuli deviating by 90Hz.

If neural representations of stimulus features held in Sensory Memory do deteriorate more rapidly in dyslexic individuals, it would be difficult to explain why MMNm responses to duration deviants were normal in Baldeweg's (1999) group.

Baldeweg and colleagues argued that the encoding of frequency information was impaired in the dyslexic group. Frequency discrimination thresholds depend on local frequency processing by peripheral filters. The graded abnormality of the dyslexic groups MMNm response to deviants with reducing degrees of frequency deviation, in addition to reports of increased frequency discrimination thresholds may reflect impairment of such local processing. McAnally and Stein (1996) proposed that frequency discrimination deficits resulted from impairments in the generation, decoding or exploitation of phase locked neural discharges, i.e. on the basis of temporal cues to pitch. However, a number of studies have disputed claims that phase locking mechanisms are disrupted in dyslexic groups (see sections 3.3.4, 3.3.5 and 3.3.6).

Hari et al. (1999) proposed an alternative account for dyslexics' frequency discrimination difficulties, not based upon peripheral processing of local frequency information. The authors suggested that the dyslexic group's deficits in the accurate identification of rapidly presented sound sequences are related to the impaired functioning of a short-term buffer in which successive sounds can interfere with one another. Such a proposal predicts that accurate perception of

auditory stimuli is disrupted by the presence of additional sounds in the sequence and that this disruptive effect is greater in the dyslexic population. This proposal is further investigate in Chapter 7.

In Chapter 5 N1m amplitudes were reduced in dyslexic participants relative to control participants. It was suggested that such a result could arise from reduced attentional capture by auditory stimuli in the dyslexic group (i.e. stimulus driven processes). Such a deficit could also account for the findings reported here. If the dyslexic listeners were not processing the stimuli as efficiently, the representations of stimulus features would not be as strong and comparisons between deviant and standard stimuli would not be as efficient. This hypothesis is considered in more detail in the next study.

6.4.6 Conclusions

The dyslexic group demonstrated pre-attentive auditory processing impairments in response to simple auditory stimuli. The MMNm component, which reflects the process of a change detection mechanism, showed graded abnormality in response to frequency deviant stimuli. This result, suggests a disruption in the encoding of stimulus features in the dyslexic population at a local level of frequency processing, possibly due to the fact that auditory stimuli capture covert attention less effectively in dyslexics.

7 TONE OMISSION MISMATCH RESPONSE

7.1 Introduction

7.1.1 Aim

Evidence of the dyslexic population's difficulties with the accurate perception and discrimination of auditory stimuli occurring in close succession, has led to the suggestion that this group has a longer than normal time window of temporal integration. The aim of the present study is to evaluate this hypothesis using a tone omission MMNm study. In the normal population a tone omission will only elicit a mismatch response if successive tone presentations have been perceptually organised into unitary auditory events. If dyslexic individuals integrate inputs over a longer time window, one would predict that the maximum interval between stimuli, resulting in a mismatch response to tone omission, would be extended.

7.1.2 Perceptual Interference of Successive Auditory Inputs

As reviewed in sections 3.3.1, 3.3.7 and 3.3.8, a large number of studies have provided evidence that dyslexic individuals demonstrate impairments in tasks requiring the processing of brief and rapidly presented auditory stimuli. Considering this evidence, it has been proposed that such difficulties might result from sluggish auditory processing in the dyslexic individuals; such a processing abnormality may lead to impaired processing of closely successive auditory stimuli, as surrounding sounds disrupt the accurate perception of current inputs. A number of studies have attempted to examine such claims.

Masking paradigms can assess the interference of closely surrounding sounds upon one another; the accurate perception of a target sound is impaired if a masking stimulus is presented before, during or after the target, within a short time window. Wright et al. (1997) presented a number of masking paradigms to a group of language impaired and control children. Brief tones were presented during, or immediately before or after (no stimulus separation) bandpass noise stimuli and Wright and colleagues measured the threshold tone level required for accurate detection of the tone. Tone level detection thresholds were higher for language-impaired children in all conditions; however, post-hoc analyses found that this was only significant in the backward masking condition (noise

immediately following tone). While none of the language-impaired children were specifically diagnosed with dyslexia, Wright et al. also reported preliminary data on twelve participants with reading difficulties. They found that five of these individuals demonstrated excessive effects of auditory backward masking, though none were as affected as the language-impaired group.

In a large scale correlation study, Ahissar et al. (2000) failed to find a significant association between reading and spelling ability and tone level detection thresholds in a backward masking condition. Their sample consisted of adults with and without a childhood history of reading difficulties. The group presented two bandpass noise bursts in each trial, one of which was preceded by a tone of adaptively varying amplitude, at ISIs between 230ms and 0ms. They employed a two-alternative forced-choice task asking the participants to judge which stimulus contained the tone. Using a similar paradigm, Ahissar et al. presented two short tones with frequencies of either 900Hz or 1100Hz, each followed by bandpass noise. Varying the tone-to-noise intervals, they asked the participants to judge whether the tones were the same or different. In contrast to the tone level detection task, performance on this task was highly correlated with reading measures.

Hari & Kiesila (1996) used an illusory sound movement paradigm to examine the effects of the timing of successive auditory inputs in dyslexic and control adults. Trains of binaural clicks with small interaural time differences were presented to participants; the first four leading from the left ear, the final four from the right. When each of the four binaural clicks are presented in isolation, the perceived origin of left ear leading clicks is the left side, while for right leading clicks it is the right side. However, when presented together in a sequence with short ISIs, participants perceive the clicks as jumping in steps of equal distance from the left to the right side. As the ISI increases, the jump over the midline from the 4^{th} to the 5^{th} click also increases and the illusion diminishes. Hari and Kiesila found that while the illusion dissipated with ISIs of 150ms and longer in their control participants, the dyslexic participants continued to perceive the illusion at far greater ISIs (up to 500ms for eight of the ten dyslexic individuals). The authors propose that the illusion demonstrates the brain's sluggishness in forming auditory

percepts: in the case of the controls, later sounds were affecting the perception of earlier sounds within a time window of 400-500ms; for the dyslexic participants this window was extended even further.

Auditory stream segregation occurs in response to sound sequences consisting of alternating low and high pitched tones: with small degrees of frequency separation between tones or slow presentation rates the perception is of a connected sequence of tones; with large degrees of frequency separation and fast presentation rates the perception is of two separate sound streams. Helenius et al. (1999b) used this perceptual phenomenon to further examine the difficulties the dyslexic population appear to show processing sound sequences. Measuring temporal coherence boundaries the group found that the dyslexic participants perceived the sound sequences as segregating into two separate streams at significantly slower presentation rates than the control participants (at mean SOAs of around 210ms and 130ms in each group, respectively). Furthermore, in the dyslexic group coherence boundaries were significantly correlated with naming speed scores, a behavioural measure thought to characterise dyslexia in adulthood (Wolf, 1986). These results were in agreement with those of Hari & Kiesila (1996), again providing evidence of a prolonged time window during which sounds can interfere with the perception of surrounding sounds.

The results of Hari & Kiesila (1996) and Helenius et al. (1999b) led Sutter et al. (2000) to question whether the dyslexic population's observed difficulties grouping sounds based on timing information extended to difficulties with perceptual judgements based on pitch. The group presented dyslexic and control groups with tone sequences consisting of two target tones (mid and high) interspersed in a repeating sequence of 1000Hz tones; the mid tone had a frequency of 1030Hz, while the frequency of the high tone was varied. As the frequency separation between the high and mid tone is increased, the mid tone becomes grouped with the background repeating stimuli and it becomes difficult to identify both targets. In addition, increasing the rate of stimulus presentation makes it more difficult to detect the two target tones. Sequences were presented at varied ISIs and degrees of frequency separation and participants were simply asked to judge whether the sequence consisted of two or three distinct tone

frequencies. As predicted, performance in both groups improved with longer ISIs, and deteriorated with increasing frequency separations. The performance of the dyslexic group was poorer than that of the control group overall but the group difference was frequency dependent; at longer ISIs the performance of the two groups was similar for small frequency separations, but the performance of dyslexics dramatically dropped at the wider frequency separations. This result suggested that the dyslexic group experienced a stronger capture effect at large frequency steps.

The results suggest that the dyslexic population have deficits relating to perceiving frequency and not solely related to stimulus timing; if the deficit were purely temporal, the dyslexics would have demonstrated impairment at all frequency steps within the same ISI conditions. Sutter et al. (2000) make a distinction between these results and findings of reduced frequency discrimination thresholds in dyslexia. In such paradigms, performance deteriorates as the frequency separation between stimuli becomes smaller. In their study, Sutter and colleagues demonstrate a deficit that is magnified as the frequency separation between the stimuli becomes wider. As such, the results are inconsistent with a low-level or peripheral processing account. Rather, they imply that the observed deficits in the dyslexic group relate to the global processing of the stimuli; with high degrees of frequency separation, the high tone affects the perception of the relationship between the mid tone and the repeating background. The authors propose that the dyslexic populations deficits in this and streaming tasks indicate impaired auditory grouping processes.

7.1.3 Physiological Processing of Sound Sequences

Rumsey et al. (1994) recorded abnormal physiological responses to tone sequences in their group of severely dyslexic men and matched controls using Positron Emission Tomography (PET). Stimuli were three- and four-tone sequences presented in pairs and the participants task was to judge whether the paired sequences were the same or different. The researchers found that their dyslexic sample's performance was significantly worse than that of controls on this complex task. Furthermore, the dyslexic group showed less activation in a

right middle temporal region and two right frontal regions, while activation patterns in left hemisphere sites did not differentiate the groups.

A number of results demonstrating abnormal mismatch responses in dyslexic groups were reviewed in section 6.1.4. In each of the studies stimuli were presented singly. However, in order to examine processing of sound sequences researchers have also employed MMN paradigms requiring discrimination of tonal patterns (see section 3.4.6).

Schulte-Korne et al. (1999a) constructed complex stimuli consisting of four pure tone segments of differing pitch and duration. These stimuli were presented to their dyslexic and control adults in a MMN paradigm. Deviant stimuli were the same tone sequences, identical except that the order of two of the segments was reversed, resulting in a change in the duration order but not the pitch order of the segments. Schulte-Korne and colleagues found that the area under the MMN curve between 250-600ms was significantly reduced in the dyslexic group.

Supporting these results, Kujala et al. (2000) also recorded reduced MMN response to temporal pattern stimuli in their group of dyslexic adults. Tones with identical frequencies and durations were separated by gaps of varying duration, thus resulting in rhythmic patterns. In deviant trials the order of these gaps was changed (the third tone in the sequence occurred earlier in the deviant pattern). An additional control condition was included; tone pairs were presented to participants with a decreased ISI in deviant trials. While MMN response to tone pair deviants did not differ between groups, MMN responses to tone pattern deviants did. In the case of control participants, tone pattern deviants elicited two consecutive MMNs in response to the two early third tone, an 'addition' and an 'omission' response. In contrast, no significant differences in standard and deviant traces were found in the dyslexic group prior to 400ms, interpreted as evidence that the 'addition' response was absent. Furthermore, there was evidence of hemispheric differences between groups; while responses were larger in the right hemisphere of the control group, they were similarly distributed over the two hemisphere in the dyslexic group. The absence of an 'addition' MMN in the tone pattern condition is in contrast to the normal response found with the

same stimulus change in the simpler tone pair context. This dissociation suggests that the critical factor in the anomalous processing was the interfering influence of surrounding inputs.

In a review article considering the usefulness of MMN paradigms in examining auditory processing abnormalities in dyslexia, Kujala & Näätänen (2001) report as yet unpublished data in a study examining responses to tone pair order reversals either preceded or followed by a masking tone (Kujala, Belitz, Tervaniemi and Näätänen). The MMN responses in the dyslexic group were diminished to the tone order reversals, particularly so under backward masking conditions. This result again suggests that in the dyslexic population the influence of surrounding, and especially following, sounds is more disruptive on the accurate perception of auditory inputs than in the control population.

7.1.4 Persistence in Sensory Memory

Merzenich et al. (1993) has proposed that the deficits dyslexic individuals' demonstrate when processing brief and rapidly successive auditory stimuli may result from impairment in a pre-attentive event synthesis mechanism (the Temporal Window of Integration in Sensory Memory), a hypothesis first forwarded by Cutting and Pisoni (1978, cited in Loveless & Koivikko, 2000). Stimuli occurring in close succession are integrated in Sensory Memory within a time window of around 150ms (see section 3.4.1).

Loveless & Koivikko (2000) set out to examine whether the observed processing deficits in dyslexia could be accounted for by an extension of this integration process to a longer than normal time window. This study is reviewed in section 3.4.2. Briefly, the group examined the N1m component of the auditory field in response to tone pair stimuli. When the second tone of the pair is presented within a short time window after the initial tone, the N1m component is enhanced, due to persistence in a temporal integration process. The prediction was that if dyslexic individuals do have an extended time window of temporal integration, the enhancement effect should be displaced to longer intervals in these participants. The results of the dyslexic group revealed that, not only was the enhancement effect not displaced to a longer than normal time window, it was

attenuated with shorter SOAs in the dyslexic group. This directly contradicts the hypothesis of a prolonged time window of temporal integration in this population.

A further physiological measure of temporal integration is afforded by examining mismatch responses to stimulus omissions. Yabe et al. (1997) successfully recorded mismatch responses to complete stimulus omissions, allowing the group to estimate the duration of the Temporal Window of Integration. When the delay between sounds is so large that successive inputs fall outside the window of integration (SOAs greater than 150ms), the trace formation in Sensory Memory is that of a single auditory percept. As mismatch responses are not elicited by cessation of stimulus sequences, a stimulus omission under such conditions fails to elicit a mismatch response. In contrast, when the stimuli are presented in close succession (SOAs of 150ms or less) and the second stimulus enters during the window of integration, the trace formation in Sensory Memory is that of a compound stimulus, with a short temporal gap. Thus, a random omission of a stimulus in the sequence triggers change-detection mechanisms and an MMN response is formed. By varying the interval between tones it is therefore possible to estimate the duration of the time window within which successive auditory inputs are integrated.

If the dyslexic population do integrate percepts in Sensory Memory over a longer than normal time window, one would predict that omissions occurring in stimulus sequences presented at slower rates (SOA of 175ms) would continue to elicit MMN responses in these participants. In contrast, considering the results of Loveless & Koivikko (2000) the dyslexic participants may fail to integrate the inputs presented with short SOAs (100ms), resulting in absence of the MMN response to tone omission. The two possible outcomes are investigated in the present study.

7.2 Methods

7.2.1 Participants

Six dyslexic (D1, D2, D3, D4, D5 and D7) and six control (C1, C2, C4, C5, C6, C7) individuals, as described in Chapter 4, completed the study. One participant from each of the initial groups of seven (control and dyslexic) withdrew their

participation before data for this study was collected. The remaining participants were all students from Aston University and groups were matched for age, sex and IQ. The dyslexic group's performance on tests of auditory short-term memory, phonological skills and literacy measures was significantly worse than the control groups performance on the same measures (see section 4.1.4).

7.2.2 Stimuli

Stimuli (Figure 8-1) were 1800 pure tones with a frequency of 1000Hz and duration of 50ms (5ms Hanning Window) presented binaurally at 65dBSPL. In one condition the SOA (onset-onset) was 100ms, while in the other condition the SOA was 175ms. At a probability of 0.1, a stimulus was randomly omitted from the stimulus sequence, with the constraint that at least five tones should occur between each omission. The two conditions were presented in separate blocks, with the order of presentation randomised across subjects.

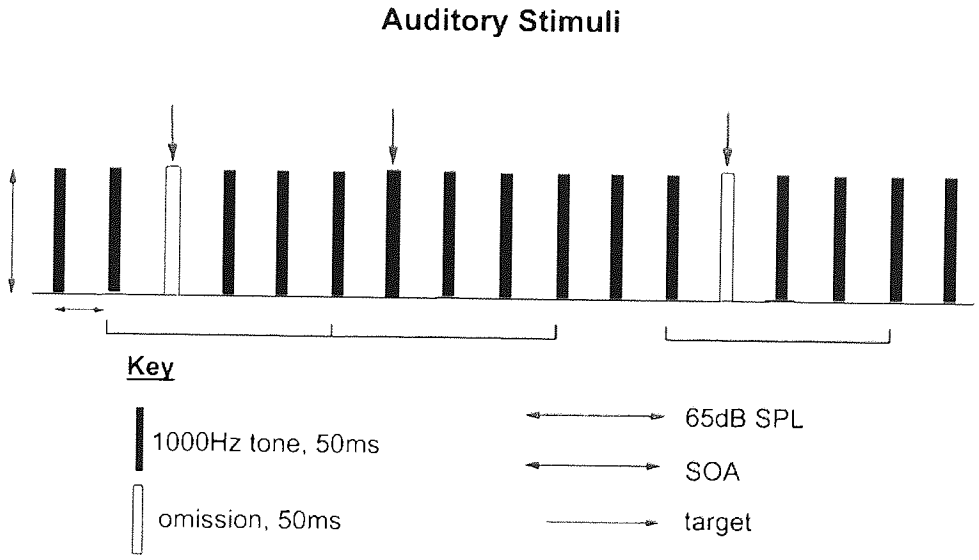

Figure 7-1 Tone Omission Stimuli
Graphical representation of the auditory stimuli.

7.2.3 Data Acquisition

Physiological data were collected with the CTF 151-channel whole-head MEG system outlined in Chapter 4. Participants were instructed to ignore the auditory stimuli and watch a cartoon video, which was viewed via mirrors from a television screen placed at a fixed distance outside the magnetically shielded

room. Data were recorded at a sampling rate of 625Hz, with a low pass filter of 200Hz. For each of the condition blocks, data were recorded in a single epoch; in the 100ms SOA condition the epoch length was 190s including a pre-stimulus period of 500ms; in the 175ms SOA condition the epoch length was 320s including a pre-stimulus period of 500ms. 5mins resting time was provided on completion of each of the condition blocks.

7.2.4 Data Processing

Initially, datasets were DC corrected based on the whole trial. In addition the data was comb filtered to remove the 50Hz powerline and its harmonics.

The data were then marked in order for them to be split into standard and deviant blocks. For deviant blocks the omissions were marked as targets and the analysis period extended from the onset of the tone preceding the target to the onset of the third tone after the target. For standard blocks a tone was marked as the target and the analysis period extended from the onset of the tone preceding the target to the onset of the third tone after the target. Deviant blocks were marked initially and the overlap tolerance was set at zero; thus only a standard tone occurring at least four places behind a target could itself be marked as a target (see Figure 7-1). In each of the SOA conditions the onset of the target was taken as time point zero. Therefore, for the 100ms SOA condition, the analysis period was 400ms including a pre-stimulus period of 100ms; for the 175ms SOA condition, the analysis period was 700ms including a pre-stimulus period of 175ms.

For each of the SOA conditions new datasets were created for participants, with each block (standard or deviant) saved as a single trial. The first omission block was omitted and thus, resulting datasets consisted of 179 deviant trials and 206 standard trials.

These datasets were then analysed with the GLM program, described in Chapter 4. Standard trials were compared to deviant trials over the 1-30Hz range. The analysis period extended from 100ms after target onset to 140ms after target onset. For each analysis, chi values were obtained for 20 degrees of freedom. The resulting p values were recorded and a significant difference between the

standard and deviant tone trials was assumed if p was less than 0.01. Due to the short analysis period, the plotted canonical modes yielded little information about difference peaks between standard and deviant trials.

Average datasets were then created for standard trials and deviant trials in each of the SOA conditions. The data were bandpass filtered from 0.626-40Hz. The averaged response of a control participant to standard and deviant blocks in the 100ms SOA condition can be seen in Figure 7-2. Small deflections can be seen in the standard response, with a phase related to the presentation of each tone. A large deflection in the deviant response can be seen peaking at around 200ms. This is likely to be an enhanced response to the tone presented after the omission (at 100ms). In addition, the deflection peaking at 110ms appears to be slightly enhanced in the deviant response, this deflection commences before the presentation of the next tone after omission and can therefore be interpreted as a response to the stimulus omission.

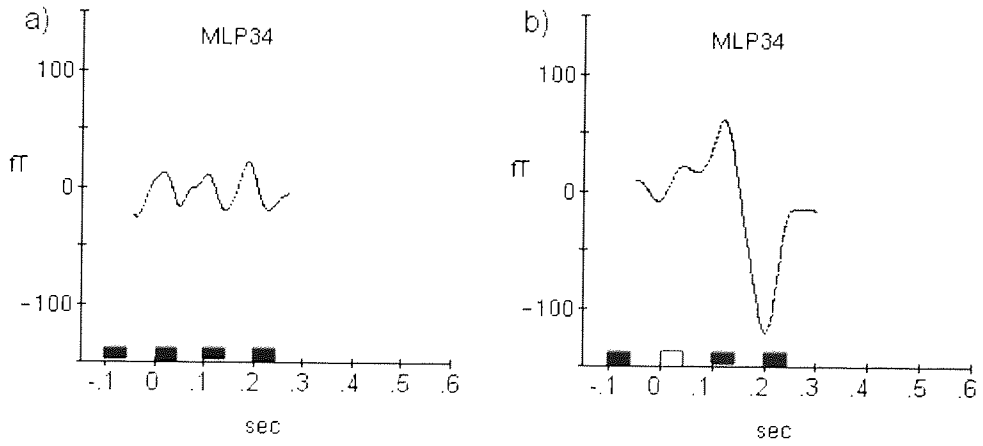

Figure 7-2 Single Channel Response to Standard and Deviant Stimulus Blocks: 100ms SOA
The response to a) standard and b) deviant stimulus blocks in the 100ms SOA condition for a representative control participant, in the channel showing the largest response to deviant stimulus blocks. Tone presentation is indicated by a filled black square; tone omission is indicated by an unfilled black square.

The averaged response of a control participant to standard and deviant blocks in the 175ms SOA condition can be seen in Figure 7-3. Deflections can be seen in the standard response, with a phase related to the presentation of each tone. These deflections are larger in amplitude than those seen in the standard response in the

100ms SOA condition (Figure 7-2(a)); clearly, the cortical response to the tonal stimuli is far more suppressed with faster rates of presentation. A large deflection in the deviant response can be seen peaking at around 275ms. This is likely to be an enhanced response to the tone presented after the omission (at 175ms). Examining the waveform immediately preceding the onset of the tone after omission, a reduction in amplitude is noted. This suggests that the deflection to tone omission, which peaks 100ms after target tone onset in the standard response, is missing in the deviant response.

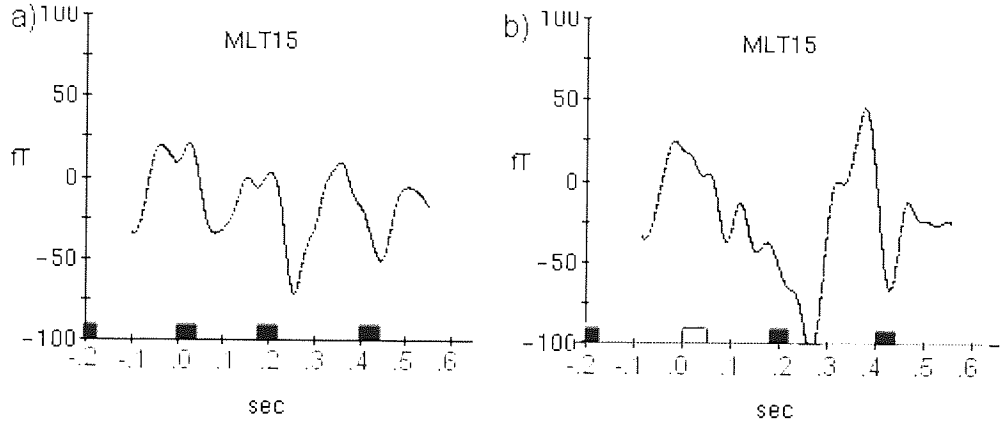

Figure 7-3 Single Channel Response to Standard and Deviant Stimulus Blocks: 175ms SOA
The response to a) standard and b) deviant stimulus blocks in the 175ms SOA condition for a representative control participant, in the channel showing the largest response to deviant stimulus blocks. Tone presentation is indicated by a filled black square; tone omission is indicated by an unfilled black square.

For each averaged and filtered data set created, the Global Field Power (GFP) response was plotted, taking the signals from all 151 channels into account. The peak amplitude of the deviant averaged response within the latency range 100ms to 140ms after target onset was noted from the resulting plots, as well as the amplitude of the standard averaged response at the same latency.

7.2.5 Source Modelling

With such fast stimulus presentation rates, stimulus onset responses (N1m's) were small and there was a large degree of temporal smearing. Physiological responses to stimulus omissions (MMNs) were also weak with large amounts of temporal overlap. Consequently, the creation of subtraction averages was deemed inappropriate (in line with Yabe et al., 1997). Furthermore, due to the weak

signals, dipolar source models could not be reliably fitted in the majority of datasets (11 of the 12 participants' datasets). The use of a source estimation models is critical in the analysis of MEG data in order to account for signal to noise variability and source depth (see section 4.2.5). The failure to generate reliable source estimates in the present study limits the possible statistical comparisons; absolute values for amplitude cannot be compared across datasets, or indeed participants. However, as responses to standard and deviant events are recorded within a single dataset in the MMNm paradigm, their relative signal strength can be compared.

In the single participant where reliable dipoles could be fitted to the MMNm response (with Monte Carlo Volumes of less than $3cm^{3)}$, illustration of the dipoles, superimposed on the participant's MRI, serves to clarify that the response was generated from left and right auditory cortices (Figure 7-4).

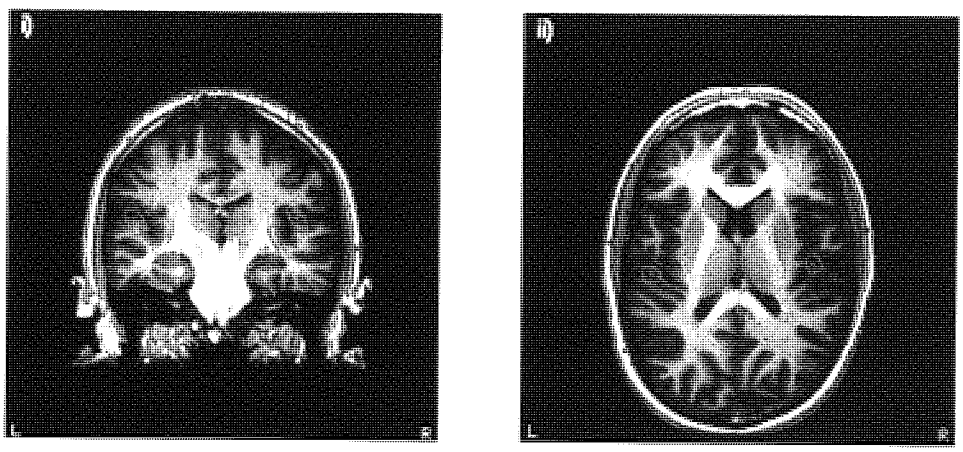

Figure 7-4 MMNm Dipoles Superimposed on MRI Slices

The dipoles modelled to explain the MMNm field response in the 100ms SOA condition, superimposed onto a coronal (i) and axial (ii) MRI slice in a control participant. Small dots indicate dipole location while spheres represent the 95% Confidence Volume calculated from Monte Carlo analysis.

7.2.6 Criterion for Assessing the Presence of an MMNm Response

As noted in chapter 4, GLM analyses do not directly assess the presence or absence of an MMN response. Rather, they consider whether data elicited in

response to standard and deviant stimuli are significantly different (a prerequisite for the presence of the MMNm in the deviant response). Additional criteria were required to determine the presence of an MMNm response; GFP plots for each of the participants were examined in order to identify peaks within the 100ms to 140ms post trigger latency range. In addition, field maps generated at the peak of the deviant response, within the 100-140ms post omission onset latency, were inspected to determine whether patterns of activation resembled those of a mismatch response.

7.2.7 Statistical Analyses

For each participant, amplitude values at the peak of the GFP response to deviant blocks (between 100-140ms) were recorded along with the GFP amplitude to standard blocks at the same latency. The difference between these amplitude values (MMN amplitude) was taken as the dependant variable.

The study was originally designed as a 2x(2) factorial experiment, both participant groups being assessed in the two frequency deviant conditions. The results of retrospective power analyses (Appendix 1, Table A-4) reveal that to obtain 80% power in the group by SOA interaction, 10 participants would be required. Due to the small participant numbers, in addition to unequal variance between participant groups in many measures, non-parametric statistical tests were used.

7.3 Results

7.3.1 GLM Analyses

Chi-square values obtained from GLM analyses are given for each participant in Table 7-1. There was a significant difference in the response to standard and deviant blocks in all control participants in the 100ms SOA condition and for one of the dyslexic participants. On the other hand, analyses comparing standard and deviant block responses in the 175ms SOA were significant for four of the control participants and four of the dyslexic participants.

Table 7-1 Chi-square Values Obtained from GLM Analyses
A table of chi-square values obtained in the two SOA conditions for each of the participants. Values were computed for 20 degrees of freedom.

Participant	100ms SOA	175ms SOA
C1	45.63*	24.53
C2	56.55*	86.44*
C4	57.87*	29.32
C5	120.89*	73.14*
C6	58.86*	60.87*
C7	59.18*	77.94*
D1	48.37*	45.26*
D2	35.53	27.02
D3	35.26	57.28*
D4	24.00	27.73
D5	23.62	44.18*
D7	34.73	44.17*

Chi-square values, calculated with df=20. * $p<0.01$

7.3.2 100ms SOA, Control Participants

The GFP plots to standard and deviant tone blocks in the 100ms SOA condition are shown for each control participant in Figure 7-5.

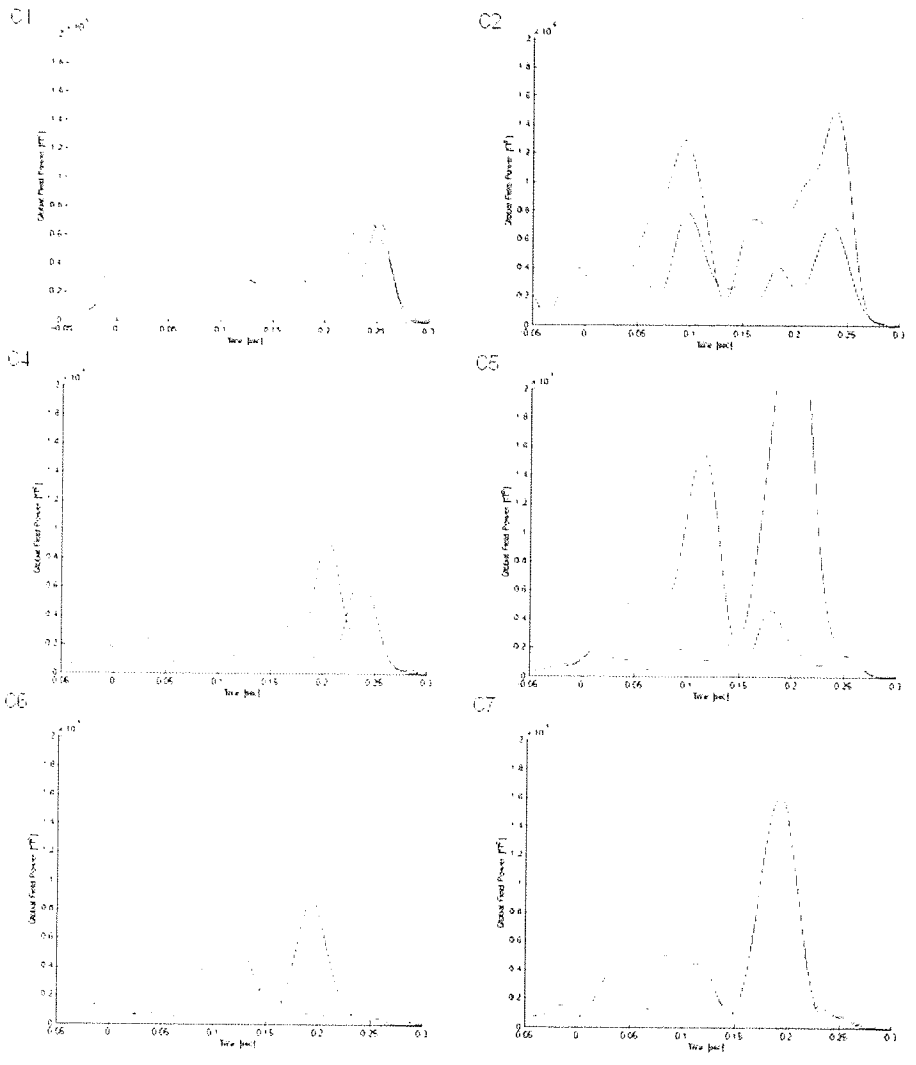

Figure 7-5 100ms SOA Condition, Control Group: GFP Responses to Standard and Deviant Stimulus Blocks
GFP waveforms to standard (red) and deviant (black) stimulus blocks are shown in the 100ms SOA condition for all control participants.

As seen from Table 7-1, GLM analyses revealed significant differences between these responses for each control participant. Traces to standard trials can be considered as baseline values as they contain all components found in deviant traces other than the omissions. In the majority of the plots a large deflection in the deviant trace is seen at a peak latency of around 200ms. This is likely to be the response evoked by stimuli occurring immediately after the omission (onset at 100ms). Considering the response to stimulus omission, the time interval extending 100-140ms after omission onset is the period of interest (Yabe et al., 1997). Within this latency range, the responses to deviant blocks are clearly

higher than those to standard blocks, in C2, C4, C5, C6 and C7. For C1 the difference is less obvious.

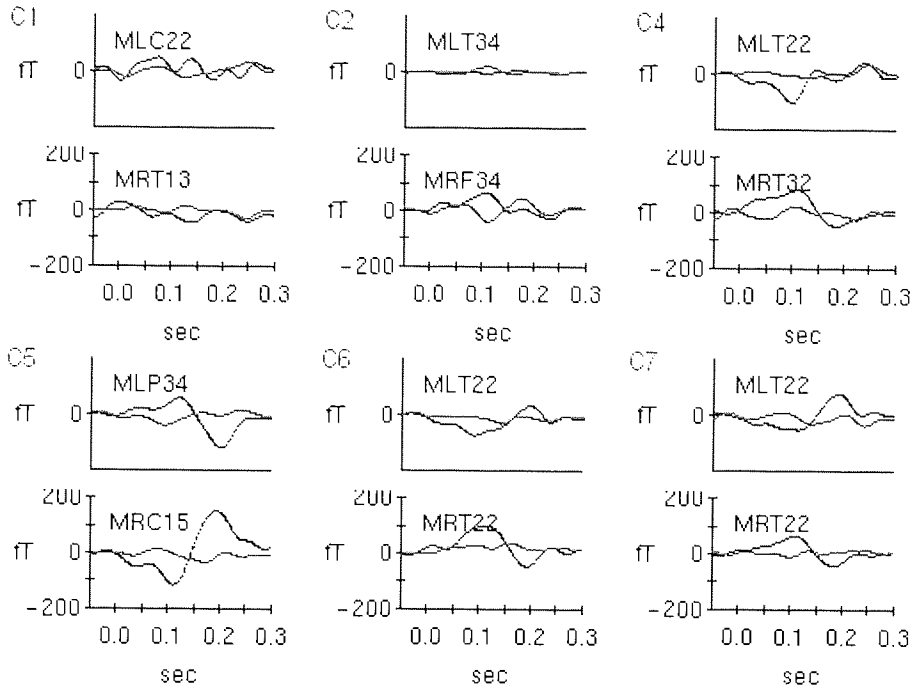

Figure 7-6 100ms SOA Condition, Control Group: Single Channel Responses to Standard and Deviant Stimulus Blocks
Waveforms to standard (red traces) and deviant (black traces) stimulus blocks in the 100ms SOA condition for all control participants. Responses are shown in the channels with the largest response to deviants over each hemisphere (top traces correspond to left hemisphere channels, bottom traces correspond to right hemisphere channels).

Differences between standard and deviant responses are seen more clearly in the traces of single channels (Figure 7-6). In each case, a deflection in the deviant response waveforms can be seen between 100-140ms post omission onset. As this deflection commences before the onset of the next tone in the sequence (100ms onset), it can be identified as a mismatch response to the tone omission.

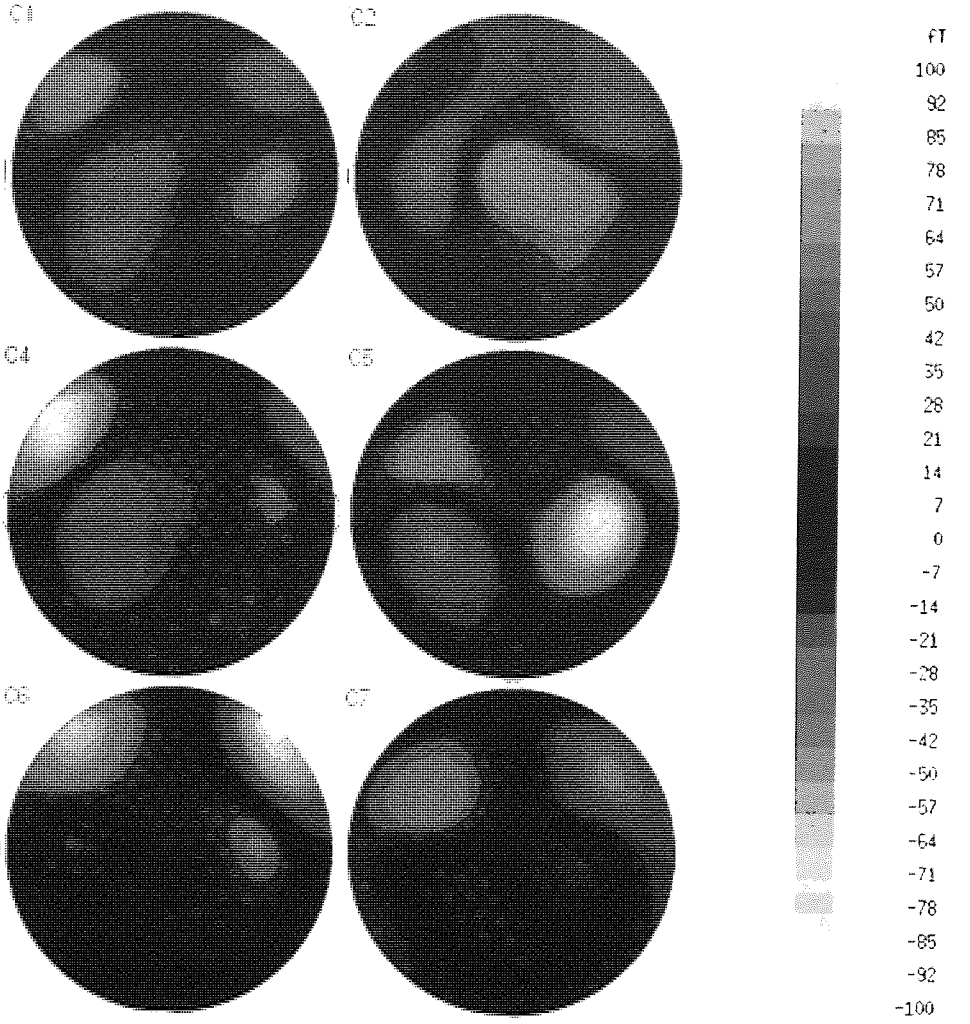

Figure 7-7 100ms SOA Condition, Control Group: Field Map at the Peak of the Deviant Response
Field maps generated at the peak of the deviant response between 100-140ms post omission onset in the 100ms SOA condition for all control participants.

Figure 7-7 shows the field maps generated at the peak of the deviant response for each of these participants. Activation patterns reveal bilateral, dipolar activity over the temporal lobes, suggesting a generator source in auditory cortex.

7.3.3 100ms SOA, Dyslexic Participants

The GFP plots to standard and deviant tone blocks in the 100ms SOA condition are shown for each dyslexic participant in Figure 7-8. As seen from Table 7-1, GLM analyses revealed significant differences between these responses for only one dyslexic participant (D1). In four of the plots (D1, D2, D3, and D7) a clear deflection in the deviant trace is seen at a peak latency of around 200ms. Again, this is likely to be the response evoked by stimuli occurring immediately after the

omission (onset at 100ms). Considering the 100-140ms latency range, the response to deviant blocks is clearly higher than that to standard blocks in D1, corresponding with the significant GLM result. A small peak in this latency range is also evident for D5.

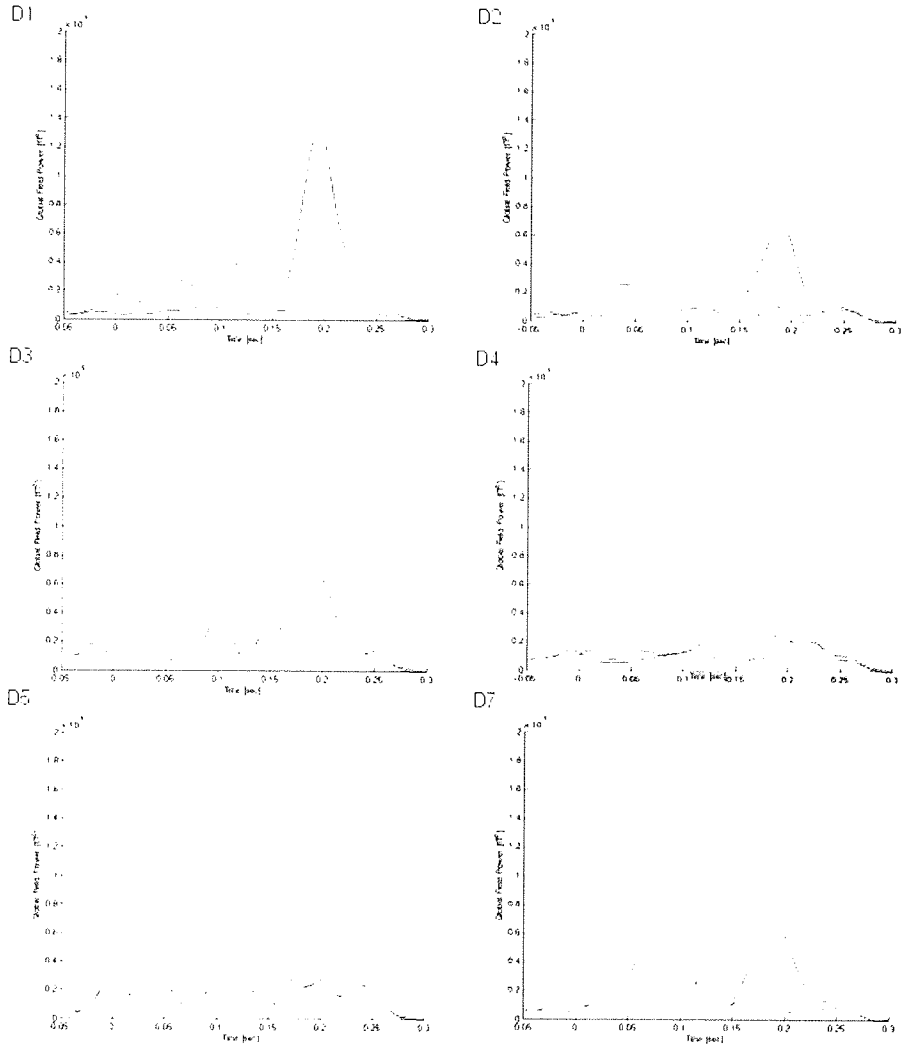

Figure 7-8 100ms SOA Condition, Dyslexic Group: GFP Responses to Standard and Deviant Stimulus Blocks
GFP waveforms to standard (red) and deviant (black) stimulus blocks are shown in the 100ms SOA condition for all dyslexic participants.

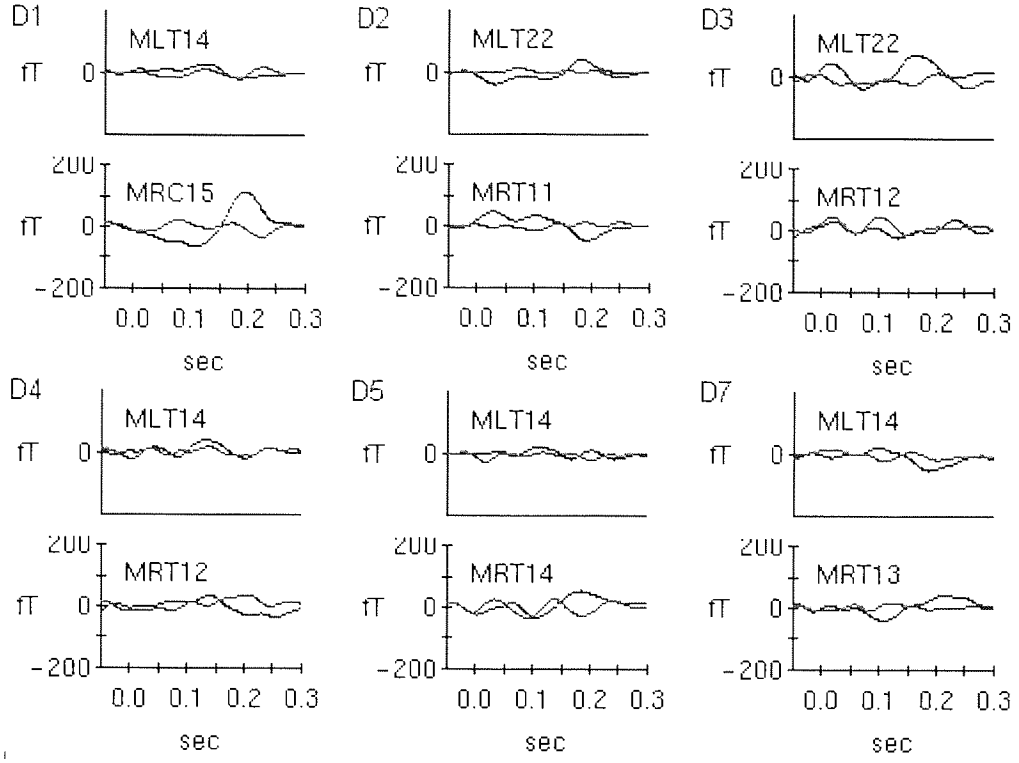

Figure 7-9 100ms SOA Condition, Dyslexic Group: Single Channel Responses to Standard and Deviant Stimulus Blocks
Waveforms to standard (red traces) and deviant (black traces) stimulus blocks in the 100ms SOA condition for all dyslexic participants. Responses are shown in the channels with the largest response to deviants over each hemisphere (top traces correspond to left hemisphere channels, bottom traces correspond to right hemisphere channels).

Differences between standard and deviant responses were also inspected in the traces of single channels (Figure 7-9). A convincing deflection between 100-140ms post omission onset is evident in the deviant response of D1 and D7. The presence of a deflection in the case of D1, though not D7, is in agreement with the results of the GLM analysis. As this deflection commences before the onset of the next tone in the sequence (100ms onset), it can be identified as a mismatch response to the tone omission.

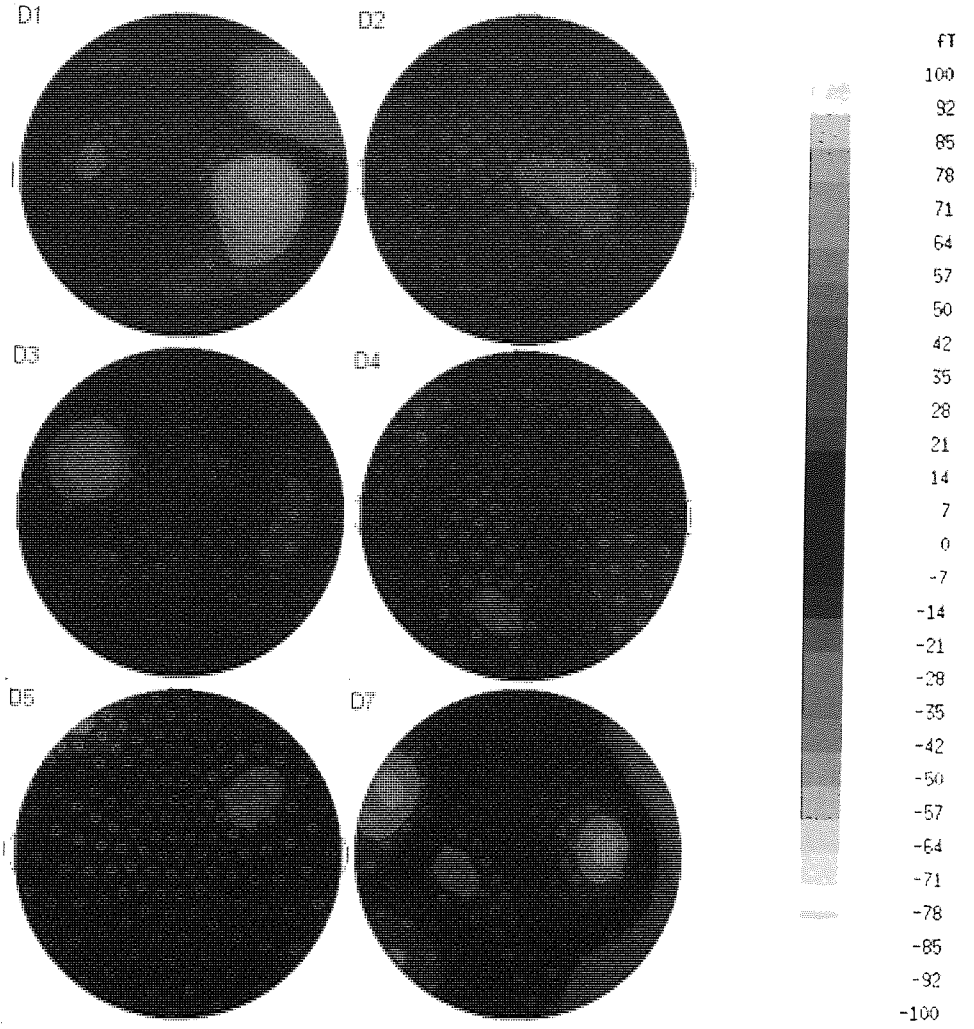

Figure 7-10 100ms SOA Condition, Dyslexic Group: Field Map at the Peak of the Deviant Response
Field maps generated at the peak of the deviant response between 100-140ms post omission onset in the 100ms SOA condition for all dyslexic participants.

The field pattern of activation generated at the peak of the deviant response in D1 reveals bilateral, dipolar activity over the temporal lobes, suggesting a generator source in auditory cortex (Figure 7-10).

7.3.4 175ms SOA, Control Participants

The GFP plots to standard and deviant tone blocks in the 175ms SOA condition are shown for each control participant in Figure 7-11. As seen from Table 7-1, GLM analyses revealed significant differences between these responses for C2, C5, C6 and C7. In all plots a large deflection in the deviant trace is seen at a peak latency of around 260ms. This is likely to be the response evoked by stimuli occurring immediately after the omission (onset at 175ms). In the case of C5 a deflection can be seen in the GFP trace to deviant trials within the 100ms to

140ms latency range; thus, this participant appears to demonstrate a mismatch response to stimulus omission at this longer SOA. For C2, C6 and C7 there are no clear peaks in deviant response waveforms, suggesting that no mismatch response is present.

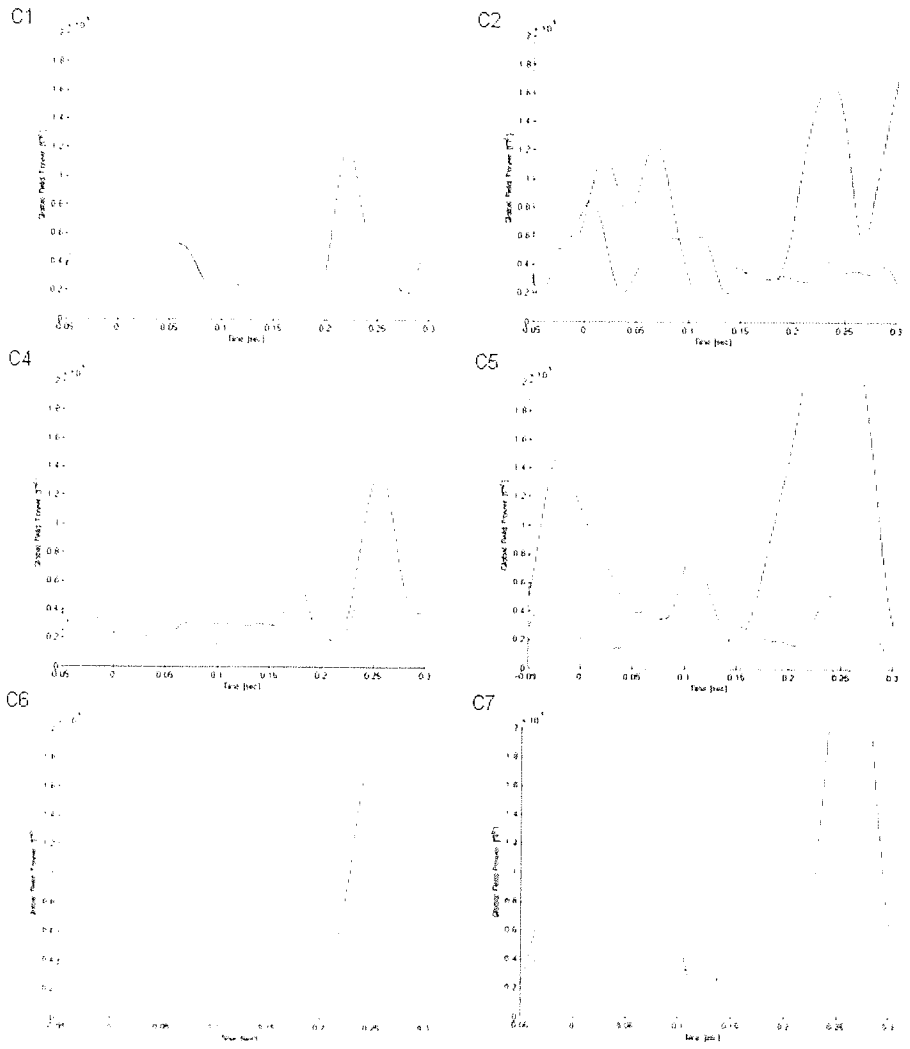

Figure 7-11 175ms SOA Condition, Control Group: GFP Responses to Standard and Deviant Stimulus Blocks
GFP waveforms to standard (red) and deviant (black) stimulus blocks are shown in the 175ms SOA condition for all control participants.

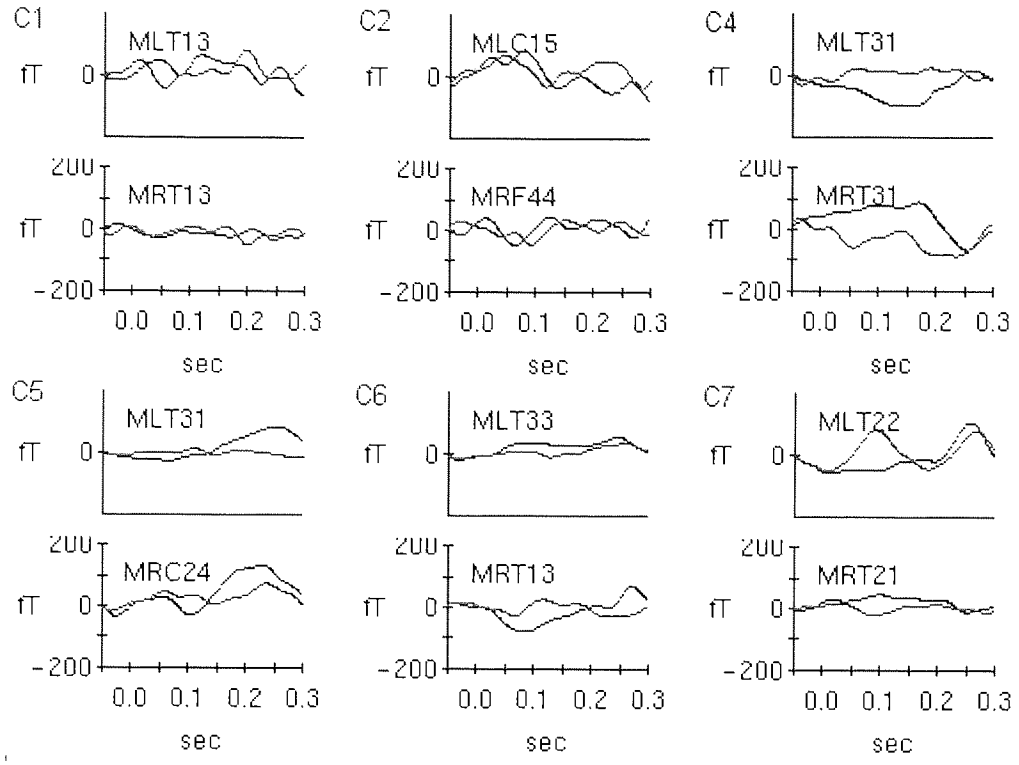

Figure 7-12 175ms SOA Condition, Control Group: Single Channel Responses to Standard and Deviant Stimulus Blocks
Waveforms to standard (red traces) and deviant (black traces) stimulus blocks in the 175ms SOA condition for all control participants. Responses are shown in the channels with the largest response to deviants over each hemisphere (top traces correspond to left hemisphere channels, bottom traces correspond to right hemisphere channels).

Differences between standard and deviant responses are seen more clearly in the traces of single channels (Figure 7-12). In the case of C5, a small deflection in the deviant response waveforms can be seen between 100-140ms post omission onset. However, no clear deflections can be identified in the other participants' data.

Figure 7-13 shows the field maps generated at the peak of the deviant response for each of these participants. None of the field maps demonstrate clear bilateral, dipolar activity over the temporal lobes. This is true in the case of C5 also, and as such, it seems unlikely that the deflection found in this participant's deviant response represents a genuine mismatch response.

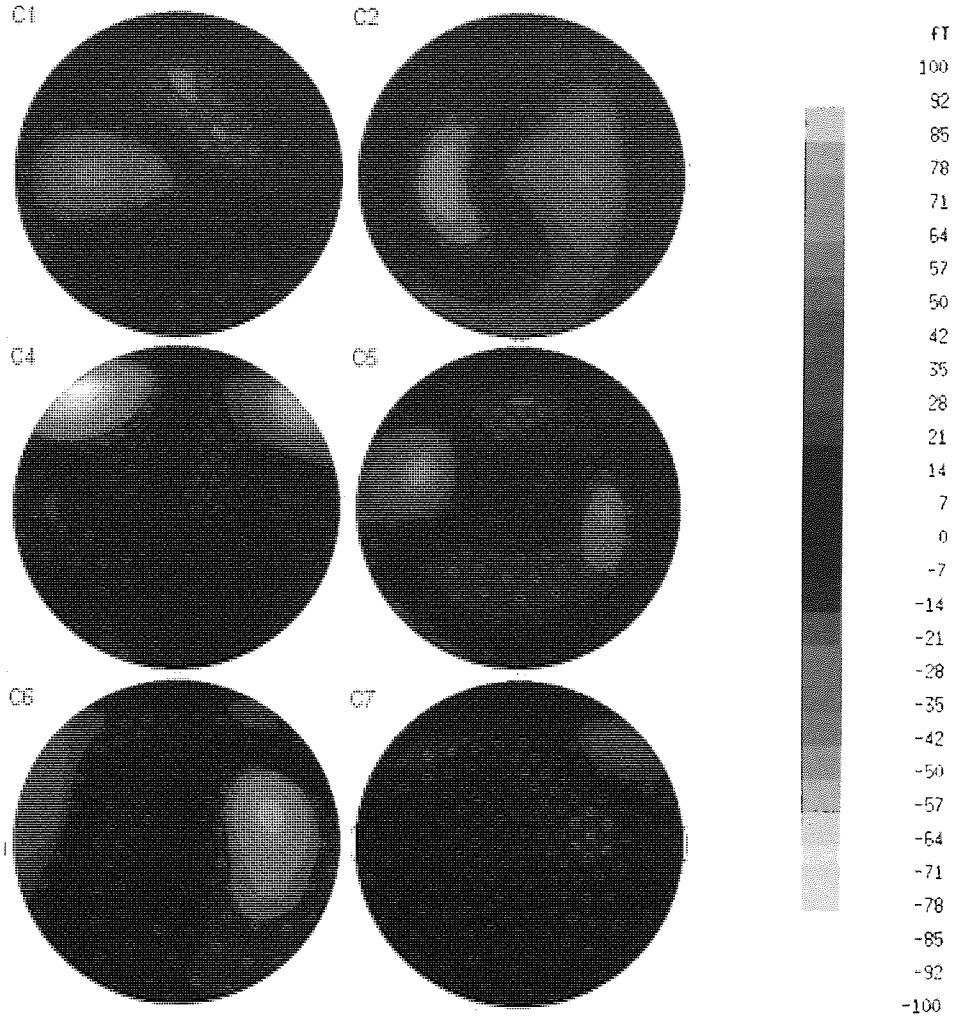

Figure 7-13 175ms SOA Condition, Control Group: Field Map at the Peak of the Deviant Response
Field maps generated at the peak of the deviant response between 100-140ms post omission onset in the 175ms SOA condition for all control participants.

7.3.5 175ms SOA, Dyslexic Participants

The GFP plots to standard and deviant tone blocks in the 175ms SOA condition are shown for each dyslexic participant in Figure 7-14. As seen from Table 7-1, GLM analyses revealed significant differences between these responses for D1, D3, D5 and D7. In all plots a deflection in the deviant trace is seen at a peak latency of around 260ms. Again, this is likely to be the response evoked by stimuli occurring immediately after the omission (onset at 175ms). None of the GFP plots reveal a clear deflection in the deviant response within the 100-140ms latency range.

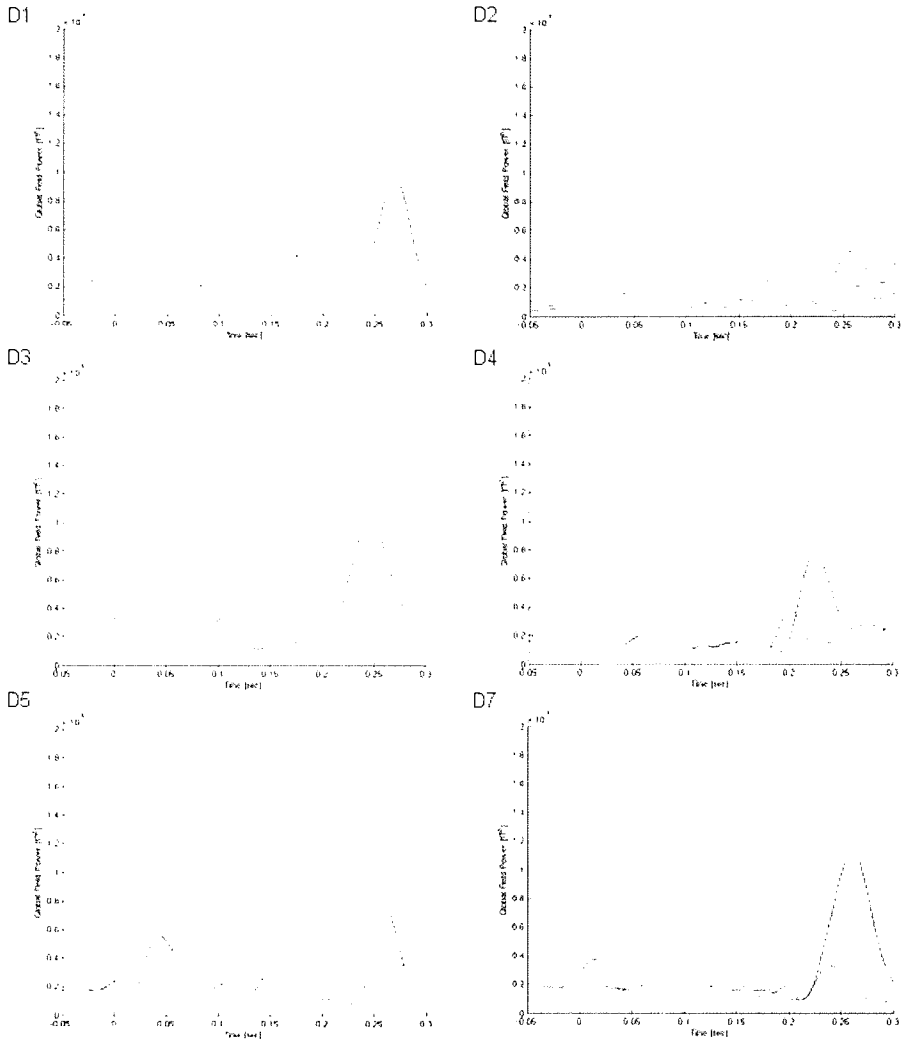

Figure 7-14 175ms SOA Condition, Dyslexic Group: GFP Responses to Standard and Deviant Stimulus Blocks

GFP waveforms to standard (red) and deviant (black) stimulus blocks are shown in the 175ms SOA condition for all dyslexic participants.

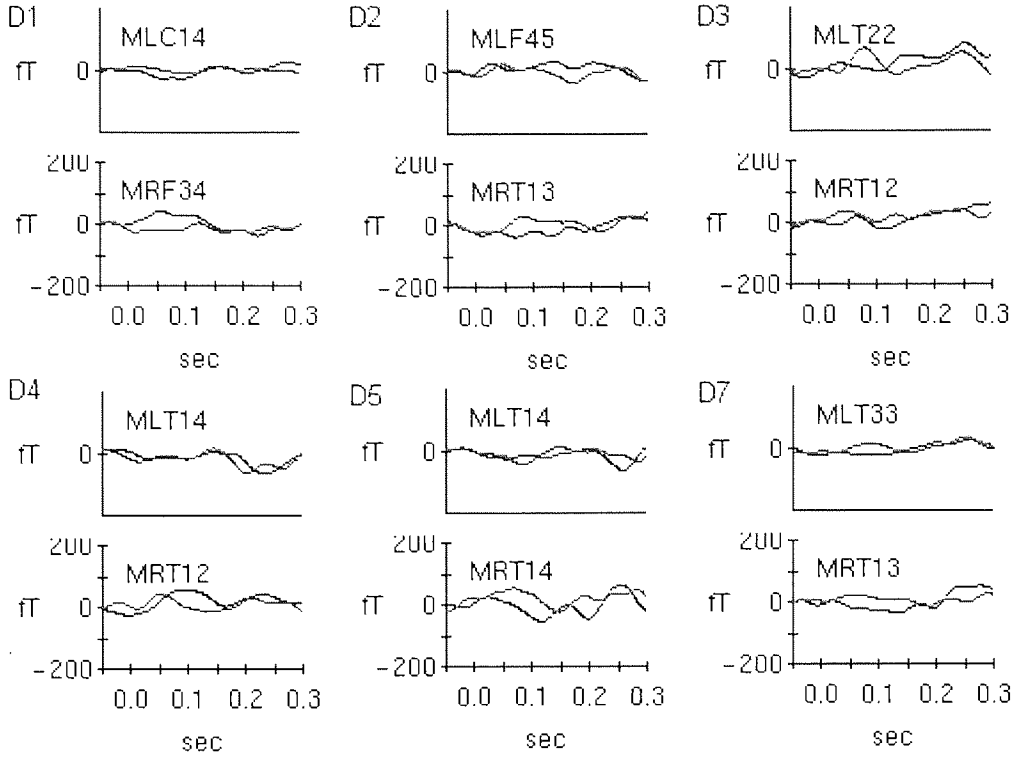

Figure 7-15 175ms SOA Condition, Dyslexic Group: Single Channel Responses to Standard and Deviant Stimulus Blocks
Waveforms to standard (red traces) and deviant (black traces) stimulus blocks in the 175ms SOA condition for all dyslexic participants. Responses are shown in the channels with the largest response to deviants over each hemisphere (top traces correspond to left hemisphere channels, bottom traces correspond to right hemisphere channels).

Differences between standard and deviant responses were also inspected in the traces of single channels (Figure 7-15). None of the plots reveal a convincing deflection between 100-140ms post omission onset, in agreement with the inspection of the GFP traces.

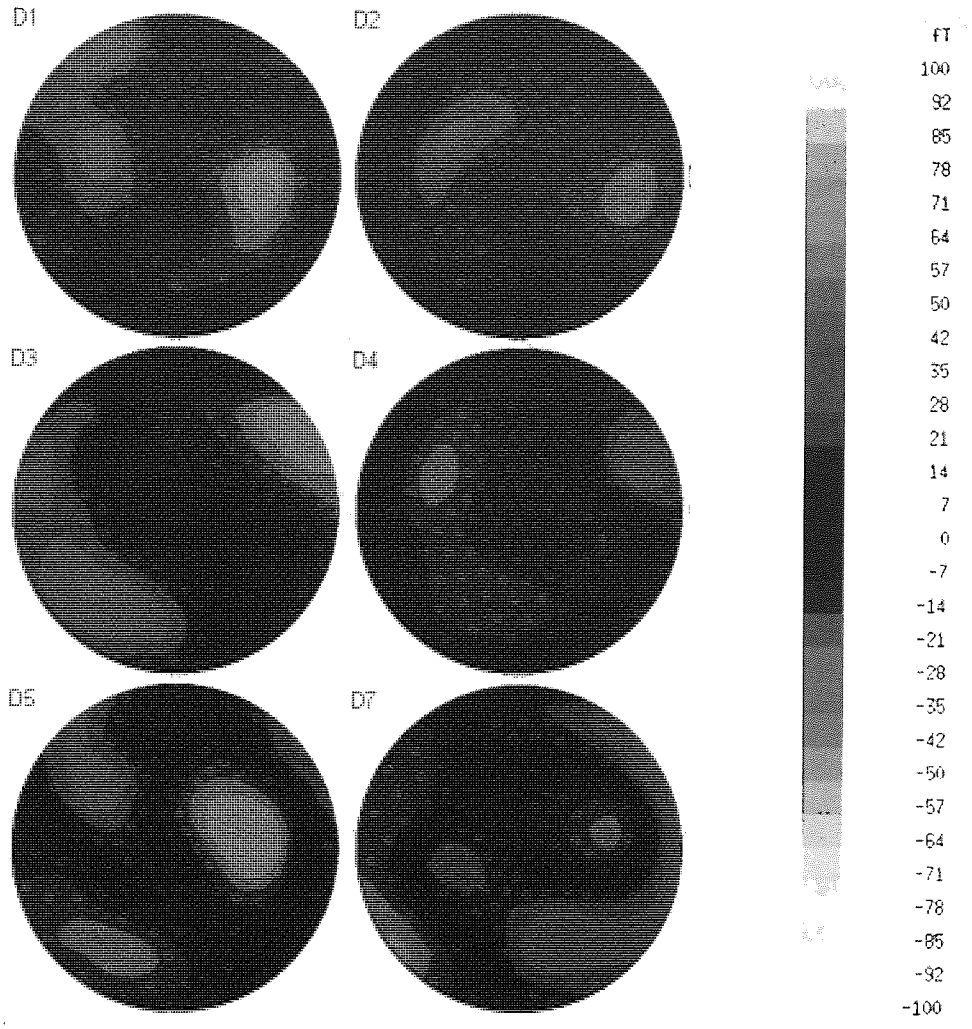

Figure 7-16 175ms SOA Condition, Dyslexic Group: Field Map at the Peak of the Deviant Response
Field maps generated at the peak of the deviant response between 100-140ms post omission onset in the 175ms SOA condition for all dyslexic participants.

Figure 7-16 shows the field maps generated at the peak of the deviant response for each of the dyslexic participants. None of the field maps demonstrate clear bilateral, dipolar activity over the temporal lobes. As such, it is concluded that deviant stimuli do not elicit a mismatch response in any of the dyslexic participants in this SOA condition.

7.3.6 Group Analyses

As noted in section 7.2.7, the sample size limited the statistical analyses available; as an alternative to the originally planned 2x(2) factorial design, MMNm amplitude was compared between the participant groups in the two SOA

conditions using a Mann-Whitney test. In the 100ms SOA condition the MMN amplitude was significantly larger in the control group (U = 4.00, $p=0.025_{(2\text{-tailed test})}$). In contrast, with a 175ms SOA the MMN amplitude did not significantly differ between the two groups (U = 12.00, p=0.337). The distinction across the two SOA conditions is supported by the results of retrospective power analyses, which report power of 63% in the 100ms SOA condition but power of only 20% in the 175ms condition (Appendix 1, Table A-5). Finding a significant group difference in the 100ms SOA condition supports the qualitative evidence provided above; while all control participants appear to demonstrate an MMNm to tone omission in this condition, there is only evidence of an MMNm in the data of one of the dyslexic participants. Furthermore, the failure to find a group difference in 175ms SOA condition is in agreement with qualitative evidence that an MMNm was not elicited in response to tone omissions in either control or dyslexic participants.

Individual GFP amplitudes are plotted (Figure 7-17). While GFP values in response to deviants were exceptionally large in C5 and C2, the group as a whole do seem to have larger responses to deviant stimulus blocks as opposed to standard stimulus blocks. In contrast, examining the dyslexic participants GFP amplitude values to standard and deviant stimulus blocks reveals much more overlap. In the 175ms SOA condition there is very little difference in GFP amplitude values to standard and deviant stimulus blocks in either participant group. The exception is C5, where the amplitude difference between standard and deviant responses is notably large. Indeed the presence of a MMNm at 175ms SOA in this participant was suggested when considering the qualitative data presented above.

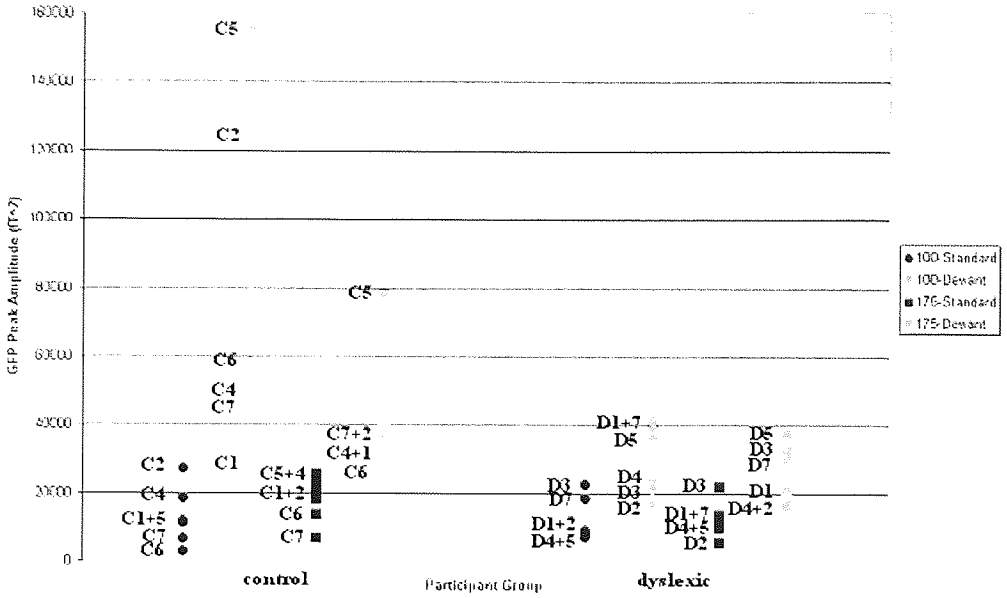

Figure 7-17 GFP Peak Amplitude Values: Individual Data
Graph illustrating the GFP peak amplitudes recorded at the peak of the deviant response in the 100-140ms post omission range, for the 12 participants. Black data points represent the standard tone response; grey data points the deviant tone response. Data point markers identify each of the individual participants.

7.4 Discussion

7.4.1 Summary of Results

The results of the present study confirm that an extended time window within which auditory percepts are integrated in Sensory Memory cannot account for deficits in auditory processing observed in the dyslexic population. Furthermore, the integration of percepts falling within the window of temporal integration is abnormal in this population. Mismatch responses to tone omissions occurring in a sequence of repeating auditory stimuli were elicited in all control participants when the SOA between tones was 100ms. However, under the same condition, significant MMNm responses were elicited in only one of the dyslexic participants.

7.4.2 Criterion for Assessing Deviant Responses

The presence or absence of MMNm was assessed on the basis of a number of criterion: i) a significant difference between responses to standard and deviant stimulus blocks 100-140ms after deviant onset, as assessed by GLM; ii) an observable peak in the GFP/single channel signal in response to stimulus omission within the 100-140ms time window, commencing before the onset of the next

tone in the sequence; iii) a field pattern of activation at the peak of this response revealing bilateral dipolar activation over the temporal lobes, consistent with an auditory cortex generator source. Considering these criteria, the results of all participants in the two SOA conditions are summarised in Table 7-2.

Table 7-2 Summary of Results

Participant	100ms SOA			175ms SOA		
	GLM	GFP/Single Channel Peak	Dipolar Field	GLM	GFP/Single Channel Peak	Dipolar Field
C1	+	+	+	-	-	-
C2	+	+	+	+	-	-
C4	+	+	+	-	-	-
C5	+	+	+	+	+	-
C6	+	+	+	+	-	-
C7	+	+	+	+	-	-
D1	+	+	+	+	-	-
D2	-	-	-	-	-	-
D3	-	-	-	+	-	-
D4	-	-	-	-	-	-
D5	-	-	+	+	-	-
D7	-	+	-	+	-	-

With an SOA of 100ms all control participants fulfilled each of the set criteria, suggesting that tone omissions elicited MMNm responses. In contrast, only one dyslexic participant (D1) met all criteria. As such it is assumed that an MMNm response was evoked by tone omissions only for this individual from the dyslexic group. While these data are qualitative in nature, the consistency in results across the findings supports their validity (e.g. no individual obtained two out of three).

Considering results in the 175ms SOA condition, four of the control (C2, C5, C6 and C7) and four of the dyslexic (D1, D3, D5 and D7) participants obtained significant results in the GLM analysis. However, field map and latency metrics suggested that this difference could not be attributed to the MMN in seven of these cases. The exception was found in the case of C5 where, alongside the significant GLM result, GFP plots indicated a deflection in response to deviant tones during the critical latency period. Examination of the field pattern evoked at the peak of this deflection revealed that this peak did not generate the typical

MMNm field pattern of activation and it was concluded that no MMNm was present in the data.

In the 100ms SOA condition all significant GLM analyses were supported with further evidence of the presence of an MMNm response (peak deflection in the GFP/Peak Channel and a field map distribution suggesting bilateral dipolar activation over temporal lobes). Considering the data from the 175ms SOA condition is more complicated. In the case of three control and four dyslexic participants a significant GLM result was found, without corresponding evidence of an MMN response in the GFP/Peak Channel traces or resulting field maps. In these cases it appears that the GLM analyses returned false positive results.

A possible explanation for such a high rate of false positive results lies in the nature of the comparison. In chapter 6, standard and deviant trials differed only in terms of the frequency of the stimuli presented. In the absence of an MMNm response there would have been very little difference in the signal generated in response to standard and deviant trials, resulting in a non-significant GLM result. In the present study the difference between standard and different trials is more substantial, namely the presence or absence of a stimulus. As such, one would predict that, even in the absence of an MMNm response, a difference in the signal generated in response to standard and deviant trials would be evident. Thus, a significant GLM result is more likely to be obtained in error in the present study.

While the potential for obtaining false positive results with GLM analyses should be acknowledged as a weakness of the procedure applied to such data, it continues to be useful at least for initial stages of data exploration. Where an MMNm response is present, the GLM program should be able to detect the difference in signals to standard and deviant stimuli. Thus, the programs potential for obtaining false negative results is low. By employing a range of criterion it is possible to determine the presence or absence of an MMNm response with some degree of accuracy.

7.4.3 Prolonged Time Window of Temporal Integration

Merzenich's (1996) hypothesis, that the time window within which successive auditory inputs are integrated in Sensory Memory is extended in dyslexia, cannot be supported by the results presented here. If this hypothesis were robust it would be predicted that the successive auditory inputs presented to the participants with SOAs just longer than the proposed TWI would be integrated in the dyslexic group. Occasional omissions of stimuli would in turn generate a new trace and be detected as deviants by the comparative change-detection mechanisms, resulting in the generation of an MMNm response. The absence of such responses in the data of both the control and dyslexic participants with SOAs of 175ms suggests that the auditory inputs were not being integrated within this time window for either participant group.

7.4.4 Abnormal Temporal Integration Processes

In the 100ms SOA condition, a definite MMNm to complete stimulus omission was identified for each of the control participants. In contrast, examining the results of the dyslexic group, a significant mismatch response to tone omission was evident in only one of the participants (D1). The failure of the majority of the dyslexic individuals to demonstrate an MMNm response to the tone omission with such a short SOA suggests an abnormality of temporal integration processes within this group.

Statistical analyses conducted on mean GFP peak amplitude values confirmed these findings. Examining data allowed for comparison between groups, independent of the accuracy of correctly identifying MMNm responses. The difference in peak amplitude in response to standard and deviant stimulus traces was significantly higher in the control than the dyslexic group in the 100ms SOA condition but not the 175ms SOA condition.

Similarly Loveless & Koivikko (2000) found that enhancement of the N1m response to the second tone within a pair, indexing persistence of successive inputs due to temporal integration in Sensory Memory, was attenuated in their dyslexic participants at shorter SOAs than in their control participants. A significant enhancement effect was recorded in the dyslexic group when the SOA

between tones in a pair was 150ms or shorter. However, this effect was significant in their control group with SOAs of up to 230ms. The presence of second response enhancement at shorter SOAs in the dyslexic group suggests that auditory temporal integration does occur at some level in this population. However, these processes are disrupted when the SOAs were longer.

An increased relative delay in the N1m response after a shorter silent interval was reported for control participants in Chapter 5. The failure to find a similar effect in the dyslexic group, in addition to the present results and those of (Loveless & Koivikko 2000), all suggest a disruption in normal integrative processes in the dyslexic population.

7.4.5 Impaired Attention Switching

Hari and Renvall (2001) propose a 'sluggish attentional shifting' account of dyslexia to explain observed deficits in processing rapid stimulus sequences. The authors argue that prolongations of attentional dwell time and delayed attentional capture slow down the dyslexics' speed of processing rapidly presented stimuli. This account is unable to explain the present data.

While Hari and Renvall place emphasis on the speed of attentional shifting, Loveless & Koivikko (2000) focus on the efficiency of attentional capture. In explaining their data, they suggest that sensitivity to auditory inputs is only weakly enhanced by prior stimulation in dyslexic participants. This can explain why enhancement effects were absent at longer SOAs in their study, and the absence of an increase in the relative N1m delay to stimuli occurring after a shorter silent gap in dyslexic participants, reported in Chapter 5. If initial tones did not capture as much attention in the dyslexic participants (possibly reflected in the overall N1m amplitude reduction in the dyslexic group reported in Chapter 5), their influence on following tones would be reduced. However, it is not clear how this account can explain the finding that, with the smallest SOAs (70, 150 and 230ms), the relative enhancement effect on the second tone was equivalent between experimental groups. The comparable group effect at the shorter SOAs implies that the initial tones did exert an influence on the following tones, but that the span of this interference window was reduced in the dyslexic group. Loveless

and Koivikko (2000) do not address this issue. Such a modification could account for the absence of an MMNm to stimulus omission in the dyslexic group at the short SOA reported in the present study. Indeed, shorter SOAs were not employed but may have resulted in the omission response in both groups. However, the reduced time window would need to estimated at less than 100ms in the present study and at around 230ms in the Loveless and Koivikko (2000) study.

The theory that surrounding stimuli interfere with the accurate perception of one another over longer time window in the dyslexic population was outlined at the outset of the present Chapter. Such a theory was supported by evidence from masking and stream segregation studies (section 7.1.2). Therefore, the explanation that the span of this window is shorter in dyslexic individuals seems highly improbable.

7.4.6 Perceptual Auditory Grouping Deficit

Considered simplistically, the present data suggest that the grouping of stimuli was impaired in the dyslexic group. Similarly, Sutter et al. (2000) concluded that their dyslexic sample demonstrated impairments in auditory grouping. Auditory perceptual grouping is critical in the analysis of auditory scenes (Bregman, 1990) and simplistic rules apply; sounds that are close in frequency tend to group together and segregate from spectrally distant sounds, and the effect is strongest at high presentation rates. The ability to perceptually group sounds is necessary in order to distinguish between simultaneously active sound sources and to direct attention to a particular sound source in the presence of competing sources.

Other data also identify auditory perceptual grouping problems within the dyslexic population; the results of Helenius et al. (1999b) demonstrated stream segregation abnormalities in the dyslexic group, and Dougherty and colleagues' (1998) findings suggested that their dyslexic group were less able to extract signals from noise. Likewise, the absent enhancement effect at longer SOAs reported in dyslexics by Loveless and Koivikko (2000) and the absent relative latency delay in the short SOA condition in dyslexics reported in Chapter 5 both indicate, at the simplest level, grouping abnormalities in the dyslexic population.

The presence of an MMNm response to complete stimulus omission relies on the perceptual grouping of successive auditory inputs. If no grouping occurs an omission in the repeating sequence is interpreted as complete stimulus cessation, if the successive stimuli are grouped the omission is interpreted as stimulus change and a mismatch response is evoked (section 7.1.4). Therefore, the present data reflect that even in the shorter SOA condition, successive stimuli were not being grouped by the dyslexic participants.

7.4.7 Conclusions

There is no evidence to suggest that disrupted auditory processing, demonstrated by dyslexic individuals, results from an extended time window of sensory integration. The duration of the temporal window of integration was estimated in the control and dyslexic groups with use of a tone omission MMN study. There was no evidence to suggest that this window was longer in dyslexics; with sequences of stimuli repeating at a rate just outside the proposed time window, rare tone omissions did not elicit an MMNm response in the present dyslexic sample. Moreover, while rare omissions embedded in sequences presented at a rate falling within the postulated window elicited an MMNm in the control participants, the MMNm response was only evidence in the data of one dyslexic individual (D1). The findings suggest that auditory grouping processes are disrupted in dyslexic individuals.

8 GENERAL DISCUSSION

8.1 Background to Studies

The principle aim of the present studies was to determine whether low-level auditory processing deficits were present in a compensated adult dyslexic population. Behavioural and physiological measurements were made to explore the responses of the dyslexic group to a variety of auditory paradigms and the resulting data were explored at both the group and the individual level. The nature of, and mechanisms behind, low-level auditory deficits were investigated.

The literature examining the role of low-level auditory processing in dyslexia is extensive (reviewed in Chapter 3). Tallal and colleagues (Tallal, 1980; Tallal, 1999; Tallal et al., 1993; Tallal & Piercy, 1973b) initially proposed that dyslexia could be characterised by impaired processing of brief and or rapidly presented stimuli. Evidence for such a theory has accumulated in the last three decades; at increased rates of stimulus presentation the behavioural and physiological responses of dyslexic individuals differ from those of controls.

However, when the original temporal ordering tasks used by Tallal and colleagues were simplified to explore the component processes involved, evidence emerged that the difficulties dyslexic individuals demonstrated were actually related to their inability to discriminate between the different tone frequencies. Further evidence then emerged to support the notion that the dyslexic population are impaired in their ability to discriminate between stimuli based on spectral information.

The studies presented in this thesis were designed to determine which stimulus features were more problematic for dyslexic individuals; presentation rates or spectral contrasts.

8.2 Summary of Findings

The results of the studies presented provide strong evidence of low-level auditory processing deficits in dyslexia. These deficits are measurable at the behavioural and the neurophysiological level and are sensory in nature. Their presence in a

compensated adult population suggests that they form a 'core' impairment, persistent even after the symptoms of dyslexia have largely disappeared.

The results of a frequency discrimination study are presented in Chapter 5. Participants were presented with tones in pairs and asked to judge whether they differed in frequency. In four different experimental conditions the duration of the interval between tones and the frequency separation between tones was varied. Behavioural measures assessed the control and dyslexic group's accuracy and speed of responding, and MEG data were collected to examine cortical responses, namely the N1m onset response, across the experimental manipulations. The dyslexic participants were typically slower at responding and their accuracy scores were lower, although these results were not statistically significant across the conditions (significant differences were seen across the large FS conditions only). N1m responses to the simple pure tone stimuli were consistently weaker in the dyslexic group. The group difference in N1m amplitude was not related to the frequency of the stimuli or the presentation rates. In control participants the N1m was delayed in response to stimuli occurring after 200ms but not 500ms intervals. The relative latency delay was not present in the data of the majority of dyslexic participants.

In a second study, the results of which are presented in Chapter 6, neurophysiological data were recorded in response to infrequent frequency deviants embedded in a sequence of repeating pure tones. If the degree of frequency deviation falls beyond a certain threshold, such stimuli evoke an MMNm response, even in the absence of directed attention. Dyslexic and control participants were instructed to ignore the auditory stimuli and the effect of varying the degree of the frequency deviance was measured. With 80Hz difference between standard and deviant stimuli, the mismatch responses of dyslexic participants were weaker and later that those of control participants. Furthermore, with 20Hz difference between the tone types, MMNm responses were only found in the MEG responses of four control participants and no dyslexic participants.

The final study again employed an MMN paradigm (Chapter 7). Occasional omissions were embedded in a long sequence of rapidly repeating pure-tone

stimuli. This paradigm is used to estimate the time window of temporal integration in the auditory system. As SOAs fall within the TWI, repeating stimuli are grouped and occasional omissions are interpreted as stimulus change. As SOAs fall outside the TWI, repeating stimuli remain isolated and occasional omissions are interpreted as sequence cessation. Only the former case evokes an MMN. SOAs of 100ms and 175ms were chosen to border the proposed time window of this integration process. In the 175ms SOA condition, stimulus omissions did not evoke MMNm responses in either participant group, suggesting that the temporal window of integration is not extended in the dyslexic population. In the 100ms SOA condition, stimulus omissions elicited MMNm responses in all control participants but only one dyslexic participant. This group difference suggests a disruption in the integration processes in the dyslexic group.

8.3 Theoretical Account

The principle aim of the tone pair experiment was to determine the relative effects of manipulating the frequency separation between tones and the stimulus presentation rates on the dyslexic group's performance in a frequency discrimination task. The data failed to replicate the finding of amplitude reductions to stimuli occurring after a short interval in the dyslexic group reported by Nagarajan et al. (1999). In fact there was no evidence that reducing the ISI between tones impaired the behavioural performance of the dyslexic group more than the performance of the control group. This result contradicts reports that dyslexic individuals find such tasks more difficult than controls at fast presentation rates.

In an extension to Nagarajan and colleagues' original study the contribution of the frequency discrimination component was considered. Neither behavioural nor physiological evidence suggested that the participant groups could be differentiated in their response to narrowing frequency separations. However, it was acknowledged that the tonal frequency separations used fell outside the reported thresholds for frequency discrimination in the dyslexic population. The choice of such large separations was a particular weakness of the study, which was originally designed to account for Nagarajan et al.'s (1999) data (section 5.2.2).

The results of the frequency deviant MMNm study do provide evidence of frequency discrimination deficits in the current dyslexic sample. The dyslexic participants' responses to infrequent tones that deviated in frequency by 80Hz were reduced and delayed relative to the equivalent responses in control participants. Furthermore, in the 20Hz deviant condition mismatch responses were not evident in the data of any of the dyslexic participants despite being recorded in the majority of controls. This result demonstrated graded abnormality in the dyslexic group's ability to discriminate between tones of differing frequencies, in line with reports of increased frequency discrimination thresholds. Analysis of the spectral content of stimuli occurs at a local level of processing in the auditory system. However, as noted in sections 3.3.5 and 3.3.6 the deficit cannot be explained by impaired phase locking in the dyslexic auditory system.

Considering again the data of the tone pair study, there was evidence that the manipulation of ISI did differentiate between participant groups (although not as reported by Nagarajan et al., 1999). In the control participants, N1m responses to tones presented after 200ms ISI were relatively more delayed than N1m responses to initial tones. The increased relative latency delays were not observed in the majority of the dyslexic participants and the group difference was significant. Similarly, Renvall and Hari (2002) and Loveless and Koivikko (2000) reported that the N1m enhancement found in control participants in response to sounds presented after short intervals were disrupted in their dyslexic samples. Both enhancement and delay of N1m responses in tone pair paradigms indicate temporal integration of stimuli (McEvoy et al., 1997).

The disruption of temporal integration processes was directly examined in the tone omission MMN study. An MMN response is only elicited in response to stimulus change, thus for an omission to elicit such a response successive stimuli must be integrated to form unitary percepts. By manipulating SOAs one can predict the time window of this grouping processes. MMNm responses were recorded to the infrequent stimulus omissions with SOAs of 100ms in all control but only one dyslexic participant. Again this provides evidence of abnormal sensory integration processes in the dyslexic group.

Renvall and Hari (2002) and Loveless and Koivikko (2000) suggested that the disruption of this integration process in the dyslexic population reflects impaired attentional capture by brief auditory stimuli. With short intervals between tones, responses to initial tones enhance sensitivity to second tones. If the auditory stimuli capture attention less effectively in the dyslexic population their influence on following stimuli would be reduced.

The significantly weaker N1m amplitudes recorded in dyslexic participants in the tone pair study, as well as reduced N1m responses to initial stimuli recorded by Renvall and Hari (2002), support such a theory. Näätänen's (1990) model of auditory attention (reviewed in section 3.4.3) postulates that the supratemporal N1 response (that recorded with MEG) reflects the processing of an attention triggering mechanism; incoming stimuli elicit an N1 response and if excitation reaches a given threshold the mechanism triggers an attention switch (possibly an orienting response). Thus the amplitude of the supratemporal N1 response indexes attentional capture. It is important to point out that this is a stimulus driven process; while the N1 is modulated by directed top-down attention, such low-level auditory processing can occur in the absence of overt attention.

Reduced attentional capture also plausibly explains the data presented in Chapter 6, which reported a graded abnormality in the dyslexic group's responses to frequency deviant stimuli. The component processes involved in the detection of an auditory mismatch were explored in section 6.4.5. Evidence of normal MMNm responses to deviations in other stimulus properties (e.g. duration) suggests that the comparative process itself must be functioning normally. As such, it was suggested that the deficits found in the dyslexic group must relate to inefficient encoding of the spectral properties of the stimuli. If, as suggested above, the simple tonal stimuli fail to capture attention as effectively in the dyslexic population (indexed by reduced N1m amplitudes), it would follow that the representation of inputs would be degraded, resulting in deficient mismatch detection at fine frequency separations.

However, if inefficient coding of spectral properties results from reduced attentional capture, it is unclear how other stimulus properties appear to be encoded normally in dyslexic listeners (e.g. normal responses to duration and intensity deviants). Weighing the evidence up it appears that while dyslexics do demonstrate impairments in the encoding of stimulus features, it is unlikely that such impairments result from reduced attentional capture.

Moreover, the proposal of reduced attentional capture in dyslexic individuals cannot fully account for the data of Loveless and Koivikko (2000). The authors reported that in the smallest SOA conditions (70, 150 and 230ms), the enhancement of the second tone was similar between control and dyslexic groups. This finding implies that initial tones did enhance sensitivity to second tones but that the temporal span of this enhancement was reduced in the dyslexic group.

Such a proposition does not sit comfortably with the data from masking studies. Forward and backward masking experiments demonstrate the disruptive influence of closely successive stimuli on the accurate perception of target stimuli. As the temporal separations between stimuli are reduced the masking effect is enhanced. Wright et al. (1997) have reported that masking effects are recorded in dyslexic individuals at greater temporal separations than in control participants. Such findings have been interpreted as evidence of 'sluggish' auditory processing in dyslexia, the window during which successive auditory inputs interfere with one another are extended in the population. Further evidence for this account is provided by the data of Hari and Kiesila (1996) and Helenius et al. (1999b). Exploiting an illusory sound movement paradigm and a stream segregation paradigm the investigators found that the disruptive influence of surrounding inputs is measured at slower presentation rates in dyslexic listeners. It appears contradictory to propose that; a) the window within which initial stimuli enhance sensitivity to second stimuli is reduced in dyslexia and b) the window within which successive stimuli interfere with the accurate perception of one another is extended in dyslexia.

Sutter and colleagues (2000) designed an elegant study to investigate auditory perceptual grouping processes in dyslexic individuals (outlined in section 7.1.2).

They found that capture effects exerted by surrounding stimuli were stronger in dyslexic individuals. The authors interpreted this as evidence of perceptual grouping impairments in dyslexia. This interpretation was extended to account for the findings of Helenius et al. (1999b) and Dougherty et al. (1998); evidence of abnormal perceptual grouping processes in dyslexic samples was common to all studies. Evidence of abnormalities in the temporal integration of stimuli, as reported by Loveless and Koivikko (2000), Renvall and Hari (2002) and in the data presented in Chapters 5 and 7 also fit within such a theoretical framework.

Returning to Helenius et al.'s (1999b) proposal that the temporal window of a buffer, in which surrounding sounds interfere with one another, was extended in dyslexia. Such an account predicts that the dyslexic population's performance would be abnormal in longer SOA conditions but equivalent in shorter SOA conditions. This simple effect was not evident in the data of Sutter et al. (2000); significant group differences were consistently detected at larger frequency separations but not consistently across the longer SOAs. Therefore, the interference effects were related to the temporal and spectral properties of the stimuli. Moreover, the result that group differences were evident at larger frequency separations but not smaller frequency separations suggested that deficits were not related to the difficulties dyslexics have with fine frequency discriminations. Rather, group differences at large degrees of frequency separation imply that the dyslexics' difficulties were related to the global processing of frequency in perceptual grouping.

This result is, therefore, distinct from the population's difficulties with local frequency resolution (seen in frequency discrimination impairments) and local temporal resolution (seen in increased masking effects) and suggests that both local and global auditory processing deficits are present in the dyslexic population.

In a conceptual framework developed to account for findings, Sutter et al. (2000) propose that the operation of a short-term buffer, involved in frequency discrimination, is impaired in the dyslexic population. This buffer stores tonal information and has optimal performance when input frequencies are close to the

buffer's frequency operating point (though still with minimal separation). The group further suggest that the operating point of the buffer is set by sensory expectation. The unexpected presentation of a tone that is separated from the operation point of the buffer by a large degree disrupts the predictive process and in turn interferes with storage and retrieval from the buffer. Sutter et al. suggest that delays in neural feedback loops could disrupt the functioning of this buffer in the dyslexic population. However, an account of the dyslexic population's difficulties with perceptual grouping may need to be more general. Hari and Kiesila's (1996) experiment, which demonstrated grouping deficits in dyslexic individuals, did not include a spectral component; stimuli were simply click trains. Likewise, experiments indicating disrupted integration processes, reported in the tone omission MMNm study here and Loveless and Koivikko's (2000) N1m enhancement study, employ stimuli with single spectral content.

In summary, the data presented here suggest the presence of local auditory processing deficits in dyslexia relating to the encoding of spectral information. However, they also suggest the presence of a global processing deficit in dyslexia relating to the appropriate grouping of successive auditory events with a high level role in auditory scene analysis. Importantly, the presence of both local and global processing deficits, in the same dyslexic sample, implies that they are not mutually exclusive and does not discount the data of researchers who have reported impairments in the dyslexic population relating to the fine spectral resolution or presentation rates of sounds.

8.4 Implications

The finding of non-linguistic auditory processing deficits in an adult dyslexic sample, which had largely compensated for their literacy difficulties, is significant. Frith (1999) argues that while the behavioural signs of dyslexia are likely to change over time as a result of compensation, the underlying deficit(s) is (are) likely to persist. The strong evidence for the presence of such deficits in the current sample, therefore, implicates them as 'core' biological deficits.

One important implication of identifying sensory deficits in dyslexia is their possible use as early indicators of potential dyslexic problems. A disruption in the

normal acquisition of literacy skills cannot normally be detected until a child begins to fail. However, the importance of early intervention is well documented (Hulme & Snowling, 1997; Nicolson, Fawcett, Moss, Nicolson, & Reason, 1999; Snowling, 1996; Witruk, 1993). Therefore, if early predictors of dyslexia could be identified (regardless of their causality) these would have a significant impact upon the outcomes for dyslexic children who could receive directed intervention before they fail. Studies examining early auditory indicators are currently underway and their results will be very informative (Leppanen et al., 1997; Leppanen et al., 1999; Leppanen et al., 2002; Lyytinen et al., 2001; Molfese, 2000; Pihko et al., 1999).

While the causal link between low-level auditory processing deficits and the behavioural manifestations of dyslexia has not been investigated in the present studies, the presence of such deficits implicates them in dyslexia. Indeed the proposed deficits could plausibly be reconciled with the behavioural characteristics presenting in dyslexia, by way of deficient speech perception at critical stages of development. For example, the impaired ability to discriminate between spectrally close stimuli would impact upon a listeners ability to differentiate between spectral contrasts in the speech stream, while abnormalities in auditory grouping and stream segregation could inadvertently lead to different elements of the auditory environment being assigning to the wrong auditory object. Dougherty et al.'s (1998) study directly measured the dyslexic population's difficulties in extracting target signals in the auditory environment from noise. The group propose that such a deficit could hinder the extraction of speech sounds in noisy environments, leading to poor phonological representations in dyslexic listeners. The use of an adult population in the present studies makes it difficult to evaluate such causal models. Long scale studies could assess whether the presence of these deficits in infants can predict the onset of dyslexia.

8.5 Individual Differences

Dyslexia is an extremely heterogeneous condition and the behavioural characteristics of dyslexic individuals vary widely. Hill et al. (1999) have criticised many studies reporting low-level auditory deficits (or indeed any

sensory deficits), suggesting that group differences can usually be accounted for by the data of only a few outlying dyslexic individuals. For this reason, an attempt has been made throughout the studies to present individual data and consider individual participant profiles.

The use of non-parametric statistical tests reduces the influence of exceptional or outlying data so the significant group differences reported must reflect genuine evidence that the means of the two samples are indeed different. However, variability seen in the data of the dyslexic group raises the question of degrees of impairment; it is interesting to examine whether the same dyslexic individuals demonstrate similar impairment across all the auditory processing measures and how their individual psychometric profiles might relate to physiological data.

While participant D1 demonstrated no impairment on behavioural measures in the tone pair discrimination task, his/her physiological profile indicated abnormal responses to stimuli (N1m responses were particularly delayed and weak and there was no evidence of temporal integration (as observed in the control data)). The participant's MMNm responses were delayed and attenuated in response to the 80Hz frequency deviant and absent in response to the 20Hz deviant. However, in the tone omission MMNm study D1 was the only dyslexic participant to demonstrate an omission mismatch response. Participant D1's psychometric profile indicated persisting problems with phonological and working memory tasks and some subtle deficits with literacy skills when measured under timed conditions.

Participant D2 had some problems with the tone pair discrimination task when the frequency separation was reduced. While no latency delay was measured in the N1m response to initial tones, the amplitude of this response was very weak. Responses to second tones demonstrated some evidence of temporal integration but only in the larger frequency separation condition. Considering the participants MMNm responses, graded abnormality in mismatch responses to frequency deviants was evident in addition to an absent response to the omission deviant. Psychometrically this participant was among the poorest performing individuals in the dyslexic group with some persisting problems with literacy skills in

addition to poor phonological and working memory skills and some weakness in processing speed.

The behavioural and physiological data of participant D3 was not especially disparate to that of control participants in the tone pair study. N1m's recorded in response to initial stimuli were normal with reduced amplitudes evident in only the smaller frequency separation condition. There was also some evidence of temporal integration in response to second stimuli occurring after short intervals although not across both frequency separation conditions. Likewise, while delayed and reduced MMNm responses to frequency deviants were recorded, these abnormalities were subtle when considered against the rest of the dyslexic group's data. Nevertheless, no MMNm responses were recorded in response to complete tone omissions. The participant performed well on some of the psychometric tasks considered to be indicative of dyslexia (e.g. working memory tasks) although some persisting problems were evident during tests of phonological processing and processing speed in addition to reading skills when tested under timed conditions.

Participant D4's behavioural responses in the tone pair task were slow and he/she achieved low accuracy scores in the small frequency separation conditions. N1m responses were delayed and weak and there was no evidence of temporal integration. Mismatch responses to the large frequency deviant were also delayed and attenuated and MMNm's to small frequency deviants and complete tone omissions were absent. D4 achieved average scores in tests of reading and spelling though under timed conditions difficulties surfaced. In addition the participant demonstrated some phonological weakness and processing speed scores were down.

Participant D5 achieved normal behavioural scores on the tone pair frequency discrimination task though the N1m response was delayed and weak across conditions. However, he/she was the only dyslexic participant with consistent evidence of temporal integration in the N1m response to second stimuli occurring after 200ms, with slight delays evident in both frequency separation conditions. In the frequency deviant MMNm study this participant's data reflected a graded

abnormality in the MMNm response. No MMNm was recorded to infrequent stimulus omissions. D5's psychometric profile indicated few persisting problems, relative to the data of the dyslexic group as a whole. Some weakness in phonological skills and indications of slowed speed of processing were evident.

Participant D6 was consistently the poorest in behavioural measures in the tone pair task, his/her accuracy deteriorated markedly as the frequency separation between tones was reduced. The N1m latency to initial tones was reduced in amplitude, although not consistently across the four conditions. This participant's data demonstrated no evidence of relatively later N1m responses to tones presented with a 200ms ISI, thought to suggest temporal integration in the control group. Unfortunately, D6 did not participate in either of the MMNm studies. Psychometric data for D6 reveals that this individual continued to have persisting difficulties with literacy skills as well as associated deficits in phonological awareness, working memory and processing speed.

Data for D7 was not available in the tone pair study. In the frequency deviant MMNm study the participant did not elicit a response in the small frequency deviant condition and his/her MMNm to large frequency deviants was weak. No MMNm response was evident in response to complete stimulus omissions. Psychometrically, D7 achieved well in terms of accuracy on tests of reading and spelling, although when the same skills were assessed under timed conditions some problems were observed. Phonological and working memory skills were weak.

The first important observation is that physiological abnormalities in response to simple auditory stimuli were evident in the data of each of the dyslexic participants. Thus, it would seem that in the current sample, at least, auditory processing deficits characterised all of the dyslexic individuals to some extent.

Looking at the auditory processing impairments measured in dyslexic individuals across the three studies there is some evidence of consistency. Participants D2 and D4's physiological responses in each study were notably disrupted and their behavioural performance on the tone pair discrimination task was markedly poor

relative to the group. D3's physiological responses across studies demonstrated little abnormality and performance on the tone pair task was comparable to that of control participants. On the other hand, D5 did well on behavioural measures despite consistently poor physiological responses, while D6 demonstrated relatively normal physiological responses in the tone pair task but poor behavioural ability.

Further inconsistencies in results across the paradigms are evident. The relative latency delays observed in control participants to tones occurring after short silent intervals were interpreted as potential evidence for temporal integration of the tone pairs. The data of D1, the only dyslexic participant to obtain an MMNm to complete stimulus omission (also taken as a marker for temporal integration), contained no evidence of temporal integration in the tone pair task. Meanwhile, participant D5's responses to second tones in the 200ms ISI condition of the tone pair task were slightly delayed, as were D3 and D2's (although not consistently). It is difficult to reconcile these results; a disruption in integration processes would be predicted to remain consistent in the two paradigms.

Looking at the relationship between recorded data and the individual participants' psychometric profiles there are some encouraging trends. The behavioural and physiological data of D2 were poor across the range of studies and the results of psychometric testing indicated that this participant continued to demonstrate persisting difficulties with literacy and other associated skills. In contrast, the data of D3, whose psychometric profile indicated fewer persisting difficulties, suggested only subtle physiological abnormalities.

However, this analysis also reveals contradictory results. The individual identified as the weakest in the dyslexic group on psychometric measures (D6) did not show particular impairment on physiological measures (unfortunately, this individual did not participate in the MMNm studies and therefore interpretation must be limited). While D5 demonstrated particularly abnormal physiological responses across studies was identified as strong on psychometric measures.

It is important to exercise caution when interpreting data in such a way. The degree of dyslexic impairment can only be suggested by the results of psychometric tests conducted in adulthood as the influence of environmental factors (e.g. remediation and compensation) will affect the behaviourally measured profiles of dyslexic adults.

8.6 Limitations and Directions For Future Research

While significant group differences in physiological measures indicate low-level auditory processing deficits in the present dyslexic sample, the small sample size makes it difficult to generalise findings to the dyslexic population as a whole. The results of retrospective power studies (documented in Appendix 1) indicate that many of the comparisons made across samples were underpowered. Moreover, the observed power obtained when running the studies as factorial experiments, as originally planned, is weak in many of the statistical contrasts. The factorial design in the tone pair study, particularly, was considered over complicated. Nevertheless, the ability to look qualitatively at the data of individual participants to address the issue of individual variability is an advantage of the present studies.

Another methodological weakness is the choice of frequency separations in the study presented in Chapter 5. Originally separations of 400Hz and 100Hz were chosen to allow for comparison across studies. However, the inclusion of a condition employing a frequency separation at or below the dyslexic populations predicted threshold would have been informative.

The relative latency delay seen in the N1m response to tones presented after short ISIs in the control data was interpreted as evidence of an increased contribution of the $N1m^A$ component (section 5.4.4). The absence of such latency delays in the dyslexic group may have been influenced by disruption of the $N1m^A$ component specifically. However, the distinction between $N1m^A$ and $N1m^P$ was not made when modelling responses in this study. Investigators attempting to do this could tailor the experimental design to enhance the presence of this component, perhaps using a design similar to that of McEvoy et al (1997) who explored the nature of this component in controls.

The absence of an MMNm response to complete stimulus omissions in dyslexic participants was taken as further evidence of disrupted integration processes in the group. However, it was not possible to establish whether integration was completely absent in the dyslexic group or whether it may simply be occurring over reduced time windows. The inclusion of a smaller SOA condition would be able to establish this.

It is suggested that the dyslexic populations difficulties with auditory stimuli presented in over short intervals may be related to disruption in perceptual grouping, implicating a high level role in the accurate analysis of auditory scenes. Such a disruption may mean that dyslexics find it harder to accurately perceive speech presented in noisy contexts. Dougherty and colleagues (1998) tested this using noise but the use of speech or speech like stimuli would strengthen evidence for a causal link.

It would be interesting to examine whether equivalent perceptual grouping abnormalities are present in dyslexic individuals in the visual domain and indeed whether they can explain some of the low-level visual deficits reported in the population. Studies employing paradigms with parallels in both modalities within a single dyslexic sample would be well equipped to address this issue.

The use of an adult sample allowed for the assumption that any physiologically measured abnormalities in the dyslexic group reflected core biological deficits, persistent even after the behavioural characteristics of dyslexia have largely gone. However, the use of an adult study does neglect the issue of development. It would be interesting to see if the present results can be repeated in a younger sample. Moreover, in order to make a causal connection between the recorded findings and dyslexia it would be informative to employ similar paradigms in a predictive study with an infant sample.

The results of the study presented in Chapter 8 revealed that only one of the six dyslexic participants evoked a significant MMNm in response to a complete stimulus omission. This suggested that successive stimuli were not being

integrated as unitary percepts in the dyslexic group. Data from Chapter 5 provided some speculative evidence that enhancement in a component of the supratemporal N1m ($N1m^A$), which reflects persistence due to temporal integration processes, was not evidenced in the dyslexic's data. Taken together, these findings provide evidence that temporal integration processes are disrupted in the dyslexic individuals. However, the stimulus rates employed only considered integration within a narrow band of the postulated time window of event synthesis. Therefore, two explanations are possible. Firstly, the time window of temporal integration may be reduced in dyslexic individuals. Alternatively, the functioning of integration processes may be disrupted generally in these participants. Studies examining MMN responses reflecting temporal integration over variable time windows would help to address this issue. In addition, it would be informative to examine in more detail the possibility that enhancement of the $N1m^A$ component at short interstimulus intervals is reduced or absent in dyslexic groups. For example, while the present study employed single dipoles to account for the supratemporal N1m component, future studies could attempt to model the dyslexic's response with two dipoles (see McEvoy et al., 1997).

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Appendix 1: Retrospective Power Analyses

Statistical Contrast		Dependent Variable					
		Percentage Correct	Behavioural Response Latency	Tone 1 N1m Latency	Tone 1 N1m Amplitude	N1m Latency Difference	N1m Amplitude Difference
ISI	Power	.99	.46	.14	.33	.93	.07
	N	3.1	14.5	>46.9	20.6	4.2	>46.9
FS	Power	.82	.84	.16	.91	.37	.59
	N	5.8	5.6	>46.9	4.3	18.3	10.2
Group	Power	.29	.30	.29	.90	.78	.14
	N	23.9	23.9	23.9	4.4	6.0	>46.9
ISI* Group	Power	.41	.15	.07	.07	.79	.07
	N	16.2	>46.9	>46.9	>46.9	6.0	>46.9
FS* Group	Power	.08	.27	.06	.05	.06	.05
	N	>46.9	27.8	>46.9	>46.9	>46.9	>46.9
ISI* FS	Power	.59	.05	.13	.05	.10	.09
	N	10.2	12.3	>46.9	>46.9	>46.9	>46.9
ISI* FS* Group	Power	.70	.24	.11	.07	.06	.08
	N	7.8	30.0	>46.9	>46.9	>46.9	>46.9

Table A-1 Chapter 5: Observed Power and Sample Size Required (N) for Power = .80 (Factorial Design)

The observed power (SPSS output) for each statistical contrast and for all dependent variables in the Tone Pair study, based on the originally planned 2x(2x2) mixed factorial design. Required sample estimates are based on values given in Howell (1995, Appendix D, Table D.5).

Dependent Variable	Experimental Condition							
	500ms – 400Hz		200ms – 400Hz		500ms – 400Hz		200ms – 100Hz	
	Power	N	Power	N	Power	N	Power	N
Percentage Correct	.67	8.0	.52	12.1	<.17	50.8	.29	22.7
Behavioural Latency	.40	16.3	.20	36.8	.44	13.9	.44	13.9
Tone1 Latency	.26	26.3	<.17	48.2	.32	21.2	.36	19.5
Tone1 Amplitude	.85	5.4	.77	6.6	.95	3.6	.95	3.7
Latency Difference	.20	36.5	.67	8.0	<.17	51.1	.96	3.5
Amplitude Difference	<.17	143.6	<.17	66.6	.26	29.3	<.17	91.5

Table A-2 Chapter 5: Observed Power and Sample Size Required (N) for Power = .80 (Between Samples Comparisons)
Power obtained for each between samples comparison for all dependent variables, in the four experimental conditions in the Tone Pair study. Effect size calculations are based on pooled variance. Power and required sample size estimates are based on values given in Howell (1995, Appendix D, Table D.5).

Dependent Variable	Experimental Condition	
	Large Frequency Deviant	
	Power	N
Global Field Power Peak Latency	.67	8.2
Global Field Power Peak Amplitude	.99	2.6
Right Dipole Latency	.93	4.0
Left Dipole Latency	.63	8.8
Right Dipole Amplitude	.99	2.7
Left Dipole Amplitude	.96	3.4

Table A-3 Chapter 6: Observed Power and Sample Size Required (N) for Power = .80 (Between Samples Comparisons)
Power obtained for each between samples comparison for all dependent variables in the Frequency Deviant MMNm study. Effect size calculations are based on pooled variance. Power and required sample size estimates are based on values given in Howell (1995, Appendix D, Table D.5).

Statistical Contrast		Dependent Variable
		GFP Amplitude
SOA	Power	.74
	N	6.9
Group	Power	.48
	N	13.0
SOA*Group	Power	.57
	N	10.2

Table A-4 Chapter 7: Observed Power and Sample Size Required (N) for Power = . 80 (Factorial Design)
The observed power (SPSS output) for each statistical contrast in the Stimulus Omission MMNm study, based on the originally planned 2x(2) mixed factorial design. Required sample estimates are based on values given in Howell (1995, Appendix D, Table D.5).

Dependent Variable	Experimental Condition			
	100ms SOA		175ms SOA	
	Power	N	Power	N
Global Field Power Amplitude	.63	8.8	.20	38.4

Table A-5 Chapter 7: Observed Power and Sample Size Required (N) for Power = .80 (Between Samples Comparisons)
Power obtained for each between samples comparison in the two experimental conditions in the Stimulus Omission MMNm study. Effect size calculations are based on pooled variance. Power and required sample size estimates are based on values given in Howell (1995, Appendix D, Table D.5).

Appendix 2: Sample Informed Consent Form

Informed Consent Form Subject Number

Using Magnetoencephalography to Investigate Developmental Dyslexia.

Researchers: Alison Fisher, Dr Ian Richards, Dr Ian Holliday, Neurosciences Institute.

INFORMATION FOR VOLUNTEERS

The purpose of this study is to investigate the neural correlates of Developmental Dyslexia. There will be a number of phases involved in this study; these are outlined below.

Firstly a comprehensive psychometric assessment will be conducted. This will include an intelligence test and a variety of literacy tests. Testing shall be carried out on a one-to-one basis and will take around three hours in one sitting. The results of testing are confidential but will be made available to you.

You may be asked to participate in a number of short psychophysics trials. These will involve attending to simple visual and auditory stimuli and responding by pressing a button. These trials will take no more than 1 hour in total.

Participants may also be asked to take part in neurophysiological testing with use of Magnetoencephalography (MEG). MEG is a completely non-invasive technique for recording brain activity in response to various tasks. Participants will be asked to sit in a small room and attend to visual and auditory stimuli. This procedure is likely to take around 1 hour to complete.

All procedures are known to be safe and will not involve any harm or discomfort to you. However, people with any of the following will not be eligible as participants for this study: neurological or psychiatric illness; serious head trauma; chronic substance abuse; uncorrected sensory impairment; non-English speaking background; documented history of ADHD.

If the results of testing reveal any abnormalities, arrangements will be made for you to be referred to Dr Ian Richards, Chartered Psychologist, for his opinion.

Please feel free to ask questions at any stage during your involvement in this study.

You are free to withdraw from the study at any stage without giving a reason. All of the results will be confidential and identities will not be revealed in any resulting publications.

STATEMENTS BY VOLUNTEERS

Please sign your name below to certify that:

a) The nature and procedures involved in this study have been explained to you fully.

b) You have read and understood the above information.

c) You understand that you are free to withdraw from the study at any time and for any reason.

d) You have had the opportunity to ask questions about the study.

e) You have agreed to participate in the study.

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

The patient will retain one copy of the signed Patient Consent Form and the investigator will retain the original.

Appendix 3: Summary of WAIS-III Subtests and Indices

Verbal Scale Subtests	
Vocabulary	defining words
Similarities	identifying in what way two objects or concepts are alike
Arithmetic	mental arithmetic problems involving the four basic operations
Digit Span	repeating series of numbers forwards and backwards; a test of auditory short-term memory
Information	a test general knowledge
Comprehension	reasoning/knowledge about everyday situations and social concepts
Letter-Number (L-N) Sequencing*	sequencing series of orally presented letters and numbers; a test of working memory
Performance Scale Subtests	
Picture Completion	finding the missing part in pictures of common objects and settings
Digit Symbol-Coding	a speed test in which symbols have to be matched to numbers according to a given code
Block Design	using cubes to make patterns; a test involving visuo-spatial ability
Matrix Reasoning	selecting the appropriate item to complete geometric patterns; a test of visual information processing and abstract reasoning
Picture Arrangement	sequencing series of cartoon-like picture cards to form stories
Symbol Search*	a time-limited visual search task
Object Assembly*	a jigsaw-type test involving visuo-spatial skills
Supplementary Tests	
Digit Symbol-Incidental Learning*	ability to recall the 9 symbols involved in the Digit Symbol-Coding test
Digit Symbol-Copy*	copying sequences of the 9 randomly-arranged symbols; a test of perceptual and graphomotor speed

*These tests are not used to calculate IQs.

Indices

Verbal Comprehension Index: combined scores from the Vocabulary, Similarities and Information subtests.

Perceptual Organisation Index: combined scores from the Picture Completion, Block Design and Matrix Reasoning subtests.

Working Memory Index: combined scores from the Arithmetic, Digit Span and Letter-Number Sequencing subtests.

Processing Speed Index: combined scores from the Digit Symbol-Coding and Symbol Search subtests.

Appendix 4: Summary of Administered PhAB Tests

Non-Word Reading	reading one- or two-syllable pseudo-words through knowledge of grapheme/phoneme (i.e. letter/sound) rules
Spoonerisms	replacing the first sound in a word with another sound and exchanging the initial sounds of the two words
Naming Speed (Pictures)	rapid naming of one hundred randomly arranged line drawings of five common objects
Alliteration Fluency	producing as many words beginning with the same sound as possible in 30 seconds
Rhyme Fluency	producing as many words ending with the same sound as possible in 30 seconds
Semantic Fluency	producing as many words belonging to a particular category as possible in 30 seconds. This is NOT a test of phonological processing but rather retrieval of word meaning and is included for comparison with the other two tests of fluency

Appendix 5: Common Classification of Standardised Scores

Standard Score category	Classification	Percentage within each
130 and above	'Exceptionally High'	2
120 – 129	'High' or 'Superior'	7
110 – 119	'High Average'	16
90 – 109	'Average'	50
80 – 89	'Low Average'	16
70 – 79	'Low' or 'Borderline'	7
69 and below	'Exceptionally Low'	2