Jarmo Hämäläinen

Processing of Sound Rise Time in Children and Adults with and without Reading Problems

JYVÄSKYLÄ LONGITUDINAL STUDY OF DYSLEXIA

JYVÄSKYLÄ STUDIES IN EDUCATION, PSYCHOLOGY AND SOCIAL RESEARCH 322

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Esitetään Jyväskylän yliopiston yhteiskuntatieteellisen tiedekunnan suostumuksella
julkisesti tarkastettavaksi yliopiston Agora-rakennuksessa (Ag Aud. 3)
joulukuun 10. päivänä 2007 kello 12.

Academic dissertation to be publicly discussed, by permission of
the Faculty of Social Sciences of the University of Jyväskylä,
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UNIVERSITY OF JYVÄSKYLÄ

JYVÄSKYLÄ 2007

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ISBN 978-951-39-3000-4 (nid.), 978-951-39-5190-0 (PDF)
ISSN 0075-4625

Jyväskylä University Printing House, Jyväskylä 2007

ABSTRACT

Hämäläinen, Jarmo
Processing of sound rise time in children and adults with and without reading problems
Jyväskylä: University of Jyväskylä, 2007, 46 p.
(Jyväskylä Studies in Education, Psychology and Social Research
ISSN 0075-4625; 322)
ISBN 978-951-39-3000-4 (nid.), 978-951-39-5190-0 (PDF)
Yhteenveto: Äänten nousuaikojen prosessointi lapsilla ja aikuisilla, joilla on dysleksia ja lapsilla ja aikuisilla, joilla ei ole dysleksiaa
Diss.

Two competing views on the importance of lower level auditory processing skills on speech perception and representations in dyslexia (or specific reading disability; RD) have generated several hypotheses on the role of auditory processing skills in dyslexia. The auditory problems exhibited by children with RD may be co-occurring with dyslexia, or they may have a causal role in the development leading to reading problems. The present studies focused on the hypothesis that a cue to the perception of speech stress is the more basic feature of sound rise times, perception of which is impaired in dyslexia. The relationship of rapid auditory processing (RAP) with reading problems was also investigated. In Study I, Finnish speaking adults with RD detected fewer deviations in the rise times of paired sounds when the two tones in the pair were 400 ms apart (the target deviation was in the second tone) compared to controls. In contrast, when the two tones were 150 ms apart the groups did not differ from each other. Also, the rise time detection scores were associated with several measures of literacy skills, but only when the tones were 400 ms apart. Study II found event-related potentials (ERPs) to rise time and pitch change in paired stimuli (with deviant in the second tone) to be different in children with RD than in control children. Children with RD differed from controls in responses related to detection of change in rise time when the tones were 255 ms apart. Also, children with RD had a smaller P3a component than controls in response to pitch changes when the tones were presented 10 ms apart. Study III extended the ERP findings to exogenous responses to paired tones with different rise times. The N1 component was larger in children with RD than in controls when the tones in the pair were presented 10 ms apart. P2 was smaller in children with RD than in controls to the first tone in the pair. The findings of these studies indicate that rise time processing deficits are present in a subgroup of adults and children with RD. The findings indicate that rise time processing problems might play a moderator role in relation to the development of reading skills.

Keywords: auditory processing, dyslexia, event-related potentials, rise time, children, adults

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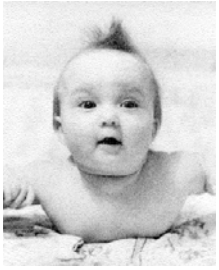

Jyväskylä Longitudinal Study of Dyslexia (JLD)

ACKNOWLEDGEMENTS

I would like to thank my supervisors Prof. Heikki Lyytinen and Dr. Paavo Leppänen for their support during these years. I would also like to thank the co-authors of the studies, Dr. Tomi Guttorm, Dr. Paavo Leppänen, Prof. Heikki Lyytinen, Dr. Kurt Müller and Minna Torppa for their contributions to the articles, and the reviewers of this work, Prof. Kenneth Hugdahl and Dr. Elina Pihko for their excellent comments. I wish to thank also Michael Freeman and Jennifer Thomson for checking the language. A special thank you to Kaisa Lohvansuu, Hanne Salminen and Annika Tanskanen for your friendship and support and all the fun we had. The Jyväskylä Longitudinal Study of Dyslexia team has created a unique, warm working atmosphere that has made everyday work exciting.

The studies comprising this doctoral dissertation were financially supported by the Finnish Centre of Excellence Programs of the Academy of Finland (#44858, "Human Development and Its Risk Factors" and #213486, "Learning and Motivation"), the Finnish Graduate School of Psychology, the Emil Aaltonen Foundation, and the Faculty of Social Sciences, University of Jyväskylä.

LIST OF PUBLICATIONS

Study I Hämäläinen, J., Leppänen, P. H. T., Torppa, M., Müller, K., & Lyytinen, H. (2005). Detection of sound rise time by adults with dyslexia. *Brain and Language, 94*, 32-42.

Study II Hämäläinen, J. A., Leppänen, P. H. T., Guttorm, T. K., & Lyytinen, H. (in press). Event-related potentials to pitch and rise time change in children with reading disabilities and typically reading children. *Clinical Neurophysiology, xx,* xx-xx.

Study III Hämäläinen, J. A., Leppänen, P. H. T., Guttorm, T. K., & Lyytinen, H. (2007). N1 and P2 components of auditory event-related potentials in children with and without reading disabilities. *Clinical Neurophysiology, 118,* 2263-2275.

CONTENTS

1 INTRODUCTION

The purpose of this dissertation was to investigate the auditory processing skills of children and adults with reading problems. Of particular interest was the detection and discrimination of amplitude envelope onsets (i.e. rise times) by individuals with dyslexia. The effect of rapid stimulus presentation on the perception of rise time was also examined. These were investigated using both behavioral and electrophysiological methods. Unique to the present studies was the use of brain event-related potentials (ERPs) to investigate rise time processing in children with dyslexia. ERPs were used to explore which processing stages might be abnormal in these children. The present studies also extended the findings on beat and rise time processing to the Finnish language environment and to shorter stimulus time ranges than those used in previous studies.

1.1 Definition of dyslexia, phonological processing and links to auditory processing

Dyslexia is a specific disability in learning to read and write despite adequate educational and motivational opportunities, intact peripheral sensory mechanisms and normal cognitive capabilities (Lyon et al., 2003). The terms dyslexia and reading disability will be used interchangeably in this dissertation. Dyslexia has been demonstrated to run in families and children born to dyslexic parents have approximately eight times higher risk for dyslexia than children born to families with no history of reading problems (Pennington & Lefly, 2001). This familiality suggests that dyslexia has a genetic basis. Four recently identified candidate genes for dyslexia have provided support for this behavioral finding (Cope et al., 2005; Hannula-Jouppi et al., 2005; Meng et al., 2005; Taipale et al., 2003).

The major underlying problem in dyslexia in most cases has been demonstrated to be a deficit in phonological processes (Bradley & Bryant, 1983;

Brady & Shankweiler, 1991; Stanovich, 1998; Wagner & Torgesen, 1987; for a review, see Vellutino et al., 2004). Phonology as a term refers to the processing of speech sounds within a given language; however, in the context of dyslexia research it has further connotations. 'Phonological awareness' refers to an individual's explicit knowledge of the segments of speech (e.g. phonemes) and to the understanding that larger speech units, for example words, can be segmented into smaller units of syllables, rhymes and phonemes. Phonological processing also refers to the ability to manipulate the phonemes of a spoken word, for example to switch the positions of two phonemes in one word to produce a word with a different meaning (cat → act).

The link between phonological processing and auditory processing is speech perception. Speech perception has been conceived as being influenced by higher level processes, such as long-term representations of phonemes (Kuhl et al., 2005), as well as by lower level processes involving the perception of basic auditory features such as pitch, intensity and duration (Shannon et al., 1995). In relation to dyslexia, two distinct theoretical approaches have formed around these two features of speech perception. One approach emphasizes the importance of higher level top-down functions while the other highlights the importance of lower level bottom-up functions. The debate on the importance of lower level sensory functions in dyslexia has continued for several decades (e.g. Farmer & Klein, 1995; Goswami et al., 2002; Livingstone et al., 1993; Nittrouer, 1999; Ramus, 2003; Rosen, 2003; Studdert-Kennedy & Mody, 1995; Tallal, 1980; White et al., 2006a, b). Proponents of the view that higher level cognitive functions are the major cause for dyslexia argue that sensory problems co-occur with dyslexia but have little or no impact on dyslexia itself (Mody et al., 1997; Ramus, 2003; Rosen, 2003). In contrast, proponents of lower level sensory function hypotheses argue that as speech is an auditory signal, problems in the auditory modality will inevitably cause difficulties in the formation of phonological representations. This in turn will impact reading and spelling (Goswami et al., 2002; Stein, 2001; Tallal & Gaab, 2006).

Even though there is much debate on the relationship between dyslexia and specific language impairment (SLI), studies that have focused upon children with SLI are referred to in this dissertation, but only when a few or no studies of children with dyslexia exist to address the issue in question. There are similarities between the two disorders such as problems in phonological awareness and possible underlying auditory processing deficits, as well as co-morbidity between the disorders (Bishop & Snowling, 2004; Corriveau et al., 2007). These similarities make it possible to draw preliminary conclusions on the auditory processing deficits in dyslexic children from studies with SLI children.

1.2 The nature of auditory processing deficits in dyslexia

1.2.1 Anatomical findings related to auditory processing in dyslexia

Anatomical findings from post-mortem studies have found several physiological differences between the brains of those with dyslexia and those with typical reading skills, including ectopias, microgyria and thalamic changes (Galaburda et al., 1985; 1994; Livingstone et al., 1991). Ectopias are clusters of misplaced neurons in the molecular layer (layer I) of the cortex that could have been caused by atypical migration of neurons from the ventricles to the cortex. Microgyria, in turn, are small, extra gyral patterns in the cortex that could also be due to abnormal neuronal migration (Galaburda, 1999; Rosen & Galaburda, 2000). Animal studies have shown that cortical ectopias and microgyria form during the development of the cortex in the uterus (Rosen et al., 1996). Numerous malformations such as those described above have been found in the perisylvian areas of adults with dyslexia (Galaburda et al., 1985). These were located in Broca's and Wernicke's areas as well as other areas also near the auditory cortex, mostly in the left hemisphere. The candidate gene findings have also suggested neuron migration problems in the early development of the cortex; in fact all the dyslexia candidate genes found to date are involved in neuronal migration mechanisms (Galaburda et al., 2006). One of these genes, ROBO1, affects axon growth between hemispheres, and animal studies have shown reduced corpus callosum and hippocampal comissure in addition to abnormal neuronal migration in the forebrain when the functioning of the robo1 gene has been compromised (Andrews et al., 2006; genes marked with capital letters refer to human genes and those with lowercase letters refer to animal genes). The other candidate genes, DYX1C1, DCDC2 and KIAA0319, affect the neuronal migration process from the ventricles to the cortex (Meng et al., 2005; Paracchini et al. 2006; Wang et al. 2006). Other anatomical differences have also been found, including magnocellular differences in auditory areas of the thalamus, and these are discussed in detail in section 1.2.2.2 (Galaburda et al., 1985; 1994; Livingstone et al., 1991).

The planum temporale (PT) is part of the secondary auditory cortex and is normally larger in size in the left hemisphere compared to the right (Shapleske et al., 1999). Some studies using magnetic resonance imaging (MRI) to investigate the hemispheric asymmetry of the planum temporale have found it to be symmetrical or even to have an opposite asymmetry between hemispheres in people with dyslexia. However, there are also conflicting findings suggesting only a subgroup of dyslexics have more symmetrical planum temporale (for reviews, see Beaton, 1997; Habib, 2000; Heim & Keil, 2004; Shapleske et al., 1999; Vellutino et al., 2004). Other MRI findings have included an increase in the size of the splenium and isthmus of the corpus callosum in dyslexics compared to controls. Both of these parts of the corpus callosum include nerve fibers connecting areas in the temporal and parietal areas and thus might be

related to the PT findings in dyslexia and possibly to auditory processing. However, there are also studies that have not found this increase in the size of the corpus callosum in dyslexics or that have found smaller corpus callosum size (for reviews, see Beaton, 1997; Habib, 2000; Heim & Kiel, 2004; Vellutino et al., 2004). Interestingly, the shape of the corpus callosum has been found to differ between children with dyslexia and typical readers (von Plessen et al., 2002). The posterior midbody or isthmus area containing nerve tracts from the auditory areas was found to be shorter in children with dyslexia.

Magnetic resonance diffusion tensor imaging (DTI) has been used to study differences in white matter nerve tracts between adults and children with dyslexia and typical readers. The left temporo-parietal area has consistently shown correlations between the anisotropy score (i.e. direction of water flow in axons) and reading score in both adults and children (Beaulieu et al., 2005; Deutsch et al., 2005; Klingberg et al., 2000; Niogi & McCandliss, 2006). Also, when comparing adults and children with poor reading skills to those with typical reading skills, group differences have been found in white matter microstructure in the same temporo-parietal area (Deutsch et al., 2005; Klingberg et al., 2000).

Most of the MRI findings have been linked to language and phonological processing (e.g. Larsen et al., 1990; Leonard et al., 2001) or to speech perception (Hugdahl et al., 2003). In contrast, data on the relationship between the auditory processing deficits and anatomical brain structure changes measured with MRI is scarce, particularly on the main focus areas of the present dissertation: rise time and rapid auditory processing.

1.2.2 Behavioral and brain activation findings related to auditory processing in dyslexia

The theory under focus emphasizes the role of amplitude envelope onsets among the auditory processing deficits in dyslexia: the suprasegmental theory (Goswami et al., 2002). In addition, the effects of rapid stimulus presentation are described from the point of view of rapid auditory processing deficits in dyslexia (Tallal, 1980; Tallal et al., 1993; Tallal & Gaab, 2006) and the magnocellular theory (Stein & Walsh, 1997; Stein & Talcott, 1999; Stein, 2001).

1.2.2.1 Rise time processing and dyslexia

The present dissertation investigated the recent hypothesis of Goswami and colleagues (2002) that the phonological problems of dyslexic children stem from an earlier developmental speech segmentation problem. This earlier problem is seen in difficulty segmenting speech sound elements larger than phonemes, for example syllables and rhymes, from the speech stream. In the development of speech perception children first learn to segment rhymes and syllables and only after that single phonemes (Curtin et al., 2005; Jusczyk et al., 1999). If children with dyslexia already have problems in segmenting larger portions of the speech stream then they will most probably also have difficulties with smaller

speech sound elements (i.e. phonemes). Goswami et al. (2002) suggested that segmenting spoken words into rhymes is related, at least partly, to the perceptual centers of words. Perceptual centers have been thought of as the perceived 'moment of occurrence' of a spoken word (Morton et al., 1976). This is not always the same as the physical onset of the spoken word. When people are asked to listen to a series of spoken numbers and asked to adjust them into equal intervals, the physical beginning to end inter-stimulus intervals of the spoken numbers will not be equal. Instead of physical length, the participants are arranging the stimuli according to the perceived 'center of gravity' of the word, i.e. the perceptual center (P-center). Perception of P-centers has been thought to be involved with segmenting word rhymes into beginning and end parts. Also, the P-center has been thought to be at least partly due to the perception of rise times (amplitude modulation of the beginning of sound) of spoken words (Scott, 1993; 1998). Based on this, Goswami et al. (2002) devised an experiment with a beat categorization task. In this task an amplitude modulated sound (with five modulation cycles) was played to children and they had to decide whether there was a beat in the sound or not. A beat is perceived more clearly when the rise time of the beginning of each modulation cycle is short and less clearly when the rise time is long. Goswami et al. (2002) found that children with dyslexia differed from chronological age-matched controls in their ability to categorize sounds in terms of their beat; the children with dyslexia had shallower categorization curves. In addition, it was found that the beat categorization slopes explained 25 % of the variance in reading and spelling skills after accounting for age, performance IQ and vocabulary. This result supported the hypothesis that children with dyslexia have difficulties processing rise times. The results also suggested that phonological problems have a lower-level auditory basis possibly related to segmenting larger speech sound elements. Other studies using spectrally impoverished speech have also shown that the temporal cues provided by the amplitude modulation in speech are important for speech intelligibility (Drullman et al., 1994; Shannon et al., 1995). Removing the slower amplitude modulations from spectrally impoverished speech makes it unintelligible. Also, sine-wave speech with only a few frequency bands but with intact amplitude modulation is enough to correctly identify speech sounds (Remez et al., 1981; Rosner et al., 2003). These studies show that both spectral and temporal information (provided by amplitude modulation) is important for speech perception.

Since the commencement of the present dissertation in 2003 several studies have appeared showing corroborating evidence for the rise time deficit in English speaking children (Richardson et al., 2004) and adults (Pasquini et al., 2007; Thomson et al., 2006) as well as in French speaking children with dyslexia (Muneaux et al., 2004). In addition, these studies have extended the finding to simpler discrimination tasks using only two modulation cycles (and thus shorter stimuli) and to stimuli with only a single rise time ramp (Richardson et al., 2004; Thomson et al., 2006).

Although most of the studies investigating rise time processing and dyslexia controlled for performance IQ, age and vocabulary, other factors in addition to auditory acuity could have affected the results. These include problems in attention, motivation and understanding instructions. Studies using event-related potentials can be used to measure auditory processing without overt attention on the auditory stimuli presented. Notably, the processing of rise times with ERPs in children with RD has not been investigated. In fact, all the ERP studies concerning the processing of rise times in normal populations have been conducted with adults.

The studies with adults have shown that rise times affect the N1 and P2 components; the longer the rise time, the longer the latency and smaller the amplitude of the component (Bierman & Heil, 2000; Kodera et al., 1979; Loveless & Brunia, 1990; Ruhm & Jansen, 1969). The N1, occurring approximately 100 ms from the sound onset, has been thought to reflect the onset, offset and transient detection of auditory signals (Näätänen & Picton, 1987). The functional significance of the P2 component remains unclear, but it has been suggested that it is involved in attention-related mechanisms (Crowley & Colrain, 2004). No systematic investigation has been carried out on the effects of rise times on ERP responses elicited by changes in sound features, such as the mismatch negativity (MMN) component. MMN is generated without active attention to the stimuli, and reflects the comparison between the memory trace that has built up for a repeated standard stimulus with the trace generated by an infrequent stimulus deviating from this (Näätänen, 1992; Näätänen & Alho, 1997). MMN has been shown to be elicited by changes in several sound features such as frequency, intensity and duration as well as by other changes in the sound stream such as omission of a sound (for reviews, see Kujala et al., 2007; Näätänen, 1992). Two studies have shown that MMN is generated by a change in rise time (Lyytinen et al., 1992; Caclin et al., 2006). In these studies, the length of rise times varied from 2 and 24 ms to 10 and 175 ms, providing evidence that, at least in adults, MMN would be generated with these parameters.

Recently the neural mechanisms for rise time processing have also been investigated with animal studies. In a series of papers Heil and colleagues (Bierman & Heil, 2000; Heil, 1997a, b; Heil & Irvine, 1997; Heil & Neubauer, 2001; 2003) showed that in the auditory cortex (primary cortex, AI) of cats the first spike of neural firing to a sound is dependent on the amplitude, length of rise time and rise function of the sounds as well as on the characteristic frequency of the neurons. Similar parameters have also been found to affect the first spike firing of auditory nerve fibers of cats, indicating that already the peripheral sensory systems are involved in rise time processing. The authors also ruled out the possibility that the relationship between these parameters was due solely to the shifting of the hearing threshold to a later time point as a result of longer rise times. The results of Heil and colleagues showed that it was the summation of energy as a function of both rise time and amplitude that affected the timing of the first spike of neural firing. In addition, they found that different neurons in the auditory cortex fire at different time points of energy

summation, i.e. at different points during rise time, depending on the slope gradient. This mechanism forms a tracking system of sound rise times: some neurons fire at the beginning while others fire at the middle and end of rise times. Corroborating results were found in human studies using magnetoencephalography (MEG) to investigate N1m response latency and amplitude to varying rise times (Bierman & Heil, 2000). The function of N1m latency and amplitude change was predicted by the energy summation mechanism found in cats. Although this temporal summation mechanism is already present at the cochlea nucleus and auditory nerve fibers, higher level structures and mechanisms are needed to separate the spontaneous firing of the nerve fibers from the stimulus-locked first spike (Heil, 2004). The neurons in this rise time tracking mechanism also lock to repetitive onsets, but at amplitude modulation (AM) rates of 10 - 20 Hz or higher the number of spikes per onset diminishes to zero (Heil, 2003). This means that AM rates of 10 – 20 Hz or higher have to be processed by some other mechanism.

1.2.2.2 Rapid auditory processing and dyslexia

Tallal's theory of rapid temporal auditory processing deficits in dyslexia was first thought of in relation to children with specific language impairment (SLI). Tallal showed that the perception of order of rapidly presented stimuli in SLI children differed from that of control children (Tallal, 1973). Later, it was shown that children with dyslexia differed from children with normal reading skills in a temporal order judgment (TOJ) task using short inter-stimulus intervals (ISI) (Tallal, 1980). In this task children listened to two sounds of different pitch and had to decide which of the sounds (lower or higher in frequency) came first and press two buttons accordingly. When the two stimuli were close to each other (305 ms or less) the children with dyslexia made more errors in TOJ than the control children but performed equally well with the control children when the ISI was 428 ms. Tallal (1980) also reported that only some (about one third) of the children with dyslexia performed below the level of the control group, even though the difference between the groups was significant.

Since this initial study of rapid auditory processing in children with dyslexia (Tallal, 1980), several studies have tried to replicate these findings and extend the theoretical basis of the rapid auditory processing theory (for reviews see Farmer & Klein, 1995; Habib, 2000; Tallal & Gaab, 2006). The theory has been extended to the perception of fast and transient elements in speech, particularly to the formant changes of stop-consonant - vowel syllables (Tallal et al., 1993). In addition, some studies have shown differential associations with literacy skills from rapid auditory and visual tasks (Booth et al., 2000). Children with reading impairment showed associations between rapid auditory processing skills and phonological skills, and between rapid visual processing skills and orthographic skills. In adults an association was found only between rapid auditory processing and phonological and orthographic skills. Their study suggests that rapid auditory processing could be the cause of, or at least have an impact on, phonological deficits. Conversely, rapid visual processing

could cause problems in fast orthographic recognition of words. One caveat of this finding, however, is that the authors did not have control groups in their study, and thus it is impossible to know whether control participants would have shown similar associations and whether the reading impaired and control groups would have differed from each other in their rapid processing skills.

In contrast to the studies reported above, some studies have found group differences for performance with stimuli presented with short ISIs, but no correlations between rapid auditory processing and reading skills (Breier et al., 2002; Bretherton & Holmes, 2003; Heiervang et al., 2002; Marshall et al., 2001). Others have suggested that it is not rapid auditory processing per se that is impaired in dyslexia but instead the phonological similarity between speech sounds that is difficult for individuals with dyslexia (Mody et al., 1997). The role of RAP deficits in dyslexia thus remains an open question.

Related to the rapid auditory processing theory and extending knowledge concerning the neural basis of RAP theory is the magnocellular theory of dyslexia (Stein & Walsh, 1997; Stein & Talcott, 1999; Stein, 2001). It was first proposed by Livingstone et al. (1991; 1993) that the magnocellular pathway of the visual system in dyslexia is disrupted and causes difficulties in rapid visual processing. Reading requires fast eye movements and thus these difficulties could be causally related to at least some forms of dyslexia. Magnocells are larger neurons in the sensory pathways, and these have been suggested to send action potentials faster than smaller cells (called parvocells; Stein, 2001). The magnocellular system is thought to relay sensory information requiring fast processing, such as motion perception and certain visual contrasts (Stein & Talcott, 1999). In post mortem autopsy studies of the brains of dyslexics Livingstone and colleagues (1991) found that the brains of dyslexic individuals had fewer and more disorganized magnocells in the lateral geniculate body of the thalamus, which is part of the visual pathway in the nervous system. Behavioral studies have provided evidence that adults with dyslexia have difficulties in perceiving, for example, coherent motion of moving dots compared to control participants and that performance in a coherent motion task correlates with nonword reading performance (Witton et al., 1998). It should be noted, however, that the visual deficits found in individuals with dyslexia do not necessarily implicate impairment exclusively in the magnocellular system (Skottun, 2000). Some studies have found no visual deficits while some have found deficits incompatible with the magnocellular deficit (Skottun, 2000).

In addition to abnormalities in the visual areas of the thalamus, similar findings have been reported for the medial geniculate nucleus of the thalamus in the auditory pathway. Although the auditory system is not divided into magno- and parvopathways as clearly as the visual system, the larger (magno) cells in the medial geniculate nucleus (MGN) have been found to be of reduced size and more disorganized in the brains of dyslexics compared to the normal population (Galaburda et al., 1994). The larger cells in the auditory system are thought to process rapidly changing information, such as amplitude and

frequency modulations (Stein & Talcott, 1999). Several studies have found differences between people with dyslexia and controls in the perception of amplitude modulated (AM) and frequency modulated (FM) sounds. For example, McAnally and Stein (1997) used the ERP technique to measure the amplitude modulation following response (AMFR) in both participants with dyslexia and normally reading controls. They also measured the auditory brainstem responses (ABR) to click sounds to investigate at which stage of the auditory system possible group differences would be observed. They found that while the ABRs of the two groups were similar, the AMFR to 20-80 Hz AM sounds differed in strength between the groups: the participants with dyslexia had smaller amplitudes than normally reading participants. This indicated that at the level of the brainstem the auditory information was processed normally but at thalamic or cortical processing stages the dyslexics showed atypicalities. Corroborating evidence for compromised perception of dynamic stimuli (involving AM and FM) in people with dyslexia has been found in several studies with ERP (Menell et al., 1999) and behavioral methods (Witton et al., 1998, 2002).

The neurobiological background of the RAP and magnocellular theories has been extensively studied recently. The brain anomalies found in individuals with dyslexia (ectopias, microgyria and thalamic malformations) have been investigated in animal models. Rats with induced cortical microgyria performed more poorly on rapid auditory discrimination tasks compared to rats without these microgyria (Fitch et al., 1994; Clark et al., 2000; Peiffer et al., 2002; 2004a, b; Threlkeld et al., 2006). Similar findings were observed in a study using mice with ectopias (caused by genetic disruption) and measuring ERPs to paired tones (Frenkel et al., 2000). These studies suggest that the cortical malformations found in the brains of dyslexics could cause auditory processing deficits.

However, when studies also involving thalamic abnormalities are included the picture becomes more complicated. In some animal studies it was found that cortical malformations induce similar anomalies in the MGN of the thalamus as those found in dyslexics' brains (Herman et al., 1997; Peiffer et al., 2002). This causal effect could be due to changes in the connections between the cortex and thalamus, as induced microgyria have been demonstrated to eliminate thalamocortical connections in the lesioned area and to increase the connections in the adjacent area (Rosen et al., 2000). Thus the abnormal connections in the cortex appeared developmentally first and caused changes in the sensory areas of the thalamus. In addition, male rats with abnormal changes in the thalamus (caused by the cortical microgyri) have been found to perform more poorly in a rapid auditory processing task compared to male rats with sham surgery that did not affect their thalamus (Herman et al., 1997). Interestingly, when cortical microgyria were induced in female rats, no thalamic changes were observed. In addition, the performance of the female rats in the RAP task was normal, indicating that it is indeed the thalamic changes that cause the RAP deficits and not the cortical changes (Herman et al., 1997; Rosen

et al., 1997). The observation of sex differences in RAP task performance of rats after induction of cortical malformations has been replicated in a study by Peiffer et al. (2004b). This sex difference was due to exposure of the rat fetuses to testosterone. Female rats exposed to testosterone showed malformations in both cortical and thalamic areas while female rats not exposed to testosterone had only cortical malformations (Rosen et al., 1999). These findings have been considered evidence against the causal effects of sensory problems in dyslexia (Galaburda, 1999; Ramus, 2004). That is, ectopias and other malformations in the language areas of the brain alone can cause the observed phonological and reading impairments. In addition, cortical changes in the language areas could cause changes in the thalamus. These changes would impair rapid auditory processing while exempting auditory deficit from any causal role in reading disorders. This would mean that auditory processing problems would only have moderator effects on phonological problems, if they affect phonology at all. However, it is not known how cortical malformations alone affect reading and spelling, how cortical anomalies combined with thalamic differences affect literacy skills, and how often cortical and thalamic differences occur in the same individuals in humans with dyslexia. Thus the role of auditory processing skills in dyslexia remains unresolved. Also, it should be noted that the ectopias and microgyria in the dyslexic brains did not occur only in language areas but also in the auditory areas (for a figure of the ectopias found across the brains of dyslexics, see Figure 3 in Ramus, 2004). The cortical anomalies found in humans in the auditory cortex might be sufficient in themselves to cause auditory processing problems without the thalamic changes.

1.3 The role of auditory processing deficits in dyslexia

Several pieces of evidence point towards the hypothesis that sensory problems co-occur with dyslexia (in contrast to being causal): (1) not all dyslexics have atypical sensory processing; (2) not all individuals with atypical sensory processing have dyslexia; (3) associations between perceptual acuity and phonology, reading and spelling skills are not shown consistently in the literature; (4) a behavior genetic study with twins shows dissociation between auditory processing and phonology in children with language impairment.

(1) Perhaps the most methodical examination of the occurrence of sensory deficits in dyslexics has been carried out by Ramus and colleagues (Ramus et al., 2003; White et al., 2006b). They found in adults with dyslexia that all 16 participants had phonological deficits, while only 10 had auditory problems (measured with speech and non-speech stimuli) (Ramus et al., 2003). Similarly, in 23 children with dyslexia 18 had phonological deficits and 6 had auditory problems (White et al., 2006b). These studies and other earlier ones (e.g. Tallal, 1980) show that there are dyslexics who have phonological problems but do not have auditory problems. Thus it would seem that auditory processing problems

are not necessary in order to have dyslexia. However, these results do not rule out the possibility that there are different subtypes of dyslexics whose underlying cause of reading difficulties is due to different factors. Maturation of phonological representations and of the auditory system could also play a role in the prevalence of auditory deficits in dyslexia (see below).

(2) Investigation of the auditory processing abilities of children with mild to moderate hearing loss have shown evidence that the detection of frequency modulation is equally poor in children with hearing loss as in those with reading disabilities (Halliday & Bishop, 2006). However, the children with hearing loss did not show poorer reading skills. Similarly, when the phonological processing and literacy skills of children with specific language impairment was compared with that of children with mild to moderate hearing loss, children with hearing loss showed phonological problems without literacy problems in contrast to children with SLI who showed both types of problems (Briscoe et al., 2001). One further study provides evidence that auditory deficits are neither necessary nor sufficient to cause dyslexia. When the auditory performance of children with autism was compared to that of children with dyslexia and typical readers, it was found that some of the children with autism had auditory deficits but normal literacy skills. In addition, some children with dyslexia did not exhibit any auditory deficits (White et al., 2006a). These studies demonstrated that auditory processing problems are not sufficient to cause reading problems on their own and that there may even be a double dissociation between deficits in reading and auditory abilities.

(3) Correlations between auditory processing abilities and phonological, reading and spelling skills have varied in different studies. In order for auditory processing to be causally related to reading skills, these two skills should show an association. Several studies have indeed found this to be the case (e.g. Goswami et al., 2002; Tallal, 1980; Witton et al., 2002). However, most studies have examined the associations across both reading disabled and typically reading populations. When the reading groups have been studied separately the association between auditory processing ability and reading has been found in control populations only (Rosen, 2003), and if reading disability is thought to be caused by auditory problems then the same correlation would be expected in the dyslexic group. In addition, some studies have not found associations between auditory processing and reading at all (Breier et al., 2002; Bretherton & Holmes, 2003; Heiervang et al., 2002); most of these studies have examined school-aged children or adults with reading disabilities. It is possible that atypical basic auditory processing skills in the early years of life could affect the development of phonological representations, and that auditory problems are ameliorated later in development. In other genetically driven disorders such as Williams syndrome, different cognitive processes have been demonstrated to show impairments only in infancy while other processes show impairments only in later ages (Paterson et al., 1999). There is also some evidence that infants at risk for dyslexia process basic auditory features differently from infants not at risk (Salminen et al., submitted). In addition, infants at risk for SLI have also

shown differences in basic auditory processing compared to controls, and the auditory processing skills of these infants have been associated with later language skills (Benasich et al., 2006). Further evidence for maturational effects were obtained by Wright & Zecker (2004), who found that children with learning disabilities showed differences in their performance on masking tasks compared to controls, but these differences were manifested in different tasks depending on the testing age of the children. Some masking tasks showed diminishing group differences with age. Other tasks showed stable group differences while some tasks showed increasing group differences with age. Also, animal studies have shown that the RAP deficits in rats caused by the induction of microgyria in the cortex show improvement with age; however, the time when the microgyria were induced also affected the pattern of improvement (Peiffer et al., 2004a; Threlkeld et al., 2006). Maturation of auditory processing skills could thus be one cause for the discrepancies in the literature.

(4) A twin study by Bishop and colleagues (1999) among children with language impairment showed that the correlations in temporal order judgment performance were of equal size between mono- or dizygotic twin pairs. Also, the scores of children showing worst performance in TOJ were of equal size between mono- and dizygotic twin pairs. In contrast, phonological short-term memory showed higher correlations in the monozygotic than in dizygotic twin pairs and the scores of the monozygotic twins showed greater similarity than those of the dizygotic twins. These results suggest that in twins with language impairment, environment has a larger effect than genetic factors on their auditory processing skills, whereas phonological short-term memory has a larger genetic component. The age at which these children were tested was approximately 10 years and, as discussed above, by this time maturation of the auditory system is more complete. Auditory perceptual development will also have been affected by environmental factors, such as musical training, that could obscure some of the genetic effects. Evidence counter to that found by Bishop et al. (1999) has, however, been shown in a recent study examining the disruption of function of the dyx1c1 gene in rats. This study found that when this dyslexia candidate gene was not working properly it caused cortical changes during neuronal migration and that juvenile and adult rats with these cortical changes showed auditory processing problems (Threlkeld et al., 2007). It would appear that the same genes as those possibly responsible for dyslexia also cause auditory processing problems.

The evidence on the role of auditory processing deficits in dyslexia thus currently allows several options: (1) auditory processing deficits co-occur with dyslexia but have no causal effect on it; (2) in a subgroup of people with dyslexia auditory deficits have caused their reading problems by interfering with speech perception and thus leaving their phonological representations less well defined; (3) auditory deficits act as moderators in dyslexia, as suggested by Bishop and colleagues (1999a, b); children with both phonological and auditory problems could be expected to show aggravated problems in reading and

spelling; (4) early in development, auditory problems could play a role in the formation of phonological representations, but with increasing age auditory processing skills have a diminishing effect on phonological and reading skills.

1.4 Aims of the empirical studies

First, we sought to find out whether Finnish speaking dyslexics would perform more poorly in rise time detection or discrimination than typical readers. Earlier studies have been carried out in English and French language environments (Goswami et al., 2002; Muneaux et al., 2004). In addition, we investigated the feasibility of using stimuli with varying rise times in ERP studies, i.e. to see if the phenomenon would be apparent also with shorter stimuli and single rise time ramps.

A second aim was to investigate at which processing stage rise time processing would show anomalies in children with RD. From behavioral findings it is difficult to discern which sensory processing stage is affected in dyslexics. Both exogenous responses (N1, P2) and responses related to stimulus change processing were examined (mismatch negativity (MMN), P3a and late discriminative negativity (LDN)).

We were also interested in how rise time is processed when the stimuli are presented rapidly. Earlier studies involving rapid auditory processing have used paired stimuli with varying frequencies (Nagarajan et al., 1999; Reed, 1989; Tallal, 1980) and some have investigated both rise time processing and rapid auditory processing in the same children but using different tasks (Goswami et al., 2002; Muneaux et al., 2004; Richardson et al., 2004).

The overall aim of these studies was in exploring the underlying causes of dyslexia with the particular focus in the role of auditory processing problems.

2 SUMMARY OF THE RESULTS

2.1 Study I

The first study was intended as confirmation that Finnish speaking dyslexics would show atypical processing of rise times. The effect of rapid stimulus presentation on the detection of rise times was also investigated. The stimulus material was different from that used in the previous literature (Goswami et al., 2002); it was chosen to test the hypothesis that the earlier findings of beat categorization could be due to atypical processing of individual rise times. The second objective of using this particular stimulus material was to investigate whether rise time processing could be measured with stimuli usable in brain event-related potential experiments.

2.1.1 Methods

The participants were parents of the children participating in the Jyväskylä Longitudinal Study of Dyslexia (JLD; Lyytinen et al., 2004). Nineteen dyslexics, 9 compensated dyslexics and 14 controls participated in the study. Rise time detection was investigated using tone pairs. Reference tone pairs with identical rise times were played repeatedly. Occasionally (23 % of the stimuli) the rise time of the second sound in the pair was changed (from 10 ms to 30 or 80 ms), and the participants had to press a button when this change occurred. Two different within-pair-intervals (WPIs) were used (150 and 400 ms) in different blocks. The pairs were separated by 1.7 seconds (onset-to-onset interval). Thirty-six repetitions of both deviant stimuli in both conditions were presented.

2.1.2 Results

The detection of the 30 ms rise time deviants was close to chance level in many of the participants and was not analyzed further due to the floor effect.

Group differences in and associations with phonological and reading skills were found only in the task with 400 ms within-pair-intervals and with 80 ms rise times. The participants with dyslexia had fewer correct detections of the different rise times compared to controls. In addition, the detection of rise times was associated with phonological, lexical decision and spelling skills. Associations were observed for the combined groups of dyslexics, compensated dyslexics and controls as well as for the dyslexics alone. The detection of rise time explained variance in phonological skills even after controlling for performance IQ, short-term memory and vocabulary. In addition, the adults with dyslexia who were particularly poor in rise time detection were poorer in phonological and spelling skills compared to those dyslexics with average or good rise time detection scores.

2.1.3 Discussion

The results provided further evidence for a rise time processing deficit in dyslexia, extending the findings to the Finnish language environment. The participants with dyslexia showed an association between rise time detection and phonology and spelling, indicating a possible causal route from basic auditory processing to higher-level literacy skills. The results also suggested that the beat categorization differences observed earlier by Goswami et al. (2002) could be due to a more basic difference in the processing of rise times. The shorter stimuli used here could be utilized in brain ERP experiments to investigate the processing stage at which children with dyslexia are impaired. Other studies carried out at roughly the same time and investigating the perception of rise times have also provided similar evidence: threshold-seeking tasks with rise times ranging from 15 to 300 ms and using either single or multiple rise times have shown processing deficits in children and adults with dyslexia for both single and multiple rise time stimuli (Richardson et al., 2004; Thomson et al., 2006).

The group differences and associations were only observed using stimuli with a 400 ms WPI. This was in contrast to the expectations of the RAP hypothesis: shorter WPIs represent more rapid auditory processing and are more likely to show associations with dyslexia. It is possible that the stimulus material affects the outcome of auditory processing tasks. With items perceptually more similar, the deficit is observed at longer stimulus intervals whilst with items perceptually more different the deficit is observed with shorter stimulus intervals. In other words, the difficulty of the task could affect the manifestation of RAP deficits.

2.2 Study II

In the second study we investigated ERP responses to rise time and pitch changes in stimulus streams and in an experimental setting requiring no active attention from the participants. The previous behavioral study showed that sound pairs with relatively short rise times could be used as stimuli. However, it is difficult from behavioral results to discern what neuronal mechanism underlies the atypical processing of rise times in dyslexia. The main aim of Study II was to investigate at which stage the atypical auditory processing of rise time change detection would occur. Change in the pitch/frequency of the stimulus was used as a control for the ERP responses to rise times, as frequency change detection has been extensively studied in previous studies (for reviews see Kujala et al., 2007; Näätänen, 1992; Näätänen & Alho, 1997). Secondly, the effects of rapid stimulus presentation on rise time and pitch processing were investigated by using stimulus pairs. Rise time processing in children with dyslexia has not previously been investigated with ERPs.

2.2.1 Methods

Participants were 9-year-old children, with and without reading disabilities, participating in the JLD project. The number of children in the short WPI condition was 30/22 (controls and children with RD respectively) and in the long WPI condition 25/21 (controls and children with RD, respectively). The event-related potentials were measured with high-density electrode nets (128 channels). The passive oddball experimental design with paired stimuli was selected to elicit the mismatch negativity (MMN) component and other components related to the processing of change (P3a, late discriminative negativity [LDN]). Stimuli were tone pairs with a change in the rise time (10 ms vs. 130 ms; 10 % of all stimuli) or pitch (750 Hz vs. 500 Hz; 10 % of all stimuli) of the second tone as deviant aspects. ERPs were recorded in two conditions: 10 ms within-pair interval (WPI) and 255 ms WPI. Tone pairs were presented with 610 ms offset-to-onset ISIs. Each deviant stimulus was presented 125 times. Children watched a silenced movie or played a silent computer game during EEG recordings. ERP data were analyzed using temporal principal components analysis that provided principal components corresponding to the MMN, P3a and LDN response time ranges. Channels showing a maximal signal (factor scores) and corresponding to earlier findings for these ERP responses were chosen for multivariate analysis of variance (MANOVA) for repeated measures. Post hoc univariate F-tests were carried out for individual channels when group effects or interactions were found.

2.2.2 Results

The ERP responses elicited by the stimuli were similar to those found in earlier studies with children of this age, showing only small, emerging N1 and P2 responses and large P1 and N250 responses (Albrecht et al., 2000; Johnstone et al., 1996; Ponton et al., 2000; 2002). For both groups, the ERP components related to the processing of change were small in response to the change in rise time when the tones in the pair were close to each other (10 ms WPI condition). This may reflect a floor effect in the amplitudes of the components.

Group differences were observed in the MMN and LDN responses to the change in rise time when the tones in the pair were farther apart (255 ms WPI condition). The response at the MMN latency was larger in the children with RD compared to typically reading children and LDN was smaller in the children with RD compared to controls (see Figure 1). In addition, group differences were observed in the P3a component in response to the change in pitch in the 10 ms WPI condition. Children with RD showed a smaller response than control children. No group-related differences were observed in the responses to the change in rise time in the 10 ms WPI condition or in the change in pitch in the 255 ms WPI condition.

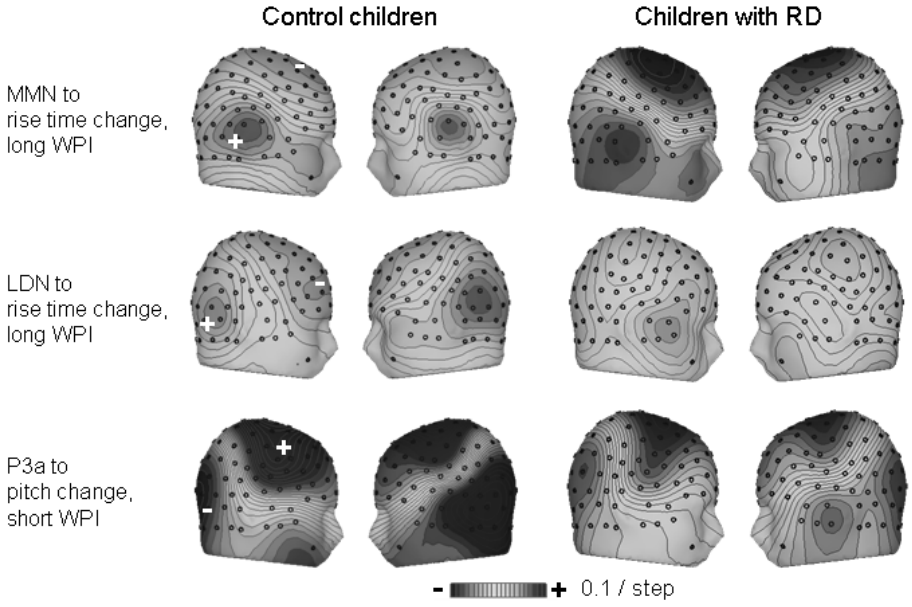

FIGURE 1 Topographic maps of the factor scores for temporal principal components (PCs) corresponding to MMN, LDN and P3a in Study II. Maps for control children are on the left and maps for children with reading disabilities (RD) on the right. Only those components showing group differences are shown. The top-most row shows the PC corresponding to the MMN elicited by rise time change in the long within-pair-interval (WPI) condition, middle row LDN to the same stimulus and bottom row P3a elicited by pitch change in the short WPI condition.

2.2.3 Discussion

This study showed atypical rise time processing in the change detection component (MMN) and at a later processing stage of the change detection process (LDN) in children with RD, but only when the tones in the pair were far apart. The finding of larger MMN in children with RD was surprising. Larger amplitudes of the MMN component have been thought to be associated with good behavioral discrimination abilities (e.g. Novitski et al., 2004; Pakarinen et al., 2007; for a review see Kujala et al., 2007) and thus we would have expected the MMN component to be smaller in children with RD than in controls. The MMN of the present study could also have reflected an overlapping N1 component and it could be that it was the N1 component that was larger in these children and not the MMN. N1 has been found to be larger in adults with dyslexia in some earlier studies (Helenius et al., 2002; Nagarajan et al., 1999). The smaller LDN component in children with RD compared to typical readers was expected. Several earlier studies have shown dyslexics to have smaller late negativity in response to a change in various stimulus features (Alonso-Bua et al., 2006; Maurer et al., 2003; Schulte-Körne et al., 1998; 1999; 2001) showing atypical later processing of the change in a stimulus feature.

In addition to the MMN and LDN components, pitch change elicited a P3a component, reflecting involuntary attention switching to the sound environment. While a P3a component was present in the children with RD, the amplitude of the component was smaller than that in the control children, but only when the tones in the pair were presented close to each other. This could indicate that compared to controls, the children with RD were less able to allocate attentional resources to novel changes in the sound environment when the stimuli were presented rapidly (see Gumenyuk et al., (2001) who found that in children the amplitude of the P3a response is associated with delay in reaction times in a cover task, indicating that this component could reflect the allocation of attentional resources).

2.3 Study III

The third study used the ERP methodology to investigate the sensory processing stages occurring prior to that of change detection: sound onset and transient detection. The N1 and P2 components have been shown to vary in amplitude and latency with ISI (Crowley & Colrain, 2004; Näätänen & Picton, 1987) and rise times (Bierman & Heil, 2000; Kodera et al., 1979; Loveless & Brunia, 1990; Rhum & Jansen, 1969). As a result, they reflect processing stages that could reveal further differences between children with RD and controls. In light of these findings we expected the children with RD studied here to show differences in their N1 and P2 components in response to different rise times. In addition, an earlier study with adults has shown that dyslexics have a

diminished N1m (magnetic counterpart of the N1) in response to the second tone of a tone pair when the two tones in the pair are presented in close succession (Nagarajan et al., 1999). Thus we expected to see atypical responses to tone pairs with short within-pair intervals if children with dyslexia exhibit rapid auditory processing deficits.

2.3.1 Methods

The participants were 19 children with RD and 20 control children and were a subgroup of the children participating in Study II. The stimuli were the same as the deviant stimuli in Study II, but the tone pairs were presented with long (1 – 5 s), random ISIs and with equal probability to elicit larger N1 and P2 responses (Ceponiene et al., 1998; 2002). Four stimuli were thus included in the study: (1) 10 ms rise time with 10 ms WPI; (2) 10 ms rise time with 255 ms WPI; (3) 130 ms rise time with 10 ms WPI; and (4) 130 ms rise time with 255 ms WPI. Each stimulus was repeated 80 times. Children watched a silenced movie or played a silent computer game during EEG recordings. Similar methods of analysis (temporal PCA and MANOVA) were used as in Study II.

2.3.2 Results

The ERP waveforms were similar to those expected on the basis of earlier studies showing the P1-N1-P2-N250 complex. The N1 and P2 responses were larger in this experiment than in Study II when the grand averages were examined. N1 to the first tone and the P2 to the second tone in the pair were of equal size between the two reading groups. The children with RD were found to have a smaller P2 response to the first tone in the pair (see Figure 2). In addition, the N1 to the second tone with 10 ms WPI and 130 ms rise time was found to be larger in children with RD compared to typical readers. Furthermore, in the control children, the N1 in response to the second tone was smaller with 130 ms rise time and larger with 10 ms rise time. In contrast, in the children with RD, the N1 in response to both rise times with 10 ms WPI was of equal size (see Figure 2).

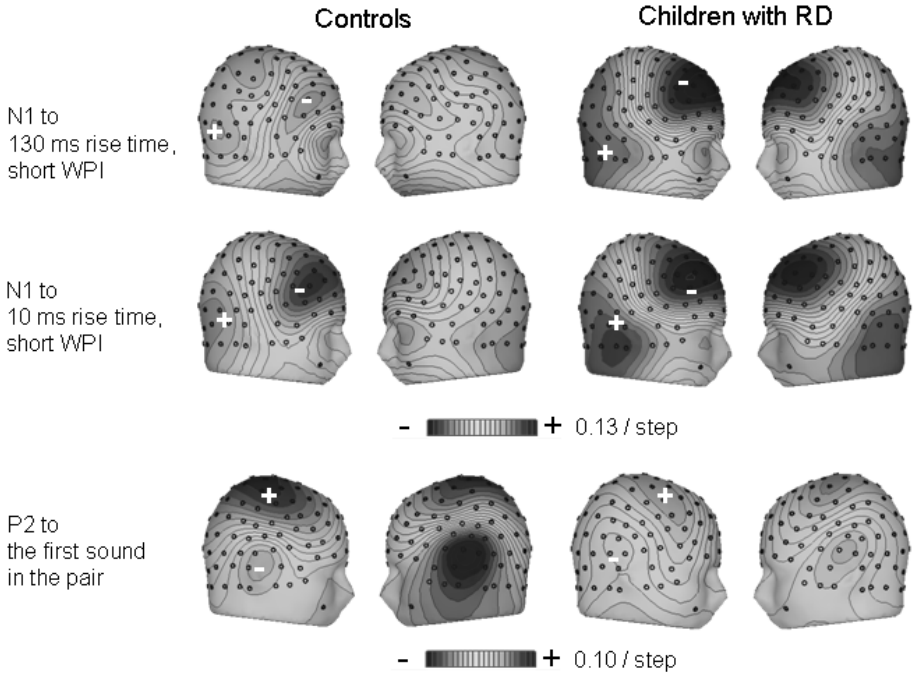

FIGURE 2 Topographic maps of the factor scores of the temporal principal components (PCs) corresponding to N1 and P2 in Study III. Maps for control children are on the left and maps for children with reading disabilities (RD) on the right. The top-most row shows the PC corresponding to N1 elicited by the second tone in the pair with 130 ms rise time and short WPI, middle row N1 elicited by the second tone in the pair with 10 ms rise time and short WPI (no group differences) and bottom row P2 elicited by the first tone in the pair.

2.3.3 Discussion

The function of the P2 component is not clear, but it has been suggested that it reflects attention-related processing (Crowley & Colrain, 2004). Moreover, the P2 has been found to become larger after auditory discrimination training (Atienza et al., 2002; Bosnyak et al., 2004; Reinke et al., 2003; Tremblay et al., 2001). The fact that the P2 difference was observed only for the first sound could indicate differences between the groups in attention switching mechanisms. The children with RD did not switch their attention away from the cover task as easily as the control children when the stimulus was preceded by a long silence interval (1 – 5 seconds). This would be supported by the P3a finding of Study II, also indicating abnormal attention-related processing.

The N1 showed differences between the groups in rise time processing. Control children reacted as expected to the rise time change: long rise times elicited smaller N1 and short rise times elicited larger N1 (Bierman & Heil, 2000; Kodera et al., 1979; Loveless & Brunia, 1990; Ruhm & Jansen, 1969). This is due to the greater amount of energy in the stimuli with shorter rise times compared to those with longer rise times. The children with RD seemed to react similarly to both long and short rise times when the auditory system was pressed for fast processing in the short WPI condition. This could possibly indicate that with these stimulus parameters the rise time and rapid auditory processing deficits converge.

3 GENERAL DISCUSSION AND CONCLUSIONS

3.1 Prevalence and nature of the rise time deficit in dyslexia

The present studies, conducted in a Finnish language environment, confirmed the earlier behavioral findings in English and French speaking dyslexics of a rise time processing deficit (Goswami et al., 2002; Muneaux et al., 2004; Pasquini et al., 2007; Richardson et al., 2004; Thomson et al., 2006). The atypical processing was observed at the behavioral level in adults and at the level of brain responses in children. However, not all the adults with RD showed poorer performance in rise time detection and not all the children with RD had atypical brain responses. Depending on the component and experimental design, 43-47 % of the distributions of the PCA factor scores of the control children and dyslexics were not overlapping, as indicated by Cohen's *d*. The behavioral study (Study I) showed 62 % non-overlap between the distributions of adults with and without dyslexia. These percentages are comparable to those in the earlier rise time studies showing non-overlap of distributions ranging from 43 % to 71 % depending on the study (see Table 1). Earlier reports have estimated the number of dyslexics with auditory deficits to be approximately 39 % (Ramus, 2003). It would appear that rise time measures yield a somewhat larger estimate of the prevalence of the auditory processing deficits in dyslexia than earlier measures conducted with other auditory processing tasks. Performance or ERP response deviating from that of the control group does not, however, necessarily indicate that the reading disability of those children is due to atypical auditory processing.

The ERP studies demonstrated that typically reading children react to rise times in a similar way as adults (Kodera et al., 1979; Loveless & Brunia, 1990; Ruhm & Jansen, 1969), as shown by the N1 response when the tones in the pair were close to each other. A smaller amount of energy in the stimulus (long rise time) elicited a smaller N1 response whilst greater stimulus energy (short rise time) elicited a larger N1 response. However, the children with reading disabilities did not react this way. N1 was insensitive to rise time changes in the

children with RD when the two sounds were presented in rapid succession. The ERP studies thus suggest that as early as approximately 100 ms from the onset of stimulus presentation the two reading groups start to differ in their processing of sound rise times. The N1 component occurring at this latency has been thought to reflect the detection of sound onsets, offsets and transient changes in sounds (Näätänen & Picton, 1987). This finding suggests that the differences observed in the present studies could be due to an abnormal rise time processing mechanism, as suggested by Heil and colleagues (Bierman & Heil, 2000; Heil, 1997a, b; Heil & Irvine, 1997; Heil & Neubauer, 2001; 2003). Of particular note is Heil's finding that the magnetic counterpart of the N1 in humans reacted to rise times as predicted by neurons found in the auditory cortex of cats. This could indicate that individuals with dyslexia have a deficit in integrating sound energy over time. A more detailed study with several different rise times would be needed for a firmer conclusion to be drawn on this matter. It should also be noted that this supposed energy integration deficit seems not to be the sole auditory processing deficit in dyslexia. For example, the detection and discrimination of sound frequencies has also been shown to be impaired in some individuals with dyslexia (Ahissar et al., 2006; Baldeweg et al., 1999; Banai & Ahissar, 2004; France et al., 2002; Halliday & Bishop, 2006; Kujala et al., 2006; Lachmann et al., 2005; Renvall & Hari, 2003; de Weirdt, 1988). The processing of different sound frequencies is not due to integrating energy over time but to the tonotopic organization of the whole auditory pathway, meaning that different neurons react more actively only to certain frequency ranges (Recanzone et al. 2000; Romani et al. 1982). This indicates the possibility that there are multiple causes for the auditory processing deficits in dyslexia. These causes should be investigated in future studies by examining both cortical and subcortical responses to both rise times and frequencies.

TABLE 1 Summary of the findings in rise time processing. The table shows the task used, age and number of participants, and effect size and percentage non-overlap between the distributions of the two groups as indicated by Cohen's *d*.

Article	**Task**	**Age (mean; SD)**	**N**	**Effect size**	**% non-overlap**
Goswami et al., 2002	Beat categorization	9.0 y (9.5 m)	25 controls 24 RD	1.4	68 %
Muneaux et al., 2004	Beat categorization	11.4 y (7 m)	20 controls 18 RD	1.5	71 %
Pasquini et al., 2007	Beat categorization	21.8 y (2.4 y)	18 controls 18 RD	0.9	52 %
Pasquini et al., 2007	2-ramp rise time discrimination	21.8 y (2.4 y)	18 controls 18 RD	0.1	8 %
Pasquini et al., 2007	1-ramp rise time discrimination	21.8 y (2.4 y)	18 controls 18 RD	0.5	33 %
Richardson et al., 2004	2-ramp rise time discrimination	8.8 y (9.5 m)	24 controls 24 RD	0.7	43 %
Richardson et al., 2004	1-ramp rise time discrimination	8.8 y (9.5 m)	24 controls 24 RD	0.8	47 %
Thomson et al., 2006	2-ramp rise time discrimination	22.3 y (ca. 3 y)	20 controls 19 RD	1.0	55 %
Thomson et al., 2006	1-ramp rise time discrimination	22.3 y (ca. 3 y)	20 controls 19 RD	1.0	55 %
Study I	Detection of rise time in tone pairs	37 y (28 – 58 y)	13 controls 19 RD	1.2	62 %
Study II	MMN and LDN to rise time change	9.4 y (4 m)	25-30 controls 21-22 RD	0.7	43 %
Study III	N1 to different rise times	9.4 y (4 m)	20 controls, 19 RD	0.7 – 0.8	43 – 47 %

When the stimuli used in the EQ experiment were presented in an oddball design, the change detection response (MMN/N1) to the change in rise time in the long WPI condition was larger in the children with RD compared to controls. On the other hand, the MMN to pitch change was of equal strength between the groups. This may be attributable to the stimulus parameters used. Earlier studies that have found differences between adults with dyslexia and typical readers in MMN response to frequency change have used a smaller frequency difference between the standard and deviant stimuli. In the present study, the frequency difference between the standard and deviant stimuli was 250 Hz, whereas in earlier studies it has been below 80 Hz when group differences were observed (Baldeweg et al., 1999; Kujala et al., 2006; Lachmann et al., 2005; Renvall & Hari, 2003) and above 80 Hz when no differences were found (Alonso-Bua et al., 2006; Baldeweg et al., 1999; Schulte-Körne et al., 2001; Sharma et al., 2006). One exception is a study with spelling-disabled children which showed MMN of equal size to that of typical spellers with a 50 Hz difference in frequency between the standard and deviant stimuli (Schulte-Körne et al., 1998). The change in rise time, in contrast, showed a larger response at the MMN time window when long WPIs were used in the control group. This could have been due to stronger afferent activation (larger neuronal population firing) to the rise time deviant. The deviant stimulus had a shorter rise time and thus more energy and it is likely that it could produce larger N1.

This would mean that the responses within the expected MMN latency were not the same for the changes in pitch and rise time respectively, and this could be one reason for the difference in the responses.

The ERP studies showed that the stimulus material and method of presentation can vary the processing stage at which auditory impairment is observed in children with RD. The early processing anomaly (N1) in the EQ experiment was found only to the short WPI stimulus in Study III whereas in the oddball experiment in Study II it was observed only with the long WPI stimulus. The difference between these experiments was in the ISI: in the EQ experiment it was 1 – 5 seconds and in the oddball experiments it was 610 ms. The N1 response to the first stimulus with long ISIs was larger than the corresponding response with short ISIs as seen from the grand averages. The preceding larger activation of the N1 neurons in the former situation could have disrupted the processing of the second stimulus in the children with RD when it was presented shortly after the first. However, with short ISIs the N1 to both the first and second tone was nearly non-existent and thus no differences between the groups were found.

In addition to the N1 difference, the P2 response also showed group differences. The smaller P2 for children with RD in response to the first sound of the stimulus pair indicates a more general auditory processing difference. This finding could be related either to stimulus feature detection, as indicated by the larger P2 after auditory training, or to attention mechanisms (Atienza et al., 2002; Bosnyak et al., 2004; Crowley & Colrain, 2004; Reinke et al., 2003; Tremblay et al., 2001).

The stimuli used in the present studies were paired non-speech tones. Using paired stimuli made it possible to investigate the effects of both rapid auditory processing and different stimulus features (rise time and frequency) with the same stimuli. The main focus was in studying the processing of different rise times. There are several options for what the more ecologically valid correlates of rise time processing in speech could be. The hypothesis of Goswami and colleagues (2002) was derived from the notion that the processing of larger speech elements would be difficult for children with dyslexia. In this case the rise time correlate would be the rhythmic changes in the speech stream due to speech stress patterns as suggested also by Pasquini and colleagues (2007). It would be of interest in future studies to compare the perceptual processing of dyslexics in both non-speech rise time and in speech elements involving changes in amplitude envelopes in order to find out whether the corresponding speech elements would be particularly problematic for those with dyslexia.

3.2 Different origins of the rise time and RAP deficits

One of the aims of the studies was to investigate the relationship between rise time and rapid auditory processing deficits. Study I showed differences between the groups and correlations with reading-related skills only when the rise times were presented with long WPIs. The oddball ERP experiment in Study II showed that rise time was processed differently in the children with RD in the long WPI condition. Earlier behavioral studies have shown small to moderate correlation between RAP and rise time tasks (Goswami et al., 2002) and also that performance in a rise time task explains additional variance in reading after performance in a RAP task is added into a regression model (Muneaux et al., 2004). These results would suggest that rise time and RAP deficits are produced by separate mechanisms and could, at least partly, be independent of each other. However, Study III demonstrated that the N1 differed between the groups only in the short WPI condition when long ISIs were used. This could suggest that, depending on the method of stimulation used, the two deficits are caused by either separate or the same mechanisms. The deficits cannot be due to the same neural mechanisms, however, as then Studies I and II should also have shown convergence for the two deficits. Other factors related to the generation of the N1 component in children must have affected the result of Study III. Such factors could include maturation of the N1 component in children and interaction with the speed of stimulus presentation (ISI).

In the oddball experiment the pitch change elicited a smaller P3a component in the children with RD, but only when the two tones were presented close to each other. On the other hand, the change in rise time elicited larger MMN/N1 and smaller LDN components in the children with RD (in the long WPI condition). This could suggest that the RAP deficit involves mechanisms associated with involuntary attention switching (P3a; Escera et al., 2000; Friedman et al., 2001; Rushby et al., 2005) and the rise time deficit involves mechanisms associated with the discrimination of sound features (MMN/N1; LDN; Cheour et al., 2001).

3.3 Role of the rise time deficit in dyslexia

The present studies showed that only a subgroup of people with dyslexia show differences in rise time processing. Study I also showed that rise time detection is associated with phonological skills and that those with poor rise time detection scores also had poor phonological test scores. In conjunction with the other evidence, it becomes possible to speculate on the possible role of auditory processing deficits in dyslexia. There are several options to be considered.

(1) The auditory deficits co-occur with dyslexia (Ramus, 2003; 2004). The behavioral results here showed associations between rise time processing and phonology and spelling, as well as an increase in the severity of phonological and spelling problems in the adults with dyslexia accompanied by poor rise time detection skills. However, behavioral measures can be influenced by motivational factors and attention mechanisms and these could be associated with reading, not the auditory processing skills. This explanation is possible but unlikely because the analyses controlled for performance IQ, short-term memory and vocabulary, and the associations were seen only with WPIs of 400 ms and not with WPIs of 150 ms. General motivational and attentional factors should affect all of these variables equally.

Even if auditory problems do not have a causal role in dyslexia they remain an interesting area of research. It would be worth investigating whether auditory problems cause other problems in children's everyday lives and whether they could be used as indicators of other disorders or of malfunctioning neural networks.

(2) In a subgroup of people with dyslexia their auditory deficits are responsible for their reading problems. The present data set cannot answer this question as all the studies were correlational in nature or examined group differences. In addition, the studies were conducted with adults or school-age children whereas data from newborns or infants would be more advantageous in seeking to answer questions of causality. Very early ERPs would not be affected by environmental factors, and cross-lagged correlations between low level auditory and speech processing development could be used to investigate influences between these variables. However, the most convincing evidence can only be produced with intervention studies using non-linguistic material for children with both dyslexia and auditory deficits. If improvements in reading and spelling were seen after non-linguistic auditory training and controlling for general attention and placebo effects, then it could be said that low level auditory processing plays a causal role in the development of reading skills.

(3) Auditory processing deficits act as moderators in the profiles of individuals with dyslexia (Bishop et al. 1999a, b). A moderator is thought here to be an intervening variable that changes the behavior of a second variable. Auditory processing deficits would affect reading disability showing differences between those with RD plus auditory deficits and those with RD minus auditory deficits. Study I provided evidence for this hypothesis: if dyslexic adults had poor rise time processing, their phonological skills were also weaker compared to dyslexic adults without rise time processing problems. It is probable that the cortical anomalies causing the phonological problems and the thalamic anomalies causing the auditory problems are affected by the same genes (e.g. dysfunction of dyx1c1 caused cortical anomalies and auditory deficits; Threlkeld et al., 2007). This could cause the high prevalence of auditory problems in individuals with dyslexia. Also, both types of deficits would be already present at birth and would interact during

development, possibly interfering with the formation of phonological representations.

(4) Maturation of the auditory system and phonological representations could obscure the effect of auditory processing on dyslexia (Galaburda et al., 2006; McArthur & Bishop, 2005; Wright & Zecker, 2004). The present studies do not support this view, although the age range used in these studies does not allow examination of early maturational effects. Approximately equal numbers of adults and children showed differences in rise time processing. This seems to be the case in the earlier studies as well: older children and adults even have slightly less overlap between the distributions of typical readers and those with RD (see Table 1). However, it is possible that during the first years of life, when phonological representations are first formed and the central nervous system shows rapid maturational changes, that a stronger relationship would be found between the auditory and phonological processing.

Taken together, the present studies show evidence of a moderator role for auditory processing deficits in dyslexia, at least where processing of rise times is concerned. This would mean that children with a risk for both auditory problems and poor formation of phonological representations have aggravated reading problems. The possibility of a causal connection in a subgroup of dyslexics cannot be ruled out altogether as the present studies were correlational in nature.

The methods used in the present studies make it difficult to obtain new information on the role of auditory processing deficits in dyslexia. The next step in research on auditory processing and dyslexia should focus on infants. Many of the current theories propose that children with RD have a maturational lag or that their auditory processing skills improve with age (McArthur & Bishop, 2005; Wright & Zecker, 2004). It is possible that impaired auditory processing at an earlier age affected their phonological representations when these were forming during the first year of life. Systematic research investigating several aspects of basic auditory processing (frequency discrimination, rapid rate processing and amplitude discrimination) should be combined with speech perception measures and followed up until phonological skills can be measured reliably to answer many of the outstanding questions of auditory processing and dyslexia.

TIIVISTELMÄ

Äänten nousuaikojen prosessointi lapsilla ja aikuisilla, joilla on dysleksia ja lapsilla ja aikuisilla, joilla ei ole dysleksiaa

Dysleksian eli lukemaan ja kirjoittamaan oppimisen vaikeuden (lukivaikeuden) taustalla on yleisesti ajateltu olevan ongelma puheen osien hahmottamisessa ja manipuloinnissa eli fonologiassa. Fonologisen prosessoinnin voidaan ajatella liittyvän puheen havaintoon ja puheesta muodostuneisiin muistiedustuksiin. Näiden fonologisten pulmien taustasyistä on käyty väittelyä pitkään. Toisaalta fonologisten pulmien on ajateltu johtuvan äänten eri piirteiden kuulemisen vaikeudesta, toisaalta korkeamman tason prosesseista kuten muistijälkien muodostumisesta.

Tämä väitöskirja keskittyi tutkimaan äänten nousuaikojen havaitsemista lapsilla ja aikuisilla, joilla on dysleksia. Nousuaikojen on ajateltu liittyvän puheessa rytmin havaintoon ja puhevirran jakamiseen pienempiin osiin, esimerkiksi tavuihin. Lisäksi väitöskirjassa tutkittiin nousuaikojen havaitsemista silloin, kun muutos nousuajassa tapahtuu toisen äänen välittömässä läheisyydessä.

Ensimmäisessä tutkimuksessa normaalisti lukevat aikuiset ja aikuiset, joilla oli lukivaikeus, kuuntelivat ääniparej a. Ääniparien jälkimmäisessä äänessä muuttui toisinaan nousuaika (10 millisekunnista 30 tai 80 millisekuntiin). Aikuisten tehtävänä oli painaa nappia kun kuulivat muutoksen nousuajassa. Ääniparej a soitettiin kahdessa erillisessä kokeessa: toisessa ääniparin äänien välinen aika oli 150 ms ja toisessa 400 ms. Tutkimuksessa havaittiin, että aikuiset joilla oli lukivaikeus, havaitsivat vähemmän muutoksia ääniparien nousuajoissa verrokkeihin verrattuna. Ero ryhmien välillä näkyi vain, kun ääniparin äänten välillä oli 400 ms hiljaisuutta. Lisäksi nousuaikojen havaitseminen oli yhteydessä fonologisiin ja lukutaitoihin, mutta vain silloin kun äänten välillä oli 400 ms hiljaisuutta. Tutkimus osoitti, että myös suomenkieltä äidinkielenään puhuvilla dyslektikoilla on vaikeuksia nousuaikojen havaitsemisessa. Aiemmat tutkimukset ovat keskittyneet englantilaisiin ja ranskalaisiin kieliympäristöihin. Lisäksi tutkimus osoitti, että äänten nopea esittäminen ei heikennä nousuaikojen havaitsemista dyslektikoilla. Aiemmat tutkimukset taajuusmuutoksilla ovat näyttäneet ärsykkeiden välin lyhentämisen heikentävän dyslektikoiden havaintotarkkuutta.

Toisessa tutkimuksessa nousuaikojen havaintoa tutkittiin aivojen herätevasteilla. Herätevasteilla voidaan seurata ärsykkeiden prosessointia aivoissa kymmenien millisekuntien tarkkuudella. Tutkimukseen osallistui lapsia, joilla oli lukivaikeus ja lapsia, joilla on normaali lukutaito. Tutkimuksessa soitettiin ääniparej a, joiden jälkimmäisessä äänessä tapahtui toisinaan joko taajuusmuutos tai muutos nousuajassa. Ääniparej a soitettiin kahdessa eri kokeessa: toisessa ääniparin äänten välillä oli 10 ms hiljaisuutta, toisessa 255 ms. Tulokset näyttivät, että lukipulmaiset lapset prosessoivat muutoksia nousuajoissa eri tavalla

kuin kontrollilapset: poikkeavuusnegatiivisuus komponentti oli suurempi ja myöhempi erotteluvaste pienempi dyslektikoilla kuin kontrollilapsilla, silloin kun ääniparin äänten välillä oli 255 ms hiljaisuutta. Lisäksi lukioppilailla oli pienempi P3a komponentti (tahattomaan tarkkaavuuden suuntaamiseen liittyvä komponentti), mutta vain silloin kun ääniparin äänten välillä oli 10 ms hiljaisuutta. Tutkimus osoitti, että lukipulmaisten lasten nousuaikojen havaintoongelmat saattavat johtua äänten piirteiden erottelun vaikeudesta. Toisaalta taas nopeasti esitettyjen taajuusmuutosten havaintopulmat saattavat johtua enemmän tarkkaavuuden suuntaamiseen liittyviin mekanismeihin.

Kolmas tutkimus laajensi toisen tutkimuksen herätevastemittareita eksogeenisiin vasteisiin. Eksogeeniset vasteet syntyvät aivoissa automaattisena reaktiona kaikkiin ärsykkeisiin ennen ärsykkeiden tietoista kognitiivista prosessointia. Tutkimukseen osallistui osajoukko toisen tutkimuksen lapsista. Tässä tutkimuksessa ääniparit esitettiin pitkillä aikaväleillä (1 – 5 sekunnin välein, kun toisessa tutkimuksessa ääniparien välillä oli 610 ms) ja yhtäläisin todennäköisyyksin. Tarkoituksena oli kasvattaa N1 ja P2 komponenttien kokoa pitkillä aikaväleillä ja ehkäistä erotteluprosessien syntymistä yhtäläisillä todennäköisyyksillä. Ärsykkeinä käytettiin samoja ääniparejа kuin toisessa tutkimuksessa. Tulokset osoittivat, että lukioppilaat eivät reagoineet nousuaikoihin odotetulla tavalla: heidän N1-vasteensa oli yhtä suuri molempiin esitettyihin nousuaikoihin, kun taas kontrollilapsilla N1-vaste oli pienempi pidempiin nousuaikoihin. Efekti näkyi ääniparin jälkimmäiseen ääneen, silloin kun ääniparin äänten välissä oli 10 ms hiljaisuutta, mutta ei pidemmällä hiljaisuusvälillä. Lisäksi havaittiin, että P2-vaste ensimmäiseen ääneen oli pienempi lukipulmaisilla kuin normaalisti lukevilla. N1-vaste heijastaa äänten alkujen, loppujen ja nopeiden muutosten havaintoa. P2-vasteen merkityksestä ei ole vielä varmuutta, mutta sen on ajateltu liittyvän tarkkaavuuden säätelyyn ja/tai äänten piirteiden analysointiin.

Osalla dyslektikoista (noin 40 – 60 %) on ongelmia havaita erilaisia nousuaikoja. Lisäksi nopeiden muutosten havaitseminen näyttäisi olevan erillinen pulma nousuaikojen havaitsemisesta. Näiden tutkimusten perusteella vaikuttaisi siltä, että auditorisen prosessoinnin vaikeudet voivat toimia moderaattoreina (muuttavana tekijänä) lukivaikeuden yhteydessä, mutta kausaalista yhteyttä ei myöskään voi sulkea pois.

REFERENCES

Ahissar, M., Lubin, Y., Putter-Katz, H., & Banai, K. (2006). Dyslexia and the failure to form a perceptual anchor. *Nature Neuroscience, 9,* 1558-1564.

Albrecht, R., Von Suchodoletz, W., Uwer, R., & von Suchololetz, W. (2000). The development of auditory evoked dipole source activity from childhood to adulthood. *Clinical Neurophysiology, 111,* 2268-2276.

Alonso-Bua, B., Diaz, F., & Ferraces, J. M. (2006). The contribution of AERPs (MMN and LDN) to studying temporal vs. linguistic processing deficits in children with reading difficulties. *International Journal of Psychophysiology, 59,* 159-167.

Andrews, W., Liapi, A., Plachez, C., Camurri, L., Zhang, J., Mori, S., Murakami, F., Parnavelas, J. G., Sundaresan, V., & Richards L. J. (2006). Robo1 regulates the development of major axon tracts and interneuron migration in the forebrain. *Development, 133,* 2243-2252.

Atienza, M., Cantero, J. L., & Dominguez-Marin, E. (2002). The time course of neural changes underlying auditory perceptual learning. *Learning & Memory, 9,* 138-150.

Baldeweg, T., Richardson, A., Watkins, S., Foale, C., & Gurzelier, J. (1999). Impaired auditory frequency discrimination in dyslexia detected with mismatch evoked potentials. *Annals of Neurology, 45,* 495-503.

Banai, K. & Ahissar, M. (2004). Poor Frequency Discrimination Probes Dyslexics with Particularly Impaired Working Memory. *Audiology & Neuro-Otology, 9,* 328-340.

Beaton, A. A. (1997). The relation of planum temporale asymmetry and morphology of the corpus callosum to handedness, gender, and dyslexia: A review of the evidence. *Brain and Language, 60,* 255-322.

Beaulieu, C., Plewes, C., Paulson, L. A., Roy, D., Snook, L., Concha, L., & Phillips, L. (2005). Imaging brain connectivity in children with diverse reading ability. *Neuroimage, 25,* 1266-1271.

Benasich, A. A., Choudhury, N., Friedman, J. T., Realpe-Bonilla, T., Chojnowska, C., & Gou, Z. (2006). The infant as a prelinguistic model for language learning impairments: predicting from event-related potentials to behavior. *Neuropsychologia, 44,* 396-411.

Biermann, S. & Heil, P. (2000). Parallels between timing of onset responses of single neurons in cat and of evoked magnetic fields in human auditory cortex. *Journal of Neurophysiology, 84,* 2426-2439.

Bishop, D. V. M., Bishop, S. J., Bright, P., James, C., Delaney, T., & Tallal, P. (1999a). Different origin of auditory and phonological processing problems in children with language impairment: Evidence from a twin study. *Journal of Speech, Language, and Hearing Research, 42,* 155-168.

Bishop, D. V. M., Carlyon, R. P., Deeks, J. M., & Bishop, S. J. (1999b). Auditory temporal processing impairment: Neither necessary nor sufficient for causing language impairment in children. *Journal of Speech, Language, and Hearing Research, 42,* 1295-1310.

Bishop, D. V. M, & Snowling, M. J. (2004). Developmental dyslexia and specific language impairment: Same or different? *Psychological Bulletin, 130,* 858-886.

Booth, J. R., Perfetti, C. A., Macwhinney, B., & Hunt, S. B. (2000). The association of rapid temporal perception with orthographic and phonological processing in children and adults with reading impairment. *Scientific Studies of Reading, 4,* 101-132.

Bosnyak, D. J., Eaton, R. A., & Roberts, L. E. (2004). Distributed Auditory Cortical Representations are Modified When Nonmusicians are Trained at Pitch Discrimination with 40 Hz Amplitude Modulated Tones. *Cerebral Cortex, 14,* 1088-1099.

Bradley, L. & Bryant, P. (1983). Categorizing sounds and learning to read: A causal connection. *Nature, 301,* 419-421.

Brady, S. A. & Shankweiler, D. P. (1991). *Phonological Processes in Literacy: A Tribute to Isabelle Y Liberman*. Hillsdale, New Jersey: Lawrence Erlbaum Associates, Inc.

Breier, J. I., Gray, L. C., Fletcher, J. M., Foorman, B., & Klaas, P. (2002). Perception of speech and nonspeech stimuli by children with and without reading disability and attention deficit hyperactivity disorder. *Journal of Experimental Child Psychology, 82,* 226-250.

Bretherton, L. & Holmes, V. M. (2003). The relationship between auditory temporal processing, phonemic awareness, and reading disability. *Journal of* Experimental *Child Psychology, 84,* 218-243.

Briscoe, J., Bishop, D. V. M., & Norbury, C. (2001). Phonological processing, language, and literacy: A comparison of children with mild-to-moderate sensorineural hearing loss and those with specific language impairment. *Journal of Child Psychology and Psychiatry, 42,* 329-340.

Caclin, A., Brattico, E., Tervaniemi, M., Näätänen, R., Morlet, D., Giard, M-H., McAdams, S. (2006). Separate Neural Processing of Timbre Dimensions in Auditory Sensory Memory. *Journal of Cognitive Neuroscience, 18,* 1959-1972.

Ceponiene, R., Cheour, M., & Näätänen, R. (1998). Interstimulus interval and auditory event-related potentials in children: evidence for multiple generators. *Electroencephalography and Clinical Neurophysiology, 108,* 345-354.

Ceponiene, R., Rinne, T., & Näätänen, R. (2002). Maturation of cortical sound processing as indexed by event-related potentials. *Clinical Neurophysiology, 113,* 870-882.

Cheour, M., Korpilahti, P., Martynova, O., & Lang, A. H. (2001). Mismatch negativity and late discriminative negativity in investigating speech perception and learning in children and infants. *Audiology & Neuro-Otology, 6,* 2-11.

Clark, M. G., Rosen, G. D., Tallal, P., & Fitch, R. H. (2000). Impaired processing of complex auditory stimuli in rats with induced cerebrocortical microgyria: An animal model of developmental language disabilities. *Journal of Cognitive Neuroscience, 12,* 828-839.

Cope, N., Harold, D., Hill, G., Moskvina, V., Stevenson, J., Holmans, P., Owen, M. J., O'Donovan, M. C., & Williams, J. (2005). Strong evidence that KIAA0319 on chromosome 6p is a susceptibility gene for developmental dyslexia. *American Journal of Human Genetics, 76,* 581-591.

Corriveau, K., Pasquini, E., & Goswami, U. (2007). Basic auditory processing skills and specific language impairment: A new look at an old hypothesis. *Journal of Speech, Language, and Hearing Research, 50,* 647-666.

Crowley, K. E. & Colrain, I. M. (2004). A review of the evidence for P2 being an independent component process: Age, sleep and modality. *Clinical Neurophysiology, 115,* 732-744.

Curtin, S., Mintz, T. H., & Christiansen, M. H. (2005). Stress changes the representational landscape: Evidence from word segmentation. *Cognition, 96,* 233-262.

Deutsch, G. K., Dougherty, R. F., Bammer, R., Siok, W. T., Gabrieli, J. D. E., & Wandell, B. (2005). Children's reading performance is correlated with white matter structure measured by diffusion tensor imaging. *Cortex, 41,* 354-363.

Drullman, R., Festen, J. M., & Plomp, R. (1994). Effect of temporal envelopment smearing of speech reception. *Journal of the Acoustical Society of America, 95*, 1053-1064.

Escera, C., Alho, K., Schröger, E., & Winkler, I. (2000). Involuntary attention and distractibility as evaluated with event-related brain potentials. *Audiology & Neuro-Otology, 5,* 151-166.

Farmer, M. E. & Klein, R. M. (1995). The evidence for a temporal processing deficit linked to dyslexia: A review. *Psychonomic Bulletin & Review, 2,* 460-493.

Fitch, R. H., Tallal, P., Brown, C. P., Galaburda, A. M., & Rosen, G. D. (1994). Induced microgyria and auditory temporal processing in rats: A model for language impairment? *Cerebral Cortex, 4,* 260-270.

France, S. J., Rosner, B. S., Hansen, P. C., Calvin, C., Talcott, J. B., Richardson, A. J., & Stein, J. F. (2002). Auditory frequency discrimination in adult developmental dyslexics. *Perception & Psychophysics, 64,* 169-179.

Frenkel, M., Sherman, G. F., Bashan, K. A., Galaburda, A. M., & LoTurco, J. J. Neocortical ectopias are associated with attenuated neurophysiological responses to rapidly changing auditory stimuli. *NeuroReport, 11,* 575-579.

Friedman, D., Cycowicz, Y. M., & Gaeta, H. (2001). The novelty P3: An event-related brain potential (ERP) sign of the brain's evaluation of novelty. Neuroscience *& Biobehavioral Reviews, 25,* 355-373.

Galaburda, A. M., LoTurco J., Ramus, F., Fitch R. H., & Rosen, G. D. From genes to behavior in developmental dyslexia. *Nature Neuroscience, 9,* 1213-1217.

Galaburda, A. M., Menard, M. T., & Rosen, G. D. (1994). Evidence for aberrant auditory anatomy in developmental dyslexia. *Proceedings of the National Academy of Sciences of the United States of America, 91,* 8010-8013.

Galaburda, A. M., Sherman, G. F., Rosen, G. D., Aboitiz, F., & Geschwind, N. (1985). Developmental dyslexia: four consecutive patients with cortical anomalies. *Annals of Neurology, 18,* 222-234.

Galaburda, A. M. (1999). Developmental dyslexia: A multilevel syndrome. *Dyslexia:* An *International Journal of Research and Practice, 5,* 183-191.

Goswami, U., Thomson, J., Richardson, U., Stainthorp, R., Hughes, D., Rosen, S., & Scott, S. (2002). Amplitude envelope onsets and developmental dyslexia: A new hypothesis. *Proceedings of the National Academy of Sciences of the United States of America, 99,* 10911-10916.

Gumenyuk, V., Korzyukov, O., Alho, K., Escera, C., Schroger, E., Ilmoniemi, R. J., & Näätänen, R. (2001). Brain activity index of distractibility in normal school-age children. *Neuroscience Letters, 314,* 147-150.

Habib, M. (2000). The neurological basis of developmental dyslexia: An overview and working hypothesis. *Brain, 123,* 2373-2399.

Halliday, L. F. & Bishop, D. V. M. (2006). Auditory frequency discrimination in children with dyslexia. *Journal of Research in Reading, 29,* 213-228.

Hannula-Jouppi, K., Kaminen-Ahola, N., Taipale, M., Eklund, R., Nopola-Hemmi, J., Kaariainen, H., & Kere, J. (2005). The axon guidance receptor gene ROBO1 is a candidate gene for developmental dyslexia. *PLoS Genetics, 1,* e50.

Heiervang, E., Stevenson, J., & Hugdahl, K. (2002). Auditory processing in children with dyslexia. *Journal of Child Psychology and Psychiatry, 43,* 931-938.

Heil, P. (1997a). Auditory cortical onset responses revisited. I. First-spike timing. Journal *of Neurophysiology, 77,* 2616-2641.

Heil, P. (1997b). Auditory cortical onset responses revisited. II. Response strength. *Journal of Neurophysiology, 77,* 2642-2660.

Heil, P. & Irvine, D. R. (1997). First-spike timing of auditory-nerve fibers and comparison with auditory cortex. *Journal of Neurophysiology, 78,* 2438-2454.

Heil, P. & Neubauer, H. (2001). Temporal integration of sound pressure determines thresholds of auditory-nerve fibers. *Journal of Neuroscience, 21,* 7404-7415.

Heil, P. (2003). Coding of temporal onset envelope in the auditory system. *Speech Communication, 41,* 123-134.

Heil, P. (2004). First-spike latency of auditory neurons revisited. *Current Opinion in Neurobiology, 14,* 461-467.

Heim, S., & Keil, A. (2004). Large-scale neural correlates of developmental dyslexia. European *Child & Adolescent Psychiatry, 13,* 125-140.

Helenius, P., Salmelin, R., Richardson, U., Leinonen, S., & Lyytinen, H. (2002). Abnormal auditory cortical activation in dyslexia 100 msec after speech onset. *Journal of Cognitive Neuroscience, 14,* 603-617.

Herman, A. E., Galaburda, A. M., Fitch, R. H., Carter, A. R., & Rosen, G. D. (1997). Cerebral microgyria, thalamic cell size and auditory temporal processing in male and female rats. *Cerebral Cortex, 7,* 453-464.

Hugdahl, K., Heiervang, E., Ersland, L, Lundervold, A., Steinmetz H., & Smievoll A. I. (2003). Significant correlation between MR measures of planum temporale and dichotic processing of syllables in dyslexic children. *Neuropsyhologia, 41,* 666-675.

Johnstone, S. J., Barry, R. J., Anderson, J. W., & Coyle, S. F. (1996). Age-related changes in child and adolescent event-related potential component morphology, amplitude and latency to standard and target stimuli in an auditory oddball task. *International Journal of Psychophysiology, 24,* 223-238.

Jusczyk, P. W., Houston, D. M., & Newsome, M. (1999). The beginnings of word segmentation in English-learning infants. *Cognitive Psychology, 39,* 159-207.

Klingberg, T., Hedehus, M., Temple, E., Salz, T., Gabrieli, J. D. E., Moseley, M. E., & Poldrack, R. A. (2000). Microstructure of temporo-parietal white matter as a basis for reading ability: evidence from diffusion tensor magnetic resonance imaging. *Neuron, 25,* 493-500.

Kodera, K., Hink, R. F., Yamada, O., & Suzuki, J. I. (1979). Effects of rise time on simultaneously recorded auditory-evoked potentials from the early, middle and late ranges. *Audiology, 18,* 395-402.

Kujala, T., Lovio, R., Lepistö, T., Laasonen, M., & Näätänen, R. (2006). Evaluation of multi-attribute auditory discrimination in dyslexia with the mismatch negativity. *Clinical Neurophysiology, 117,* 885-893.

Kujala, T., Tervaniemi, M., & Schröger, E. (2007). The mismatch negativity in cognitive and clinical neuroscience: theoretical and methodological considerations. *Biological Psychology, 74,* 1-19.

Lachmann, T., Berti, S., Kujala, T., & Schröger, E. (2005). Diagnostic subgroups of developmental dyslexia have different deficits in neural processing of tones and phonemes. *International Journal of Psychophysiology, 56,* 105-120.

Larsen, J. P., Hoien, I., Lundberg, H., & Odegaard, H. (1990). MRI evaluation of the size and asymmetry of the planum temporale in adolescents and developmental dyslexia. *Brain and Language, 39,* 289-301.

Leonard, C. M., Eckert, M. A., Lombardino, L. J., Oakland, T., Kranzler, J., Mohr, C. M., King, W. M., & Freeman, A. (2001). Anatomical risk factors for phonological dyslexia. *Cerebral Cortex, 11,* 148-157.

Livingstone, M. (1993). Parallel processing in the visual system and the brain: Is one subsystem selectively affected in dyslexia? In A.M.Galaburda (Ed.), *Dyslexia and development: Neurobiological aspects of extra-ordinary brains* (pp. 237-256). Cambridge, MA: Harvard University Press.

Livingstone, M. S., Rosen, G. D., Drislane, F. W., & Galaburda, A. M. (1991). Physiological and anatomical evidence for a magnocellular defect in developmental dyslexia. *Proceedings of the National Academy of Sciences of the United States of America, 88,* 7943-7947.

Loveless, N. E. & Brunia, C. H. M. (1990). Effects of rise-time on late components of the auditory evoked potential. *Journal of Psychophysiology, 4,* 369-380.

Lyon, G. R., Shaywitz, S. E., & Shaywitz, B. A. (2003). A definition of dyslexia. Annals *of Dyslexia, 53,* 1-14.

Lyytinen, H., Blomberg, A. P., & Näätänen, R. (1992). Event-related potentials and autonomic responses to a change in unattended auditory stimuli. *Psychophysiology, 29,* 2-14.

Lyytinen, H., Aro, M., Eklund, K., Erskine, J., Guttorm, T., Laakso, M. L., Leppänen, P. H. T., Lyytinen, P., Poikkeus, A-M., Richardson, U., & Torppa, M. (2004). The development of children at familial risk for dyslexia: Birth to early school age. *Annals of Dyslexia, 54,* 184-220.

Marshall, C. M., Snowling, M. J., & Bailey, P. J. (2001). Rapid auditory processing and phonological ability in normal readers and readers with dyslexia. *Journal of Speech, Language, and Hearing Research, 44,* 925-940.

Maurer, U. B. (2003). Altered responses to tone and phoneme mismatch in kindergartners at familial dyslexia risk. *NeuroReport, 14,* 2245-2250.

McAnally, K. I. & Stein, J. F. (1997). Scalp potentials evoked by amplitude-modulated tones in dyslexia. *Journal of Speech, Language, and Hearing Research, 40,* 939-945.

McArthur, G. M. & Bishop, D. V. M. (2005). Speech and non-speech processing in people with specific language impairment: A behavioural and electrophysiological study. *Brain and Language, 94,* 260-273.

Menell, P., McAnally, K. I., & Stein, J. F. (1999). Psychophysical sensitivity and physiological response to amplitude modulation in adult dyslexic listeners. Journal *of Speech, Language, and Hearing Research, 42,* 797-803.

Meng, H., Smith, S. D., Hager, K., Held, M., Liu, J., Olson, R. K., Pennington, B. F., DeFries, J. C., Glernter, J., O'Reilly-Pol, T., Somlo, S., Skudlarski, P., Shaywitz, S. E., Shaywitz, B. A., Marchione, K., Wang, Y., Paramasivam, M., LoTurco, J. J., Page, G. P., & Gruen J. R. (2005). DCDC2 is associated with reading disability and modulates neuronal development in the brain. *Proceedings of the National Academy of Sciences of the United States of America, 102,* 17053-17058.

Morton, J., Marcus, S., & Frankish, C. (1976). Perceptual centers (P-centers). *Psychological Review, 83,* 405-408.

Muneaux, M., Ziegler, J. C., True, C., Thomson, J., & Goswami, U. (2004). Deficits in beat perception and dyslexia: Evidence from French. *NeuroReport, 15,* 1255-1259.

Näätänen, R. (1992). *Attention and brain function*. Hillsdale, NJ: Lawrence Erlbaum.

Näätänen, R. & Alho, K. (1997). Mismatch negativity - the measure for central sound representation accuracy. *Audiology & Neuro-Otology, 2,* 341-353.

Näätänen, R. & Picton, T. W. (1987). The N1 wave of the human electric and magnetic response to sound: A review and an analysis of the component structure. *Psychophysiology, 24,* 375-425.

Nagarajan, S., Mahncke, H., Salz, T., Tallal, P., Roberts, T., & Merzenich, M. M. (1999). Cortical auditory signal processing in poor readers. *Proceedings of the* National *Academy of Sciences of the United States of America, 96,* 6483-6488.

Niogi, S, N. & McCandliss, B. D. (2006). Left lateralized white matter microstructure accounts for individual differences in reading ability and disability. *Neuropsychologia, 44,* 2178-2188.

Nittrouer, S. (1999). Do temporal processing deficits cause phonological processing problems? *Journal of Speech, Language and Hearing Research, 42,* 925-942.

Novitski, N., Tervaniemi, M., Huotilainen, M., & Näätänen, R. (2004). Frequency discrimination at different frequency levels as indexed by electrophysiological and behavioral measures. *Cognitive Brain Research, 20,* 26-36.

Pakarinen, S., Takegata, R., Rinne, T., Huotilainen, M., & Näätänen, R. (2007). Measurement of extensive auditory discrimination profiles using the mismatch negativity (MMN) of the auditory event-related potential (ERP). *Clinical Neurophysiology, 118,* 177-185.

Pasquini, E. S., Corriveau, K. H., & Goswami, U. (2007). Auditory processing of amplitude envelope rise time in adults diagnosed with developmental dyslexia. *Scientific Studies of Reading, 11,* 259-286.

Paracchini, S., Thomas, A., Castro, S., Lai, C., Paramasivam, M., Wang, Y., Keating, B. J., Taylor, J. M., Hacking, D. F., Scerri, T., Francks, C., Richardson, A. J., Wade-Martins, R., Stein J. F., Knight, J. C., Copp, A. J., LoTurco, J., & Monaco A. P. (2006). The chromosome 6p22 haplotype associated with dyslexia reduces the expression of KIAA0319, a novel gene involved in neuronal migration. *Human Molecular Genetics, 15,* 1659-1666.

Paterson, S. J., Brown, J. H., Gsödl, M. K., Johnson, M. H., & Karmiloff-Smith, A. (1999). Cognitive modularity and genetic disorders. *Science, 286,* 2355-2358.

Peiffer, A. M., Friedman, J. T., Rosen, G. D., & Fitch, R. H. (2004a). Impaired gap detection in juvenile microgyric rats. *Developmental Brain Research, 152,* 93-98.

Peiffer, A. M., Rosen, G. D., & Fitch, R. H. (2004b). Sex differences in rapid auditory processing deficits in microgyric rats. *Developmental Brain Research, 148,* 53-57.

Peiffer, A. M., Rosen, G. D., & Fitch, R. H. (2002). Rapid auditory processing and MGN morphology in microgyric rats reared in varied acoustic environments. *Developmental Brain Research, 138,* 187-193.

Pennington, B. F. & Lefly, D. L. (2001). Early reading development in children at family risk for dyslexia. *Child Development, 72,* 816-833.

Von Plessen, K., Lundervold, A., Duta, N., Heiervang, E., Klauschen, F., Smievoll, A. I., Ersland, L., & Hugdahl, K. (2002). Less developed corpus callosum in dyslexic subjects-a structural MRI study. *Neuropsychologia, 40,* 1035-1044.

Ponton, C., Eggermont, J. J., Khosla, D., Kwong, B., & Don, M. (2002). Maturation of human central auditory system activity: Separating

auditory evoked potentials by dipole source modeling. *Clinical Neurophysiology, 113,* 407-420.

Ponton, C. W., Eggermont, J. J., Kwong, B., & Don, M. (2000). Maturation of human central auditory system activity: evidence from multi-channel evoked potentials. *Clinical Neurophysiology, 111,* 220-236.

Ramus, F. (2003). Developmental dyslexia: specific phonological deficit or general sensorimotor dysfunction? *Current Opinion in Neurobiology, 13,* 212-218.

Ramus, F. (2004). Neurobiology of dyslexia: a reinterpretation of the data. *Trends in Neurosciences, 27,* 720-726.

Ramus, F., Rosen, S., Dakin, S. C., Day, B. L., Castellote, J. M., White, S., & Frith, U. (2003). Theories of developmental dyslexia: Insights from a multiple case study of dyslexic adults. *Brain, 126,* 841-865.

Recanzone, G. H., Guard, D. C., & Phan, M. L. (2000). Frequency and intensity response properties of single neurons in the auditory cortex of the behaving macaque monkey. *Journal of Neurophysiology, 83,* 2315-2331.

Reed, M. A. (1989). Speech perception and the discrimination of brief auditory cues in reading disabled children. *Journal of Experimental Child Psychology, 48,* 270-292.

Reinke, K. S., He, Y., Wang, C., & Alain, C. (2003). Perceptual learning modulates sensory evoked response during vowel segregation. *Cognitive Brain Research, 17,* 781-791.

Remez, R. E., Rubin, P. E., Pisoni, D. B., & Carrell, T. D. (1981). Speech perception without traditional speech cues. *Science, 212,* 947-950.

Renvall, H. & Hari, R. (2003). Diminished auditory mismatch fields in dyslexic adults. *Annals of Neurology, 53,* 551-557.

Richardson, U., Thomson, J. M., Scott, S. K., & Goswami, U. (2004). Auditory processing skills and phonological representation in dyslexic children. *Dyslexia: An International Journal of Research & Practice, 10,* 215-233.

Romani, G. L., Williamson, S. J., & Kaufman, L. (1982). Tonotopic organization of the human auditory cortex. *Science, 216,* 1339-1340.

Rosen, G. D., Burstein, D., & Galaburda, A. M. (2000). Changes in efferent and afferent connectivity in rats with induced cerebrocortical microgyria. *Journal of Comparative Neurology, 418,* 423-440.

Rosen, G. D. & Galaburda, A. M. (2000). Single cause, polymorphic neuronal migration disorders: an animal model. *Developmental Medicine & Child Neurology, 42,* 652-662.

Rosen, G. D., Herman, A. E., & Galaburda, A. M. (1997). MGN neuronal size distribution following induced neocortical malformations: the effect of perinatal gonadal steroids. *Society for Neuroscience Abstracts, 22,* 485.

Rosen, G. D., Herman, A. E., & Galaburda, A. M. (1999). Sex differences in the effects of early neocortical injury on neuronal size distribution of the medial geniculate nucleus in the rat are mediated by perinatal gonadal steroids. *Cerebral Cortex, 9,* 27-34.

Rosen, G. D., Sherman, G. F., & Galaburda, A. M. (1996). Birthdates of neurons in induced microgyria. *Brain Research, 727,* 71-78.

Rosen, S. (2003). Auditory processing in dyslexia and specific language impairment: is there a deficit? What is its nature? Does it explain anything? *Journal of Phonetics, 31,* 509-527.

Rosner, B. S., Talcott, J. B., Witton, C., Hogg, J. D., Richardson, A. J., Hansen, P. C., & Stein, J. F. (2003). The perception of "sine-wave speech" by adults with developmental dyslexia. *Journal of Speech, Language, and Hearing Research, 46,* 68-79.

Ruhm, H. B. & Jansen, J. W. (1969). Rate of stimulus change and the evoked response: I. Signal rise-time. *Journal of Auditory Research, 9,* 211-216.

Rushby, J. A., Barry, R. J., & Doherty, R. J. (2005). Separation of the components of the late positive complex in an ERP dishabituation paradigm. *Clinical Neurophysiology, 116,* 2363-2380.

Salminen, H. K., Hämäläinen, J. A., Guttorm, T. K., Eklund, K., Lyytinen, H. & Leppänen, P. H. T. (submitted). Event-related potentials reveal atypical pitch-change processing in newborns at-risk for dyslexia who later become dyslexic readers.

Schulte-Körne, G., Deimel, W., Bartling, J., & Remschmidt, H. (1998). Auditory processing and dyslexia: Evidence for a specific speech processing deficit. *NeuroReport, 9,* 337-340.

Schulte-Körne, G., Deimel, W., Bartling, J., & Remschmidt, H. (1999). Pre-attentive processing of auditory patterns in dyslexic human subjects. *Neuroscience Letters, 276,* 41-44.

Schulte-Körne, G., Deimel, W., Bartling, J., & Remschmidt, H. (2001). Speech perception deficit in dyslexic adults as measured by mismatch negativity (MMN). *International Journal of Psychophysiology, 40,* 77-87.

Scott, S. K. (1993). *P-centres in speech: an acoustic analysis*. University College London, UK.

Scott, S. K. (1998). The point of P-centres. *Psychological Research.Special Issue: Timing in perception and action, 61,* 4-11.

Shannon, R. V., Zeng, F. G., Kamath, V., Wygonski, J., & Ekelid, M. (1995). Speech recognition with primarily temporal cues. *Science, 270,* 303-307.

Shapleske, J., Rossell, S. L., Woodruff, P. W. R., & David, A. S. (1999). The planum temporale: a systematic, quantitative review of its structural, functional and clinical significance. *Brain Research Reviews, 29,* 26-49.

Sharma, M., Purdy, S. C., Newall, P., Wheldall, K., Beaman, R., & Dillon, H. (2006). Electrophysiological and behavioral evidence of auditory processing deficits in children with reading disorder. *Clinical Neurophysiology, 117,* 1130-1144.

Skottun, B. C. (2000). The magnocellular deficit theory of dyslexia: the evidence from contrast sensitivity. *Vision Research, 40,* 111-127.

Stanovich, K. E. (1998). Refining the Phonological Core Deficit Model. *Child and Adolescent Mental Health, 3,* 17-21.

Stein, J. (2001). The magnocellular theory of developmental dyslexia. *Dyslexia: An International Journal of Research and Practice, 7,* 12-36.

Stein, J. & Walsh, V. (1997). To see but not to read: The magnocellular theory of dyslexia. *Trends in Neurosciences, 20,* 147-152.

Stein, J. & Talcott, J. (1999). Impaired neuronal timing in developmental dyslexia--the magnocelluar hypothesis. *Dyslexia: An International Journal of Research and Practice, 5,* 59-77.

Studdert-Kennedy, M. & Mody, M. (1995). Auditory temporal perception deficits in the reading-impaired: A critical review of the evidence. *Psychonomic Bulletin & Review, 2,* 508-514.

Taipale, M., Kaminen, N., Nopola-Hemmi, J., Haltia, T., Myllyluoma, B., Lyytinen, H., Muller, K., Kaaranen, M., Lindsberg P. J., Hannula-Jouppi, K., & Kere, J. (2003). A candidate gene for developmental dyslexia encodes a nuclear tetratricopeptide repeat domain protein dynamically regulated in brain. *Proceedings of the National Academy of Sciences of the United States of America, 100,* 11553-11558.

Tallal, P. (1980). Auditory temporal perception, phonics, and reading disabilities in children. *Brain and Language, 9,* 182-198.

Tallal, P., Miller, S., & Fitch, R. H. (1993). Neurobiological basis of speech: A case for the preeminence of temporal processing. *Annals of the New York* Academy of Sciences, 682, 27-47.

Tallal, P. & Piercy, M. (1973). Defects of non-verbal auditory perception in children with developmental aphasia. *Nature, 241,* 468-469.

Tallal, P. & Gaab, N. (2006). Dynamic auditory processing, musical experience and language development. *Trends in Neurosciences, 29,* 382-390.

Thomson, J. M., Fryer, B., Maltby, J., & Goswami, U. (2006). Auditory and motor rhythm awareness in adults with dyslexia. *Journal of Research in Reading, 29,* 334-348.

Threlkeld, S. W., McClure, M. M., Bai, J., Wang, Y., LoTurco, J. J., Rosen, G. D., & Fitch, H. (2007). Developmental disruptions and behavioral impairments in rats following in utero RNAi of Dyx1c1. *Brain Research Bulletin, 71,* 508-514.

Threlkeld, S. W., McClure, M. M., Rosen, G. D., & Fitch, R. H. (2006). Developmental timeframes for induction of microgyria and rapid auditory processing deficits in the rat. *Brain Research, 1109,* 22-31.

Tremblay, K., Kraus, N., Carrell, T., & McGee, T. (1997). Central auditory system plasticity: Generalization to novel stimuli following listening training. *Journal of Acoustical Society of America, 102,* 3762-3773.

Vellutino, F. R., Fletcher, J. M., Snowling, M. J., & Scanlon, D. M. (2004). Specific reading disability (dyslexia): What have we learned in the past four decades? *Journal of Child Psychology & Psychiatry, 45,* 2-40.

Wagner, R. K. & Torgesen, J. K. (1987). The nature of phonological processing and its causal role in the acquisition of reading skills. *Psychological Bulletin, 101,* 192-212.

Wang, Y., Paramasivam, M., Thomas, A., Bai, J., Kaminen-Ahola, N., Kere, J., Voskuil, J., Rosen, G. D., Galaburda, A. M., & Loturco, J. J. (2006). DYX1C1 functions in neuronal migration in developing neocortex. *Neuroscience*, *143,* 515-522.

de Weirdt, W. D. (1988). Speech perception and frequency discrimination in good and poor readers. *Applied Psycholinguistics, 9,* 163-183.

White, S., Frith, U., Milne, E., Rosen, S., Swettenham, J., & Ramus, F. (2006a). A double dissociation between sensorimotor impairments and reading disability: A comparison of autistic and dyslexic children. *Cognitive Neuropsychology, 23,* 748-761.

White, S., Milne, E., Rosen, S., Hansen, P., Swettenham, J., Frith, U., & Ramus, F. (2006b). The role of sensorimotor impairments in dyslexia: A multiple case study of dyslexic children. *Developmental Science, 9,* 237-255.

Witton, C., Talcott, J. B., Hansen, P. C., Richardson, A. J., Griffiths, T. D., Rees, A., Stein, J. F., & Green, G. G. (1998). Sensitivity to dynamic auditory and visual stimuli predicts nonword reading ability in both dyslexic and normal readers. *Current Biology, 8,* 791-797.

Witton, C., Stein, J. F., Stoodley, C. J., Rosner, B. S., & Talcott, J. B. (2002). Separate influences of acoustic AM and FM sensitivity on the phonological decoding skills of impaired and normal readers. *Journal of Cognitive Neuroscience, 14,* 866-874.

Wright, B. A. & Zecker, S. G. (2004). Learning problems, delayed development, and puberty. *Proceedings of the National Academy of Sciences of the United States of America, 101,* 9942-9946.