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Enhancement of Brain Event-Related Potentials to Speech Sounds Is Associated With Compensated Reading Skills in Dyslexic Children with Familial Risk for Dyslexia

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Abstract

Specific reading disability, dyslexia, is a prevalent and heritable disorder impairing reading acquisition characterized by a phonological deficit. However, the underlying mechanism of how the impaired phonological processing mediates resulting dyslexia or reading disabilities remains still unclear. Using ERPs we studied speech sound processing of 30 dyslexic children with familial risk for dyslexia, 51 typically reading children with familial risk for dyslexia, and 58 typically reading control children. We found enhanced brain responses to shortening of a phonemic length in pseudo-words (/at:a/ vs. /ata/) in dyslexic children with familial risk as compared to other groups. The enhanced brain responses were associated with better performance in behavioral phoneme length discrimination tasks, as well as with better reading and writing accuracy. Source analyses revealed that the brain responses of sub-group of dyslexic children with largest responses originated from a more posterior area of the right temporal cortex as compared to the responses of the other participants. This is the first electrophysiological evidence for a possible compensatory speech perception mechanism in dyslexia. The best readers within the dyslexic group have probably developed alternative strategies which employ compensatory mechanisms substituting their possible earlier deficit in phonological processing and might therefore be able to perform better in phoneme length discrimination and reading and writing accuracy tasks. However, we speculate that for reading fluency compensatory mechanisms are not that easily built and dyslexic children remain slow readers during their adult life.

Keywords: Dyslexia, Speech perception, ERP, EEG, Phonemic length discrimination, Compensation

1 Introduction

1.1 Background

Specific reading disability, dyslexia, is a problem in learning to read and write despite adequate cognitive level, training, motivation, and other extraneous factors (Lyon, Shaywitz, & Shaywitz, 2003; Vellutino, Fletcher, Snowling, & Scanlon, 2004). Heritability and familial clustering of dyslexia has been well established pointing to genetic factors behind dyslexia (Galaburda, 2005; Lyon et al., 2003; Lyytinen et al., 2004; Vellutino et al., 2004). Phonological skills, i.e., ability to recognize and manipulate speech sound elements, is one of the key components for acquiring the ability to read, and deficit in phonological processing is one of the most relevant factors linked to dyslexia (Goswami, 2002; Ramus, 2003; Snowling, 2000; Stanovich, 1988; Torgesen, Wagner, Rashotte, Burgess, & Hecht, 1997; Vellutino et al., 2004; Wagner, & Torgesen, 1987). However, the underlying mechanism of how the impaired phonological processing mediates resulting dyslexia or reading disabilities remains still unclear. Here, we studied the brain event-related potential (ERPs) responses in dyslexic and typically reading children with and without familial risk for dyslexia to pseudo-words. Pseudo-words varied in consonant duration, i.e., phonemic length, which is a semantically distinguishing feature in the Finnish language. Also association of brain responses with outcomes in phonemic length discrimination, reading, and writing tasks were investigated.

1.1.1 Phonological processing deficit

Deficit in phonological processing is often suggested to derive from auditory or speech processing problems via inaccurate or otherwise inadequate phonological representations (Elbro, Borstrøm, & Petersen, 1998; Griffiths, & Snowling, 2002; McBride-Chang, 1995; Mody, Studdert-Kennedy, & Brady, 1997; Snowling, 2000). The brain's ability to discriminate between acoustic features in speech, crucial for formation of speech sound representations, may be insufficient in dyslexic readers. Defective representations in turn may lead to disability in reading and spelling by hindering the learning of fluent and automatic decoding of phoneme-

grapheme correspondences (Elbro et al., 1998; Share, 1995; Snowling, 2000). Several theories have been formulated for the association between auditory and speech processing deficits and reading problems. The rapid auditory temporal processing (RATP) theory suggests that dyslexics have difficulties in perceiving brief auditory stimuli when they are presented in rapid succession (Tallal, & Piercy, 1973; Tallal, 1980; 2004). It has been proposed that perception of slow modulations in speech, reflected in rise time discrimination, would be impaired in dyslexics (Goswami et al., 2002; Goswami, 2011). Furthermore, studies using functional magnetic resonance imaging (fMRI) to investigate speech processing have found deficits in access to phonetic representations without deficits at the cortical processing of speech sounds (Boets et al., 2013). However, there is no consensus yet on the mechanism how the deficit in phonological awareness is associated with the reading deficit or dyslexia. Nevertheless, there is strong evidence for neurobiological risk factors for dyslexia (for reviews see Habib, 2000; Démonet, Taylor, & Chaix, 2004; Richlan, Kronbichler, & Wimmer, 2011; Richlan, Kronbichler, & Wimmer, 2013). These neurobiological risk factors specifically related to speech include, for example, reduced gray matter volume at posterior Sylvian areas (Richlan et al., 2013), structural brain anomalies, such as neuronal ectopias around the Sylvian fissure (Galaburda et al., 1985), and abnormal activation and connectivity in posterior and perisylvian systems (Démonet et al., 2004).

1.1.2 Structural brain differences

Anomalies in dyslexic brain have been seen in autopsy and brain imaging studies (for reviews see Eckert, 2004; Habib, 2000). Reduction in gray matter volume has been found in areas relevant in speech and language processing, such as the superior temporal gyrus and the inferior frontal gyrus (Frye et al., 2010; Steinbrink et al., 2008). Gray matter volume in the left anterior fusiform gyrus/hippocampus, left precuneus, right hippocampus, and right anterior cerebellum have been found to increase during reading intervention in dyslexic children (Krafnick, Flowers, Napoliello, & Eden, 2011). Furthermore, in typical readers, gray matter thickening in the left inferior frontal cortex has been found to be associated with improving phonological skills (Lu et al., 2007). Compared to typical readers, many areas in dyslexics have been found to contain more ectopias, displacements of neurons developed during neuronal migration, near and around

Sylvian fissure, particularly in the left hemisphere (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985; Galaburda, 2005; Ramus, 2004). Also, dyslexic brains are often characterized by reduced asymmetry particularly at the posterior superior temporal gyrus, i.e., symmetrical plana temporale in the posterior Sylvian fissure (Galaburda, LeMay, Kemper, & Geschwind, 1978; Galaburda et al., 1985; Illingworth, & Bishop, 2009; Leonard, & Eckert, 2008; Sun, Lee, & Kirby, 2010). The brain symmetry in dyslexics suggest anatomical differences in areas activated heavily by speech and language and possibly differences in the distribution of activity in the left and right perisylvian cortex (Binder, Frost, Hammeke, Rao, & Cox, 1996; Galaburda et al., 1985). However, also different hemispheric symmetry patterns of posterior perisylvian areas, including planum temporale, have been observed in dyslexic individuals (Chiarello, Lombardino, Kacinik, Otto, & Leonard, 2006; Leonard et al., 1993).

1.1.3 Speech perception related brain responses

Deficits linked to the abovementioned anatomical differences include speech processing problems, which could be a cause for phonological deficits (e.g., Blomert, 2011; Price, 2012). In dyslexics, poor speech perception manifests itself as difficulties to discriminate and categorize speech sound contrasts like syllables, consonants and vowels (e.g., Bradley, & Bryant, 1978; Godfrey, Syrdal-Lasky, Millay, & Knox, 1981; Manis et al., 1997; Mody et al., 1997; Pennala et al., 2010; Reed, 1989). Nevertheless, there are studies that fail to find differences between dyslexics and controls for some speech contrasts (Blomert, Mitterer, & Paffen, 2004; Groth, Lachmann, Riecker, Muthmann, & Steinbrink, 2011). For example, Groth et al. (2011) found that dyslexics were poorer in discriminating longer vowels from shorter ones if they were made shorter by manipulation (only durational cues available), but they found no group effect for naturally shorter versus longer vowels (both spectral and durational cues available). Further, using functional magnetic resonance imaging (fMRI), Steinbrick et al. (2012) observed decreased activation of left inferior frontal gyrus and insular cortices in dyslexics during processing of the same temporal stimuli, but only in the subgroup of low performing dyslexics (Steinbrink, Groth, Lachmann, & Riecker, 2012). Also, it should be kept in mind that in certain conditions dyslexics can be even more sensitive to speech sound contrasts, i.e., dyslexics have been reported to be poorer in discriminating between phoneme categories, but more sensitive in

discriminating within category contrasts (Serniclaes, Sprenger-Charolles, Carré, & Demonet, 2001; Serniclaes, Heghe, Mousty, Carré, & Sprenger-Charolles, 2004).

Speech sound discrimination is often studied using event-related potentials (ERPs), especially the discriminative components, which are thought to be a pre-attentive index of cortical accuracy of sound processing. They capture low level processing, and therefore work as an objective measure that is not determined by level of motivation, attention or arousal (for reviews, see Bishop, 2007; Näätänen, Jacobsen, & Winkler, 2005; Schulte-Körne, & Bruder, 2010). Using ERPs to study speech sound discrimination, abnormal responses have been found in dyslexics. In most studies responses have been smaller (e.g., Bishop, 2007; Kujala et al., 2006; Maurer, Bucher, Brem, & Brandeis, 2003; Schulte-Körne, Deimel, Bartling, & Remschmidt, 1998), although in some studies larger responses have been reported (e.g., Helenius, Salmelin, Richardson, Leinonen, & Lyytinen, 2002; Hämäläinen et al., 2013). In dyslexic children, the development of ERP components has been reported to be delayed, being similar to younger typically developing children (Blomert, 2011; McArthur & Bishop, 2004), but the brain responses of children who have a history of reading difficulty but are currently reading age appropriately, i.e., compensated readers, have been found to follow those of same aged controls (Sharma et al., 2006). Sharma et al. (2006) studied three groups of school-aged children: children with current reading difficulty, compensated readers, and age appropriately reading controls. They found that compensated readers were similar in their brain responses and in behavioral auditory tasks as was the control group, whereas children with reading difficulty differed from other groups in their performance in both brain and behavioral measures.

1.1.4 Atypical quantity perception

In the ‘Quantity languages’ like Finnish, Japanese, and Swedish, phonemic length is a semantically distinguishing feature (Lidestam, 2009; Tervaniemi et al., 2006). Two qualities exist: a phoneme can be perceived either as short or long in relation to other phonemes in the word, although physically both phoneme durations vary and may even overlap in duration (Suomi, Toivanen & Ylitalo, 2008; Vainio, 2001). Differences between children at risk for dyslexia and non-risk control children have been seen in ERP responses to syllables with vowel or consonant duration changes already at birth and early childhood (Leppänen, Pihko, Eklund, & Lyytinen, 1999; Leppänen et al., 2002; Pihko et al., 1999). More recently, corresponding results

have been found in children and adults with dyslexia (e.g., Hämäläinen et al., 2013; Kujala et al., 2006; Lovio, Näätänen, & Kujala, 2010; Sharma et al., 2006). Impaired perception of phonemic length has also been found using behavioral tasks (e.g., Hämäläinen et al., 2009; Pennala et al., 2010; 2013; Richardson, Leppänen, Leiwo, & Lyytinen, 2003; Richardson, Thomson, Scott, & Goswami, 2004).

Although corresponding group differences between dyslexic and control children have been found, speech perception abilities change during development. In early childhood, native language environment starts to shape the perception of speech sounds (Kuhl, Williams, Lacerda, Stevens, & Lindblom, 1992; Kuhl et al., 2006; Ortiz-Mantilla, Hämäläinen, Musacchia, & Benasich, 2013), and improvements in speech perception accuracy are still seen during the first three grades (Pennala et al., 2010; 2013). Further, longitudinal studies have found that the differences in speech perception ability between children with and without dyslexia vary depending on age (Pennala et al., 2010), and suggestions have been made of different developmental trajectory of the perceptual abilities of children with language related difficulties (McArthur & Bishop, 2004; Wright & Zecker, 2004). Similar changes in perceptual abilities during development have been found using non-linguistic stimuli as well (Stefanics et al., 2011).

1.1.5 Maturation of ERP components

During development, brain physiology slowly changes because of, for example, myelination and changes in synaptic density, affecting also auditory brain responses (Bishop, Hardiman, Uwer, & Von Suchodoletz, 2007; Johnstone, Barry, Anderson, & Coyle, 1996; Moore & Guan, 2001; Ponton, Eggermont, Kwong, & Don, 2000; Ponton, Eggermont, Khosla, Kwong, & Don, 2002). In early infancy, broad ERP waveforms are typical, but already by the age of six months the auditory ERPs are well defined (see e.g. Leppänen et al., 2002). By pre-school and school-age, childhood ERPs are dominated by obligatory responses P1 and N250 with peaks around 100 and 250 ms, respectively (Čeponienė, Rinne, & Näätänen, 2002; Hämäläinen et al., 2013). Around 9 years of age, the most prominent auditory ERP components in adulthood, N1 and P2, begin to emerge, while P1 and N250 diminish (Hämäläinen, Leppänen, Guttorm, & Lyytinen, 2007; Ponton et al., 2000; Ruhnau, Herrmann, Maess, & Schröger, 2011). However, these changes do

not purely follow the chronological age, because also (auditory) environment, i.e., sounds surrounding us, shapes the system, e.g., through exposure to music (Partanen, Kujala, Tervaniemi, & Huotilainen, 2013). The auditory mismatch response (MMR), a component reflecting change detection process, which is detectable from a very early age, is also affected by developmental changes and acquires the waveform similar to that of an adult mismatch negativity (MMN) by school-age with a negative deflection for a deviating sound around 150-200 ms (Cheour, Leppänen, & Kraus, 2000; Cheour, Korpilahti, Martynova, & Lang, 2001; Csépe, 1995; Leppänen et al., 2004; Lohvansuu et al., 2013; Näätänen et al., 2005; Näätänen, Paavilainen, Rinne, & Alho, 2007). Late discriminative negativity (LDN) reflecting a cognitive-level preattentive processing of the deviant stimuli has been suggested to diminish in amplitude with age (Čeponienė et al., 2004; Cheour et al., 2001; Kraus et al., 1993).

1.2 Research questions

We studied auditory event-related potentials (ERPs) of school-aged children to pseudo-words differing in phonemic length, i.e., varying in the duration of a silent gap between syllables which determines the perception of a consonant duration as short or long. Stimuli were presented in unattended condition. Group differences were investigated between three groups: reading disabled children with a familial risk for dyslexia (RDFR), typically reading children with a familial risk for dyslexia (TRFR), and typically reading control children with no familial risk for dyslexia (TRC). Based on the previous studies reviewed above, we expected to see group differences between the RDFR group and typically reading groups to phonemic length contrasts. In the RDFR group the smaller amplitudes for the change detection responses whereas larger responses for the obligatory responses were expected. Previous studies have also suggested that auditory ERP amplitudes could be associated with reading and spelling skills as well as phonological skills. However, the associations could have a different direction in the three groups. Therefore, the associations between ERPs and outcomes in phonemic length discrimination, reading accuracy, reading fluency, and writing accuracy tasks were also investigated for deeper understanding of brain activation differences between groups.

2 Material and methods

2.1 Participants

Data were collected in the Jyväskylä Longitudinal Study of Dyslexia (JLD; for reviews see Lyytinen et al., 2001, 2004, 2008) when the children were at a mean age of 9.41 years (SD .34; range 8.18 - 10.23). The ERP data of 139 children (73 girls, 66 boys) were included in this study[1]. The children had no neurological disorders and their performance IQ was at least 80, as tested with the Wechsler Intelligence Scale for Children – Third Edition (WISC-III: Wechsler, 1991). The hearing levels of the children were measured with an audiogram and determined normal with the average hearing threshold (average of the both ears) being at or below 25 dB (BSA). The children were grouped into three groups according to their reading performance at the end of 2nd grade at the age of 9 years and their family risk status. Familial risk for dyslexia was defined when at least one parent had a diagnosis of dyslexia and at least one other close relative was reported to have reading disability (see Leinonen et al., 2001). The children were determined to have a reading disability if their reading performance outcome at the end of 2nd grade fell below the10th percentile of the performance of the JLD control children (N = 89) on at least three of four measures of reading/writing accuracy, at least three of four measures of reading speed, or two reading accuracy, and two reading speed tasks (for details see Eklund, Torppa, & Lyytinen, 2013). Otherwise, child's reading skills were considered to be typical. The data of 58 typically reading control children with no familial risk for dyslexia (TRC), 51 typically reading children with a familial risk for dyslexia (TRFR), and 30 children with a familial risk for dyslexia and reading disability (RDFR) were included in the current study. No

[1] Out of 164 children participating in EEG measurements altogether 25 participants were excluded from this study: 12 children whose EEG data were noisy and/or had inadequate number of accepted epochs (≤ 60), 3 children with reported reduced hearing, 4 children with performance IQ lower than 80, 3 children with ADHD, 1 children with Asperger's syndrome, 2 children with other neurological reason (one with distended cerebral ventricles and one with exceptional findings in EEG).

significant group differences were found between the groups in age or performance IQ (see Table 1).

2.2 Behavioral measures

Phonemic length discrimination, reading accuracy, reading fluency, and writing accuracy were assessed at the end of 2nd grade. The phonemic length discrimination task consisted of 22 two-, three- and four-syllable pseudo- and non-word pairs. Children were asked to determine whether words in the pair were identical or not. Reading accuracy was determined by a composite score based on reading accuracy in three- and four-syllable word (20 items) and non-word list reading tasks (20 items), whereas a composite score for reading fluency comprised of the average reading times of the abovementioned word and non-word lists. Writing accuracy was defined by a composite score of the accuracy of writing performance in four-syllable non-word dictation tests (altogether 12 items). (For details on the tests see Pennala et al., 2010; Puolakanaho et al., 2007).

2.3 Stimuli

Two naturally produced pseudo-words were used as stimuli: the short /ata/, with a total duration of 300 ms, and the long /at:a/, with a total duration of 460 ms (Figure 1). For both stimuli, the duration of the first part of the stimulus, including the initial glottal stop and the vowel /a/, was 72 ms, and the duration of the second part, comprising of the explosion of the /t/ and the final vowel /a/, was 133 ms. The short and the long stimuli differed only in the length of the silent gap, the voiceless stop of 95 ms or 255 ms, respectively, between the initial vowel and the following stop consonant. The stimuli were presented to the participants with an interstimulus interval (ISI) of 610 ms at an intensity of 75 ± 0.5 dB(A) via a loudspeaker located approximately 1 meter above the participant's head. The intensities of the stimuli were measured with a Brüel & Kjær sound level meter (type 2235) at the estimated head position of the participant.

2.4 Procedure

During the experiment, four passive oddball experiments (each lasting 20–25 min) and one equal probability (EQ) experiment (ca. 35 min) were conducted. The results of the consonant quantity stimuli from two speech oddball experiments are reported in the current paper (the results considering stop consonant change stimuli are reported elsewhere, and the results from the experiments with paired non-speech stimuli using frequency and rise time change were reported in Hämäläinen, Leppänen, Guttorm, & Lyytinen, 2008). The speech stimuli analyzed in this study were presented in two oddball paradigms (Figure 1): first with the short /ata/ as a standard (80%, 1010 trials) and the long /at:a/ as a deviant (10%, 125 trials); and second with the long /at:a/ as a standard (80%, 1010 trials) and the short /ata/ (10%, 125 trials) as a deviant (results for the other two deviants in the above paradigms, short /apa/ and long /ap:a/ (10%, 125 trials each), are reported elsewhere). The experiments were carried out in this order for each child. During the experiment, participants watched a silenced video or played a computer game and were instructed not to pay any attention to the sounds.

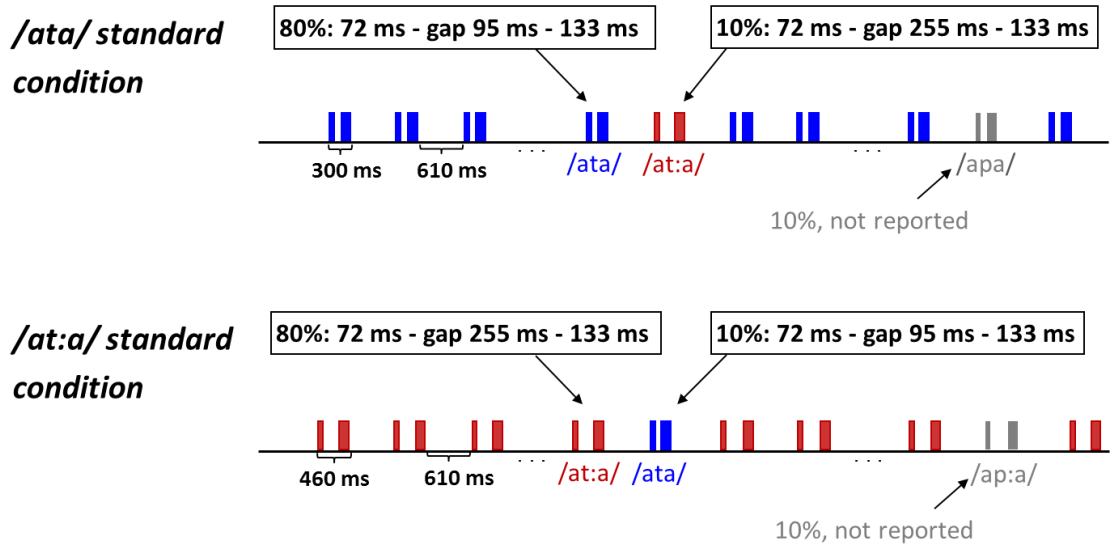

Figure 1. Schematic illustration of the experiments and stimuli.

2.5 EEG Recording

The EEG was recorded with Ag-AgCl electrodes using 128-channel Geodesic Sensor Nets (Electric Geodesics Inc.). The EEG was referred to the Cz electrode and recorded with the sampling rate of 500 Hz and the bandpass filter of 0.1 – 100 Hz. Electro-oculogram (EOG) was recorded with electrodes located above, below, and lateral to both eyes. During the experiment, impedances for the majority of the electrodes were kept below 50 kΩ. For the few electrode locations where the impedances were higher, the quality of the EEG was visually ensured. Individual EEG channels with excessive electric or other extra-cerebral noise were marked and later interpolated.

2.6 Preprocessing of the EEG Data

EEG data were preprocessed using BESA software. The raw EEG data were filtered offline with a highpass filter of 0.53 Hz (forward 6 dB) and a notch filter of 50.0 Hz and re-referred to an average reference. Eye blinks in the data were corrected before averaging with an individual eye blink correction algorithm, implemented in BESA, using principal component analysis (PCA; Ille, Berg, & Scherg, 2002). ERPs to each stimulus type were obtained by averaging EEG epochs of the time window of -300 – 1060 ms around the stimulus onset and baselined to -50 – 0 ms. Channels with multiple artifacts throughout the data were omitted from the averaging and interpolated later (see below). EEG epochs with peak-to-peak deflections of over 200 µV within the epoch time window or transient peaks over 115 µV were also excluded from the averaging. For the standard stimuli, only the responses to the pre-deviant standard stimuli (preceding either of the deviants) were included in the average. Participants having at least 60 good epochs per stimulus type in the oddball experiments were included in the analyses (the average number of accepted epochs (standard deviations) and percentages, respectively, for the RDFR group were 95.1 (14.4) and 76.08 % for the deviant and 189.2 (28.7) and 75.68% for the standard stimuli; for the TRFR group 96.2 (12.6) and 76.96% for the deviant and 190.6 (23.7) and 76.24% for the standard stimuli; for the TRC group 93.6 (11.6) and 74.88% for the deviant and 186.3 (24.2) and 74.52% for the standard stimuli). The amount of accepted epochs did not differ statistically between the groups. After averaging, a lowpass filter of 35 Hz (zero-phase 12 dB) was applied,

and the data for the channels previously omitted from the averaging were interpolated using a spherical spline interpolation method (Perrin, Pernier, Bertrand, & Echallier, 1989). The average number (standard deviation) and percentage of the interpolated channels, respectively, for the RDFR group were 11.23 (4.60) and 8.77%; for the TRFR group 8.51 (5.40) and 6.65%; for the TRC group 9.72 (4.93) and 7.59%.

2.7 Statistical Analyses

2.7.1 Permutation tests

Individual averaged ERPs were analyzed with BESA Statistics 1.0 for between and within group stimulus related differences. Permutation tests with channel and time point clustering for paired comparisons for the responses (2 standards, 2 deviants) and groups (RDFR, TRFR, TRC) were carried out. Number of permutations was set to 1000 for each contrast, channel cluster distance to 3 cm, analysis time window to 50 - 900 ms, and cluster alpha level to 0.05 (for further information on the permutation testing, see Bullmore et al., 1999; Ernst, 2004; Maris & Oostenveld, 2007).

2.7.2 Correlation analysis

Brain responses in time window showing significant group differences were correlated within the groups channel by channel with phonemic length discrimination, reading and writing accuracy, and reading fluency measures using Matlab (for details regarding these measures, see Pennala et al., 2010). Significant correlations were plotted as topographic maps separately for each group using EEGLAB toolbox (see Figure 7). Furthermore, significance of the differences in the correlation topographies between the groups was tested using Matlab (for further information on correlation testing, see McNemar, 1969).

2.7.3 Phase-locking analysis

In order to further examine the group differences for all stimuli across the whole analysis time window, phase locking values were calculated, using the coherence module in Besa Research 6.0, across the trials for each child. The data were first transformed to 26 channels corresponding to the 10-10 system. No offline filters were applied to the raw EEG data before the time-frequency calculations. Frequencies between 2 – 46 Hz were examined with 1 Hz frequency resolution and 50 ms time resolution. A complex demodulation method built in BESA was used to examine the inter-trial phase locking (ITPL) values. Differences between groups in ITPL were examined in paired comparisons using BESA Statistics 1.0.

2.7.4 Source analysis

The source localization was carried out for the grand average ERP waveforms of the groups to reveal the approximate areas generating the activity for the short /ata/ deviant stimulus, which showed most significant group differences in permutation tests (see Results). A time window of 264 – 324 ms showing the most significant group differences between the RDFR (N = 30), TRFR (N = 51), and TRC (N = 58) was used for dipole fitting. For the source localization analysis the RDFR group was divided into 3 equally sized groups on the basis of their reading accuracy performance (N = 10 for each) to explore the effect of the stronger ERP amplitudes correlating with better reading accuracy within the RDFR group. A realistic approximation head model for 8-10-year-old children, available in the BESA software, was used with brain-to-skull conductivity ratio of 30 (Hoechstetter, Berg, & Scherg, 2010). The time window used showed a stable topography for the source analysis.

3 Results

3.1 Within group comparisons

3.1.1 Deviant /ata/ vs. standard /ata/

Within all groups, the response to the deviant /ata/ was statistically significantly stronger (more negative at frontal and central areas and more positive at occipital, parietal, and temporal areas, if not mentioned otherwise) in amplitude than response to the standard /ata/ (see Figures 2A and 3). In the TRC group, the response to deviant /ata/ was stronger frontocentrally at the time window of 136 – 338 ms and at temporal-parietal-occipital area at 158 – 364 ms (p = .001 and p = .017, respectively). In the TRFR group, two clusters were significant between responses: one beginning with central distribution and shifting to bilateral temporal sites at 126 – 618 ms, being weaker in positivity between 126 – 290 ms, and another at temporal-parietal-occipital area between 88 – 372 ms, being weaker in positivity between 375 – 440 ms (p < .00001 and p = .003, respectively). In the RDFR group, responses to deviant /ata/ were stronger frontocentrally at 88 – 450 ms and at 494 – 900 ms (p < .00001 and p = .002, respectively), and bilaterally at temporal-parietal-occipital site at 108 – 448 ms and moving from right to left between 572 – 900 ms (p = .002 and p = .001, respectively). Based on the timings and topographies, these differences most likely occurred in several different components, including MMN, and, for the TRFR and RDFR groups, also LDN response at the later time window. The response at the time window of the earliest differences at 88 – 167 ms (before the onset of the second /ta/ syllable of the short /ata/) is due to a violation of a context effect created by a longer SOA when the longer /at:a/ was the standard stimulus. The consecutive time window from 170 ms onwards is likely to reflect afferent activation for the earlier second syllable /ta/ onset when the longer /at:a/ was the standard stimulus. Later on, from ca. 270 ms the deviant-standard response differences reflect overlapping effects of change detection (MMN) and N250. Similar effects also explain comparable deviant-standard response differences in relation to a shorter SOA when short /ata/ was the standard stimulus (see Figure 1).

3.1.2 Deviant /at:a/ vs. standard /at:a/

Within all groups, the responses to the deviant /at:a/ differed from the responses to the standard /at:a/ (see Figures 2B and 3): in the TRC group frontocentral activation between 124 – 280 ms was more negative for the standard (p = .011). In the TRFR group, responses were stronger for the deviant as compared to the response to the standard stimulus at frontocentral area, being more negative at 266 – 424 ms, and occipital site, being more positive at 278 – 670 ms (p = .002 and p = .010, respectively). In the RDFR group, centrally distributed activation between 256 – 520 ms was more negative for the deviant stimulus, and frontally distributed activation between 146 – 264 ms was more negative for the standard stimulus (p = .003 and p = .049, respectively).

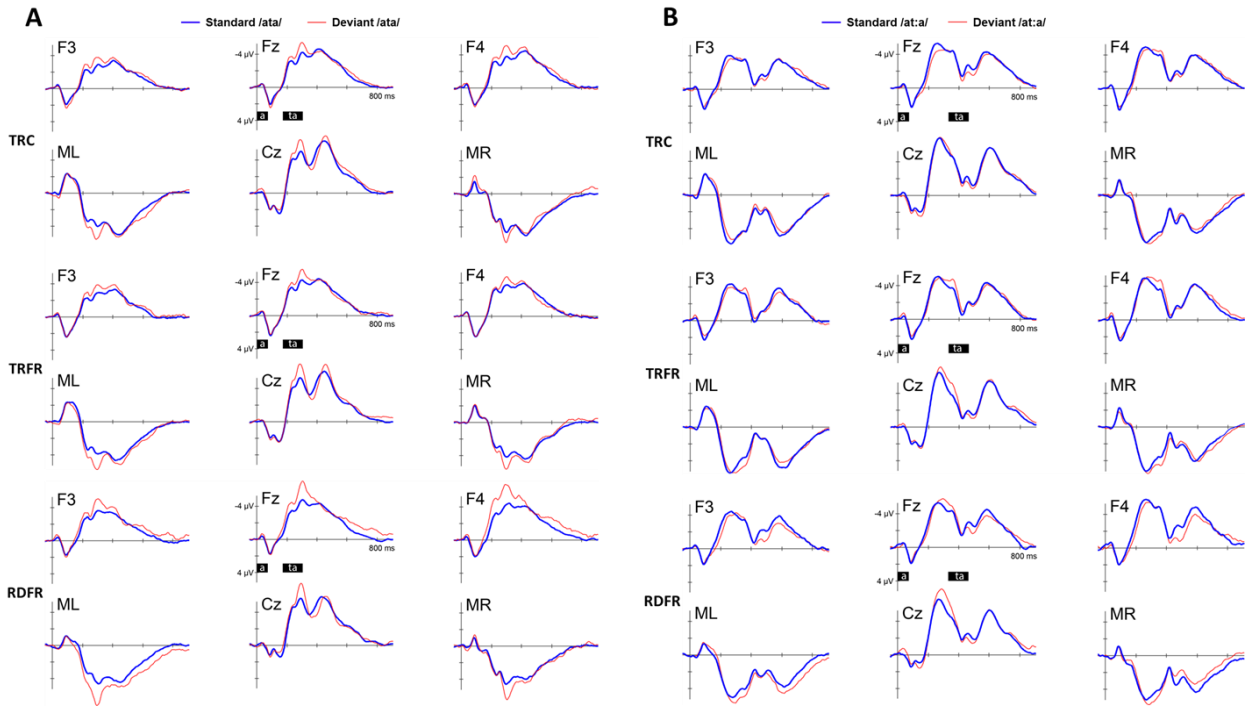

Figure 2. Grand average ERP waveforms for the stimuli with a short (A) and for long (B) consonant length in the three groups: children with a familial risk for dyslexia and reading disability (RDFR, N = 30), typically reading children with a familial risk for dyslexia (TRFR, N = 51), and typically reading controls (TRC, N = 58). Vertical tick marks represent 2 µV and horizontal tick marks 200 ms (negativity up).

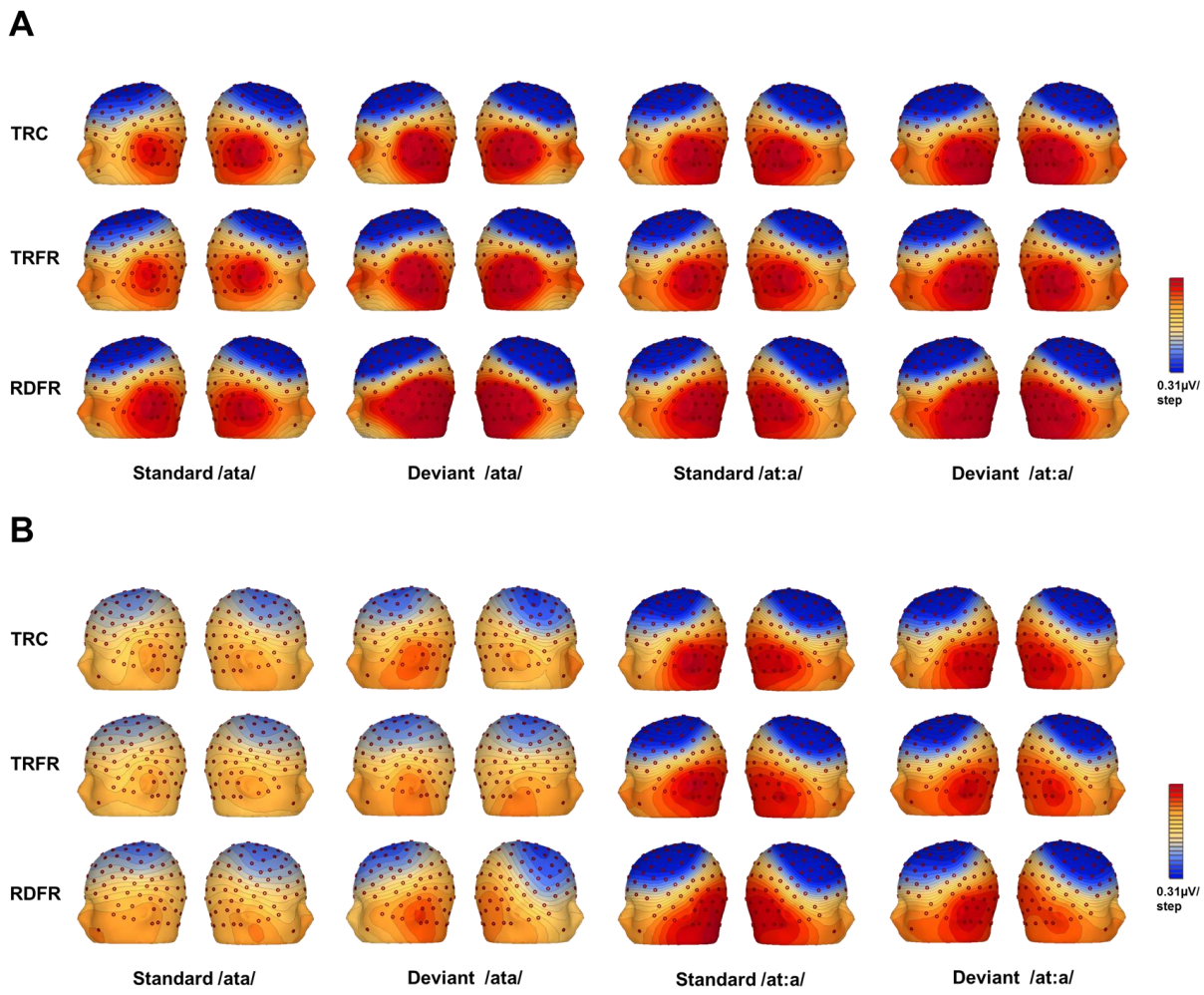

Figure 3. Topographic maps for responses to all stimuli at 294 ms (A) and at 600 ms (B) by groups: children with a familial risk for dyslexia and reading disability (RDFR, N = 30), typically reading children with a familial risk for dyslexia (TRFR, N = 51), and typically reading controls (TRC, N = 58).

3.2 Between group differences

Responses to the deviant /ata/ in the RDFR group differed statistically significantly from responses of the other groups, TRFR and TRC, for several channel clusters and time windows (see Figures 4 and 5). The RDFR group showed significantly more negative and more right-lateralized responses as compared to the TRC group at the frontal area between 132 – 900 ms after stimulus onset and more positive at occipital site between 50 – 378 ms (p = .001 and p = .038, respectively). When compared to the TRFR group, the RDFR group showed significantly

larger responses towards negative voltages at frontocentral area at 50 – 900 ms and more positive responses at occipital site at 56 – 380 ms and at 486 – 830 ms ($p < .00001$, $p = .043$ and $p = .005$, respectively). No statistically significant group differences were found for responses to the other stimuli.

3.2.1 Phase-locking and source analysis

Larger ERP responses could be due to better phase-locking of the single trials to the stimulation. Therefore, we also examined the inter-trial phase locking values in each group, but did not find statistically significant differences between any of the groups. Another cause for differences in the ERP amplitudes could be due to the underlying source structure of the ERPs. Equivalent current dipole fitting to the grand average data revealed that the source locations between the TRC and TRFR groups were the same near left and right auditory cortices (see Figure 6). However, when examining the source locations of the subgroup of RDFR children who had the largest amplitudes (N = 10), a right hemisphere source location was found approximately 20 mm posterior to of the sources in all the other groups, including other children of the RDFR group (N = 20) with amplitudes close to those of the TRC group. Source in the left hemisphere, in the subgroup of RDFR children who had the largest amplitudes (N = 10), was close to that of the other groups.

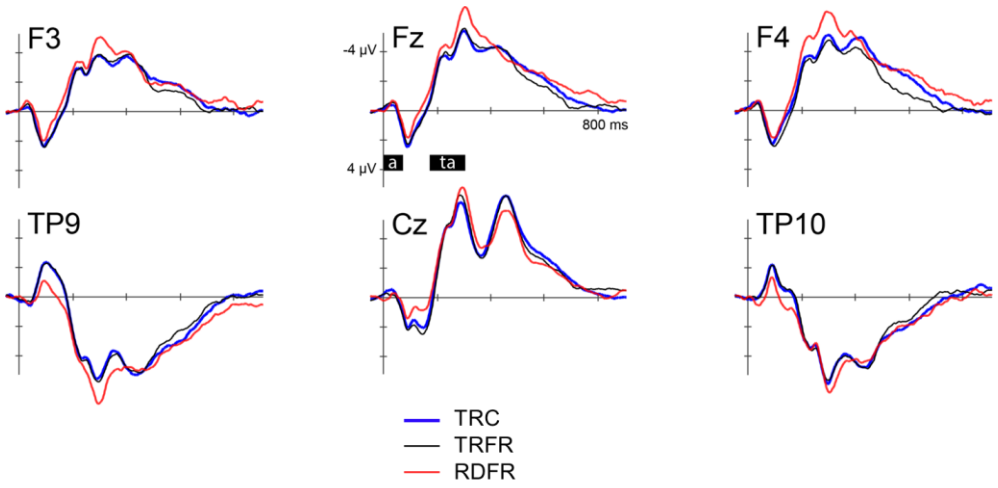

Figure 4. Grand average ERP waveforms for the responses to the short deviant /ata/ stimulus in the three groups: children with a familial risk for dyslexia and reading disability (RDFR, N = 30), typically reading children with a familial risk for dyslexia (TRFR, N = 51), and typically reading controls (TRC, N = 58). Vertical tick marks represent 2 µV and horizontal tick marks 200 ms (negativity up).

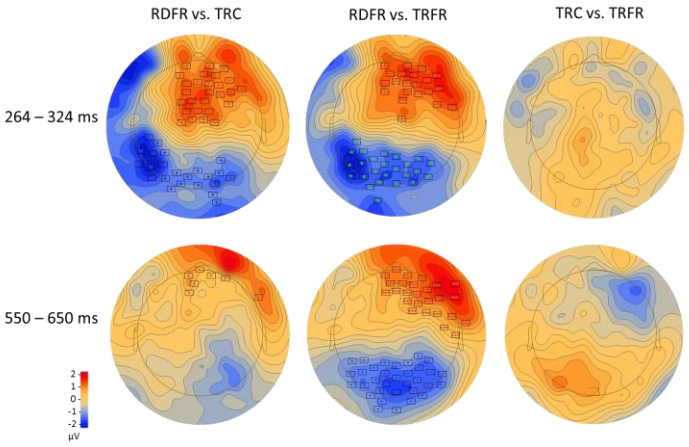

Figure 5. Group difference topographies between children with a familial risk for dyslexia and reading disability (RDFR, N = 30), typically reading children with a familial risk for dyslexia (TRFR, N = 51), and typically reading controls (TRC, N = 58) for the deviant /ata/ stimulus response at 264 – 324 ms (N250/MMN) and 550 – 650 ms (LDN) time windows. Statistical clusters marked with rectangles differ significantly between the groups.

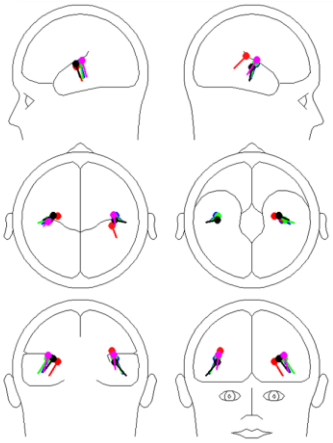

Figure 6. Source localization for the short deviant /ata/ at a time window of 264 - 324 ms. Dipoles for groups are denoted with different colors as follows: red = the most accurate readers of the RDFR group (N = 10), black = the intermediate readers of the RDFR group (N = 10), pink = the poorest readers of the RDFR group (N = 10), green = TRFR group (N = 51), and blue = TRC group (N = 58).

3.3 Short deviant /ata/ and correlations to behavior

The time windows showing group differences were selected for correlation calculations. Amplitude values around N250/MMN peak (294 ms ± 30 ms) and LDN time window (600 ms ± 50 ms) were averaged across time. The averaged amplitudes were correlated to behavioral measures within groups in each measured channel. Significant correlations (*p*s < .05) are seen plotted as a topographic map for each group in Figure 7. Statistical significances of within group correlations differences were also tested between groups. Figure 8 shows scatterplots of the correlations from a representative channel. As can be seen, the correlation coefficient is overall clearly larger for the children with dyslexia as compared to the other groups and that the correlations are not produced by outlying cases (one participant from the RDFR group was excluded as an outlier in reading fluency).

3.3.1 Phonemic length discrimination

At the N250/MMN time window in the RDFR group, right frontocentral and occipital brain responses to the deviant /ata/ showed correlations with speech perception (phonemic length discrimination) scores (*p*s < .05), but only the correlations at the frontal area differed from the other groups (*p*s < .05). Significant correlations within at-risk and dyslexic groups were found at the LDN time window as well as at frontocentral and occipital brain areas, but those were not significantly different between groups.

3.3.2 Reading accuracy

The brain processing of consonant length at the right frontocentral and occipitoparietal areas at the N250/MMN and LDN time windows was found to be associated with reading accuracy, but in the RDFR group only. The frontal correlations of the RDFR group were significantly different from the correlations in the other groups (*p*s < .05).

3.3.3 Reading fluency

Significant correlations between brain measures and reading fluency were found only for the N250/MMN time window. Correlations of the RDFR group at the frontal area and correlations of the TRFR group at the occipital area differed significantly from those of the TRC group (*p*s < .05).

3.3.4 Writing accuracy

Brain measures at the N250/MMN time window at the right frontal and occipital brain areas showed significant correlations with writing accuracy scores in the RDFR group (*p*s < .05), but only correlations at the frontal area differed significantly (*p*s < .05) from the correlations of the other groups. At the LDN time window at right frontal area, the TRC group showed correlations significantly different from the other groups (*p*s < .05).

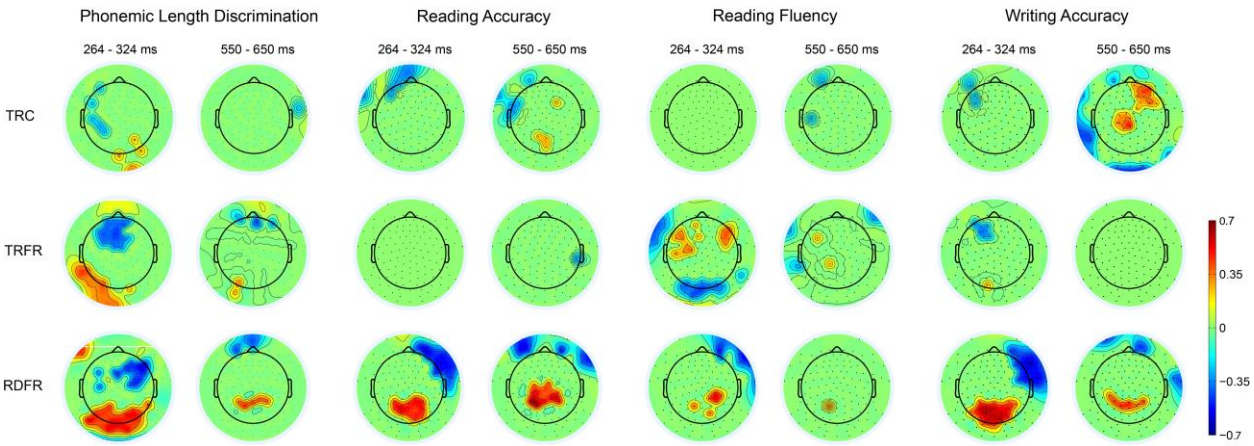

Figure 7. Significant correlations (*p* < .05) indicated by blue (negative) and red (positive) for responses to the short deviant /ata/ stimulus (averaged over the time windows of 264 – 324 ms (N250/MMN) and 550 – 650 ms (LDN)) with phonemic length discrimination, reading accuracy, reading fluency, and writing accuracy measures. One participant from the RDFR group was excluded as an outlier in reading fluency.

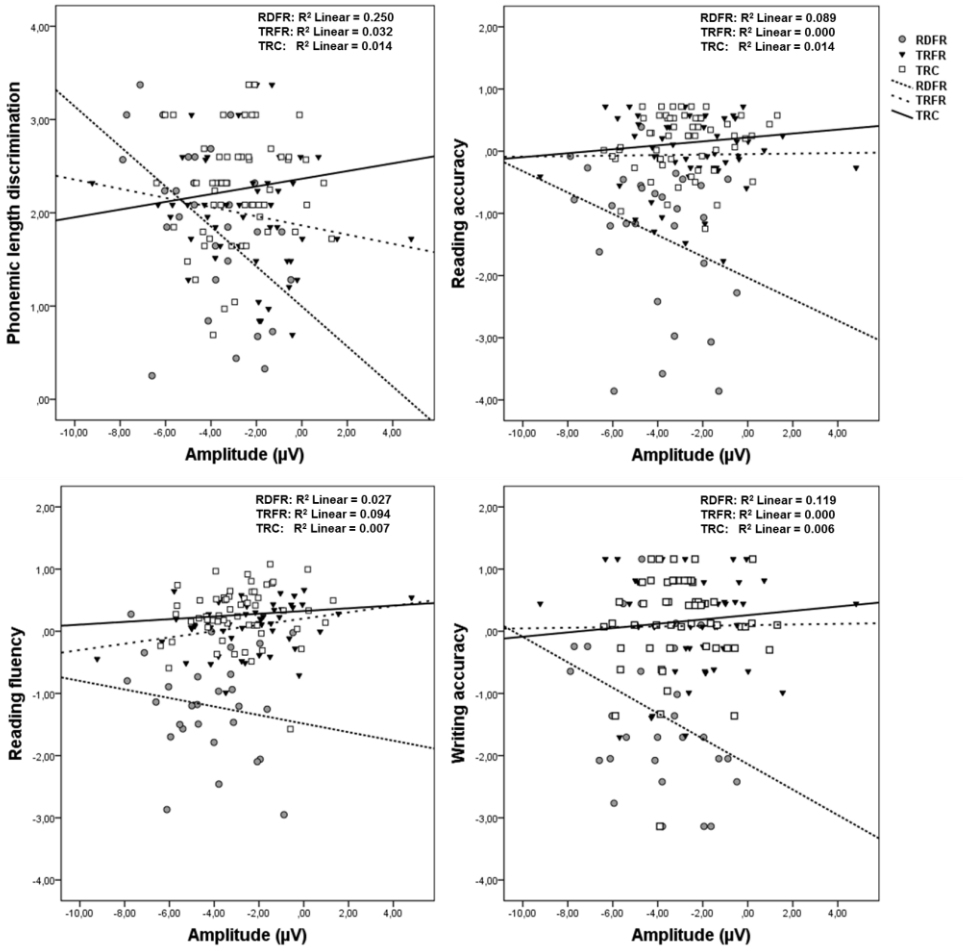

Figure 8. Scatter plots of average amplitude (μV) of responses to the short deviant /ata/ between 264 – 324 ms at the channel 123 (near F4) and phonemic length discrimination, reading accuracy, reading fluency, and writing accuracy scores in the three groups: children with a familial risk for dyslexia and reading disability (RDFR, N = 30), typically reading children with a familial risk for dyslexia (TRFR, N = 51), and typically reading controls (TRC, N = 58). One participant from the RDFR group was excluded as an outlier in reading fluency.

4 Discussion

In the current study, consonant quantity perception was investigated in school-aged children with and without familial risk for dyslexia and with and without reading disorder using electroencephalography (EEG). Enhanced ERPs were found for shortening of the pseudo-word stimuli (/ata/ presented among /at:a/ in an oddball/ MMN paradigm) in dyslexics with familial risk for dyslexia (RDFR) as compared to both typically reading groups (TRFR and TRC). Group differences were not found for lengthening of the consonant duration (see Figure 2). Visual inspection of topographic maps (Figure 3) and source localization analysis (see Figure 4) revealed that a subgroup of the RDFR group with highest reading performance had the largest brain responses and that the source of their ERPs was located more posteriorly at the right auditory areas as compared to the all other participants. Further, correlations between brain responses to the speech sounds and reading and writing accuracy, reading fluency, as well as behavioral discrimination of phonemic length were assessed. The correlations showed that the responses within the dyslexic group (RDFR) to short deviant /ata/ at N250/MMN time window were associated with phonemic length discrimination (Figures 7 and 8), as well as reading and writing accuracy: the stronger the potential, the better performance in behavioral tasks. Associations in the other two groups were less systematic. These findings suggest that different brain areas are involved in processing of these tasks in the different groups.

Previously, mainly diminished brain event-related responses in dyslexic children or in children at familial risk for dyslexia for any change in auditory stimulus train have been reported (Schulte-Körne et al., 1998; Maurer et al., 2003; Lachmann, Berti, Kujala, & Schröger, 2005; Lovio et al., 2010; Sharma et al., 2006). Instead, in the current study we found atypically large and enhanced response for shortening of the consonant length in pseudo-word stimuli in the dyslexic group. A few studies reporting enhanced ERPs in dyslexics to auditory stimuli also exist. For example, Hämäläinen et al. (2013) found enhanced N250 responses in 6.5-year-old kindergarten children with dyslexia as compared to at-risk and control groups. In their study, though, the enhancement occurred for lengthening of consonant duration, whereas in the current study, this was found only for the shortening, which was not studied in the study by Hämäläinen and colleagues (2013). Furthermore, the enhanced responses in their study were associated with poorer reading accuracy and slower reading speed later at the 2nd grade. In adult dyslexics, parents of the children of the

current study, enhanced N100m responses to first /a/ syllable of the pseudo-word /ata/ have been reported in active discrimination condition (Helenius et al., 2002). However, because of the differences in experimental design (e.g., in instructions (active/passive), stimulation rate, and presentation), the results are not fully comparable with our findings. In their study, Helenius et al. (2002) did not examine associations to behavioral measures, and therefore it remains unknown whether participants with the largest amplitudes were the best discriminators and readers within the adult dyslexic group. The enhanced responses in the current study could be due to larger cortical area activating to stimulation reflected also in the different source location at the right hemisphere for the sub-group of children with largest responses within the RDFR group.

4.1 Correlations of brain responses to reading related skills

Interestingly, it was found that, within the dyslexic group, those with the largest N250/MMN responses were the best in behaviorally discriminating phonemic length and they were also the most accurate readers and writers within the dyslexic group (Figures 7 and 8). To our knowledge, no such result has been reported previously. We speculate it could reflect a compensatory mechanism in some individuals with dyslexia, in whom the auditory and speech perception network is organized differently leading to improved speech perception, reading, and writing skills. This is supported by our earlier finding, that within partly overlapping population of dyslexics tested three years before, the enhanced brain responses were related to poorer performance in reading at the 2nd grade (Hämäläinen et al., 2013).

Many studies show anomalies in children with dyslexia in their brain functionality and anatomy. For example, dyslexics have been suggested to have more symmetrical hemispheres in general, as well as symmetrical specific brain structures such as plana temporale in the posterior Sylvian fissure, which might affect the brain activation originating from these areas involved in speech and language processing (Binder et al., 1996; Galaburda et al., 1978; Galaburda et al., 1985; Illingworth, & Bishop, 2009; Leonard, & Eckert, 2008; Sun et al., 2010). Regardless of the commonly reported reduced asymmetry, also asymmetry has been reported: adults with familial risk and earlier history of clinically diagnosed dyslexia, but whose reading skills were later

compensated, showed leftward asymmetry of planum temporale (Chiarello et al., 2006; Leonard et al., 1993).

Leonard et al. (1993) studied compensated adult dyslexics as well as their first or second-degree unaffected relatives. They found that the relatives had less cerebral anomalies and better scores in phonological awareness as compared to compensated dyslexics, yet more anomalies and lower scores than in the control group. This was interpreted to mean that all anomalies in the brain are linked to certain processing or perceptual strategies, of which some would be compensable by alternative strategies, while multiple and bilateral anomalies would be more difficult to compensate. Source localization analysis of the current data revealed that, for the subgroup of the best reading dyslexics with the largest EEG responses, the source was located about 20 mm more posterior at the right auditory areas as compared to the others in the RDFR, TRFR, and TRC groups. This suggests a *more* asymmetrical brain response pattern between the hemispheres in the anterior-posterior direction in the subgroup of dyslexics, possibly reflecting compensation mechanisms. Using fMRI during a same-different word identification test, Kovelman et al. (2012) found greater activation in the right temporoparietal neocortex in dyslexic children as compared to typical readers who suppressed this region, suggesting atypical reliance on right posterior cortex in phonological processing in dyslexics. Kovelman et al. (2012) suggested that this is due to a compensatory mechanism in dyslexics related to their impaired phonological processing. Some reading studies have also reported hyperactivation of right temporal and parietal regions, which has been interpreted as an enhanced compensatory neural mechanism due to the reading process being more demanding for dyslexic children (Shaywitz, & Shaywitz, 2005; Simos et al., 2002). Also, hyperactivation in the left inferior frontal gyrus in dyslexic group has been reported and assumed to reflect increased effort related to phonological coding (Georgiewa et al., 2002). In the current study, discrimination performance as well as reading and writing accuracy showed significantly differing correlations (the larger the amplitudes the better the scores) in the dyslexic group at the right frontal areas as compared to other groups. These areas have been found to be involved in reading in dyslexics and assumed to compensate for the underachievement of corresponding left temporal and parietal areas (Pugh et al., 2000; Shaywitz, & Shaywitz, 2005).

An important point, when comparing the present study with the earlier studies in children of the same age, is that the stimuli used in several of those studies substantially differ from those used in the present study. Although speech sounds have been used, stimulus sets have typically consisted of CV syllables differing in consonant quality rather than in consonant quantity, which was the modification in the current study. However, using the same pseudo-word stimuli /ata/ and /at:a/ and partly the same sample as in the current study, enhanced responses have been observed for the quantity change, at an earlier age before reading instruction and acquisition (Leppänen et al., 2002; Hämäläinen et al., 2013). These findings refer to the fact that the complexity/type of the stimuli and experimental design highly affect the observed group differences between dyslexics and good readers. Further, the severity of dyslexia phenotype and the age of the participants with dyslexia also seem to affect the results, as well as the fact that in some cases there is a familial, i.e. genetic, background, and in others there is not. It should also be noted that there is considerable overlap in the responses of children with dyslexia and typical readers and that not all dyslexic children display an atypical response. These differences should be taken into consideration when comparing studies.

4.2 Maturation

Although our finding of the enhancement of the N250/MMN in the dyslexic group deviates from the main line of findings of group differences in children of the same age, the morphology of the brain event-related potentials as a whole is very similar as in the previous studies (Bishop et al., 2007; Čeponienė et al., 2002; Ponton et al., 2000; Ponton et al., 2002). In line with earlier studies of children at early school-age, the predominent ERP components in the current study were P1, a positive deflection around 100 ms, and N250, a negative deflection around 250 ms, for all groups and in response to all stimuli. With the relatively short ISI of 610 ms, N1 was not yet clearly visible at the frontal area, but the TRC and the TRFR groups showed significantly larger amplitudes to all stimuli around 100 ms as compared to the RDFR group, which could suggest a more immature activation of the supratemporal source of the N1 in the RDFR group (see Figures 2 and 4). In addition, the TRC and TRFR groups showed smaller amplitudes at the N250 time window as compared to the RDFR group (see Figures 2 and 4). These group differences seen between the RDFR group and the other two groups indicate a possible slower maturation and

differential brain development in dyslexic group, although earlier studies suggest that no clear developmental lag exist in children with reading difficulties at the behavioral level (Felton, Naylor, & Wood, 1990; Francis, Shaywitz, Stuebing, Shaywitz, & Fletcher, 1996; Shaywitz et al., 1999). Unlike in the RDFR group, in the TRC and TRFR groups relative diminishing of the N250 (see Figure 4) during maturation may already have begun, as well as emerging of the supratemporal subcomponent of the N1 (Hämäläinen et al., 2007; Ponton et al., 2000; Ruhnau et al., 2011). Late discriminative negativity (LDN) was seen in all groups emerging at around 550 ms for the short deviant stimuli and after 700 ms for the long deviant stimuli (in both cases at about 400 ms after the stimulus deviancy). This finding is in line with earlier findings in children of this age (e.g., Cheour et al., 2001; Čeponienė et al., 2004).

It might be possible that the above group differences arise because of a larger change detection processing (MMN) being embedded in the brain responses of the RDFR group within these time windows. However, the N250 responses to the other short stimuli as well, i.e., to the standard /ata/, was smaller in amplitude in the TRC and TRFR groups in comparison to the RDFR group, and the response to the deviant /ata/ was clearly larger in all groups when compared to the responses to the other stimuli with a short gap (see Figure 2A). This indicates that the larger response in the RDFR group cannot purely be due to the chance detection process, although, in the current study, the identification of the MMN for the consonant length change was difficult with confidence, because the short deviant /ata/ and the short standard /ata/ were presented in different conditions, most likely causing some differing context effects. However, it is likely that the change detection processes contributes to the responses after 150 ms after the stimulus deviancy.

4.3 Conclusion

In this study, we found that the subgroup of dyslexic children who had enhanced brain responses performed better in phonemic length discrimination and reading and writing accuracy, but not at reading fluency, when compared to the other dyslexics who did not have enhanced brain responses. We also discovered that the brain responses of those dyslexic children with the largest amplitudes for the pseudo-word with a short consonant length originated from a more posterior

area of the supra-temporal cortex in comparison to the other groups. The best readers within the dyslexic group have probably developed alternative strategies which employ compensatory mechanisms substituting their possible earlier deficit in phonological processing and might therefore be able to perform better in phoneme length discrimination and reading and writing accuracy tasks. However, it seems that for reading fluency possible compensatory mechanisms are not that easily built and, as usually has been seen, dyslexic children remain slow, although become rather accurate readers during their adult life.

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