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Research report

Basic auditory processing is related to familial risk, not to reading fluency: An ERP study

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ABSTRACT

Less proficient basic auditory processing has been previously connected to dyslexia. However, it is unclear whether a low proficiency level is a correlate of having a familial risk for reading problems, or whether it causes dyslexia. In this study, children's processing of amplitude rise time (ART), intensity and frequency differences was measured with event-related potentials (ERPs). ERP components of interest are components reflective of auditory change detection; the mismatch negativity (MMN) and late discriminative negativity (LDN). All groups had an MMN to changes in ART and frequency, but not to intensity. Our results indicate that fluent readers at risk for dyslexia, poor readers at risk for dyslexia and fluent reading controls have an LDN to changes in ART and frequency, though the scalp activation of frequency processing was different for familial risk children. On intensity, only controls showed an LDN. Contrary to previous findings, our results suggest that neither ART nor frequency processing is related to reading fluency. Furthermore, our results imply that diminished sensitivity to changes in intensity and differential lateralization of frequency processing should be regarded as correlates of being at familial risk for dyslexia, that do not directly relate to reading fluency.

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1. Introduction

Developmental dyslexia is characterized by persistent difficulties in word reading and/or spelling that are discrepant with intelligence and that are not attributable to sensory deficits or environmental factors such as poor educational

opportunities (e.g., Snowling, 2000; Vellutino, Fletcher, Snowling, & Scanlon, 2004). Dyslexia is known to run in families, suggesting an active genetic component (for a review see Carrion-Castillo, Franke, & Fisher, 2013). A phonological processing deficit is generally considered to be at the core of reading problems (de Jong & van der Leij, 2003; Pennington & Lefly, 2001). Poor awareness of the phonological structure of

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language is thought to hamper reading acquisition, as it may compromise the mapping of speech sounds to letter symbols (phoneme to grapheme mapping; [Elbro, 1996](#)). What underlies the phonological deficit is still debated, but it has been hypothesized that a decreased ability to process basic (non-speech) auditory information may underlie the phonological problems ([Farmer & Klein, 1995](#); [Hämäläinen, Salminen, & Leppänen, 2013](#); [MacAnally & Stein, 1996](#); [Tallal, 1980](#)).

One aspect of basic auditory processing that is thought to affect phonological processing, is the processing of amplitude rise time (ART) ([Goswami et al., 2002](#)). ART refers to the speed with which the amplitude of an acoustic signal rises from sound onset. The hypothesis that ART influences phonological processing stems from the idea that speech units can be segmented into parts like syllables. An important factor underlying segmentation of speech is stress- or rhythm processing, which is specifically influenced by modulation of ART, for modulations in ART will lead to perceived differences in rhythm ([Goswami et al., 2002](#)). Perception of rhythm aids speech segmentation because it is thought to be important to the perception of onset (the word initial phoneme), and rime (the string of phonemes that follow the onset), in a syllable. Hence, if subtle differences in ART are not registered, then this may affect the perception of speech sounds, which, in turn, may have negative consequences for the acquisition of phonological skills because speech segmentation into meaningful phonological units is hampered ([Goswami et al., 2002](#)).

The theory that problems in ART processing underlie literacy problems is supported by empirical data from several studies. [Goswami et al. \(2002\)](#) found that dyslexic readers were poorer at detecting amplitude envelope modulations. Moreover, they showed that amplitude modulation detection was related to individual differences on phonological processing measures, such as performance on rhyme oddity tasks. Participants who performed poorly on this task, also performed poorly on tasks tapping phonological skills. [Richardson, Thomson, Scott, and Goswami \(2004\)](#) examined ART processing in school-aged children with and without reading disability and found that controls were better at discriminating between differences in ART compared with the dyslexic group. A study with adult participants by [Hämäläinen, Leppänen, Torppa, Müller, and Lyytinen \(2005\)](#), found similar results. They found correlations between ART processing and (syllable level) phonological awareness (PA) tasks, and between ART processing and reading. Deficits in ART processing do not appear to be dependent on mother tongue and may thus be universal, as differences have been found in a variety of languages, both in transparent and opaque orthographies, i.e., languages in which there is a simple one-to-one mapping of speech sound to letters and languages in which this is not the case ([Muneaux, Ziegler, Truc, Thomson, & Goswami, 2004](#); [Richardson et al., 2004](#); [Surányi et al., 2009](#)).

Most studies investigating sensitivity to subtle differences in rise time have focused on the behavioral level. In order to meet the task demands, attention from the participants is required. Attention may, therefore, have been a confound in these studies, mediating the perception of, and the response to amplitude modulations. Given the high comorbidity between dyslexia and ADHD (e.g., [Light, Pennington, Gilger, &](#)

[DeFries, 1995](#)), it is important to disentangle the relationship between attention and ART processing to be able to assess the relationship between ART processing and reading ability directly. Neurophysiological measures may provide a solution by means of the mismatch negativity (MMN, [Näätänen, 1995](#); [Näätänen et al., 2012](#)), an event-related potential (ERP) component which reflects pre-attentive auditory discrimination. The MMN is considered to be a pre-attentive measure of discrimination because the MMN can be recorded without subjects attending to the stimuli: they can for instance perform an unrelated primary task or watch a video (e.g., [Näätänen et al., 2012](#)). Nevertheless, MMN amplitude, duration and onset latencies are related to (subsequently measured) behavioral discrimination skills (e.g., [Dehaene-Lambertz et al., 2005](#); [Tiitinen, May, Reinikainen, & Näätänen, 1994](#)). The MMN typically occurs after an occasional deviant stimulus is presented in a train of repeated standard stimuli. It is thought that the repetition of the standard stimulus leads to the buildup of an auditory memory trace of sound features (e.g., frequency, intensity) contained in the standard. When a sound feature in the deviant stimulus does not match the memory trace, the auditory system detects this change and an MMN is elicited ([Näätänen, 1995](#)). The MMN is characterized by a frontally negative deflection in the ERP waveform, around 200 msec after stimulus onset in adults.

In addition to MMN, another ERP component can be identified that reflects processing of deviance: the late discriminative negativity (LDN, sometimes also referred to as “late MMN”; e.g., [Čeponienė, Korpilahti, Martynova, & Lang, 2004](#); [Cheour, Korpilahti, Martynova, & Lang, 2001](#)). It is elicited under the same circumstances as the MMN, but typically only occurs between 300 and 600 msec after stimulus onset (e.g., [Schulte-Körne, Deimel, Bartling, & Remschmidt, 2001](#)). LDN is suggested to reflect automatic processing of change in auditory and linguistic stimuli ([Cheour et al., 2001](#)). It occurs in both adults and children, though its amplitude appears to decrease throughout development ([Čeponienė et al., 2004](#)). Several studies have shown LDN to be attenuated in dyslexia (e.g., [Neuhoff et al., 2012](#); [Schulte-Körne et al., 2001](#)).

If ART processing is indeed related to reading fluency, it follows that the MMN and/or LDN of poor readers to changes in ART will be smaller or absent compared to the MMN and/or LDN to changes in ART of good readers. [Hämäläinen, Leppänen, Guttorm, and Lyytinen \(2008\)](#), investigated the effects of rise-time changes on sensory processing in 9 year-old children with reading problems using the MMN. Differences in processing were found between good and poor readers, as reflected in MMN amplitude. However, it was larger in poor readers compared to control children, reflecting enhanced processing of ART information. However, when looking at LDN, [Hämäläinen et al. \(2008\)](#) found control children to show enhanced processing of ART stimuli. Several other studies provide neurophysiological support for abnormal processing of rise time changes in dyslexia as they find smaller amplitudes of the N1 ERP component (also reflecting sensory processing) in the dyslexic group (see for example [Hämäläinen, Leppänen, Guttorm, & Lyytinen, 2007](#); [Stefanics et al., 2011](#); for a review see [Hämäläinen et al., 2013](#)).

From the studies mentioned above it seems that there is a relation between ART processing and reading although the picture is not completely clear. In addition, these studies have compared children or adults with and without dyslexia, but did not control for familial risk (FR, i.e., one or more close relatives have a history of dyslexia). This may lead to a confound given the heritable component of dyslexia, as most children in the poor reading group will have a familial risk, whereas children with the same genetic risk but no poor reading were not included in these studies. Control children typically do not have a familial risk. The lack of differentiation between at risk children who do or do not develop dyslexia influences the interpretation of the results, since it remains unknown whether poorer ART processing is a characteristic of familial risk children, or whether it is related to reading skill directly. To support the notion that an impairment in ART processing is causing reading problems, it is important to disentangle this and include at risk children who do not develop dyslexia (e.g., [van der Leij et al., 2013](#)).

Longitudinal studies on good and poor reading at risk children have been executed to investigate basic auditory processing at a pre-reading age retrospectively, once it is known which children became good and poor readers. [Leppänen et al. \(2010\)](#), using data of the Jyväskylä Longitudinal Dyslexia (JLD) project, showed that less proficient frequency processing was related to being at risk for reading problems, but not to reading directly. They found that at-risk newborns could not process differences in frequency as opposed to typically developing controls, as indicated by the mismatch response (MMR; the MMN can be both frontally positive [e.g., [He, Hotson, & Trainor, 2007](#)] as well as negative in infants [e.g., [Alho, Sainio, Sajaniemi, Reinikainen, & Näätänen, 1990](#)], when positive it is called the MMR). As part of the Dutch Dyslexia Programme (DDP), [Plakas, van Zuijen, van Leeuwen, Thomson, and van der Leij \(2013\)](#) studied ART processing differences in 41-month-old children at risk of dyslexia and controls. Differences in MMN amplitude were found between children at-risk of dyslexia and controls. Typically developing children were able to discern differences in ART, as indicated by MMN presence, whereas at-risk children did not show an MMN. However, in both studies the differences were independent of whether the at risk children developed into good and poor readers later on. The findings support the view that atypical basic auditory processing is related to having a familial risk for reading problems but not causally related to deficiencies in reading fluency.

However, the absence of differences in early auditory processing does not exclude the possibility that the influence of certain factors contributing to reading problems may gradually change over time, or that the influence of these factors becomes manifest later on. From this perspective, it is not unlikely that the influence of neurophysiological factors as investigated by [Leppänen et al. \(2010\)](#) and [Plakas et al. \(2013\)](#) would change over time. To investigate this issue, the present study has investigated basic auditory processing skills in children with a familial risk of dyslexia. Pre-attentive sensitivity to changes in ART were studied at the end of primary school using MMN and LDN. Of particular interest, and unique to this study, was the intention to disentangle characteristics of children with a familial risk from factors that

relate directly to reading by investigating differences in MMN and LDN amplitude elicited by modulations in rise time between good and poor reading at-risk children.

To reach our aim, we investigated children at-risk of dyslexia with and without dyslexia and control children, who participate in the DDP. A basic auditory multi feature paradigm ([Kujala, Lovio, Lepistö, Laasonen, & Näätänen, 2006](#); [Lovio et al., 2009](#); [Pakarinen, Takegata, Rinne, Huotilainen, & Näätänen, 2007](#)) was used to record MMN and LDN to changes in ART. Two control measures were included to investigate whether poor ART processing was specifically related to reading, in contrast to other aspects of auditory processing. Changes in frequency (FREQ) were included in the paradigm to assess whether an ART deficit is specific to reading, or whether multiple aspects of basic auditory processing relate to fluent reading, as some studies have shown that children with dyslexia have difficulty discerning changes in frequency (e.g., [Bishop, 2007](#); [Hämäläinen et al., 2013](#)). Including both these deviant types enables us to disentangle the influence of both aspects of basic auditory processing on reading fluency. Additionally, intensity (INT) manipulations were included in the paradigm to control for the possibility of an ART processing impairment being due to problems in processing of intensity information, because a relatively longer ART results in an overall softer sound ([Stefanics et al., 2011](#)). In a multi feature paradigm, a feature deviant is presented after each standard. The feature deviant differs from the standard on one out of three features ART, FREQ or INT, but serves as a standard for the other features. Each feature change is, therefore, in itself rare. Each of these deviant types has three levels of deviance, resulting in a total of 9 deviants in our study. The brain builds a representation of all features of the stimuli, and if one of the features deviates, an MMN is elicited ([Pakarinen et al., 2007](#)). Following the MMN elicitation, an LDN is expected as well. A great benefit of the multi feature paradigm over the classic oddball paradigm ([Näätänen, 1995](#)) is that a great amount of information can be recorded in a short amount of time.

2. Methods

2.1. Participants

The children who participated in this study comprised a subsample of the children who participated in the DDP. Fifty-five children were invited to take part in the current study based on the following inclusion criteria.

Children were assigned to the familial risk group if one or both parents were dyslexic. Whether parents experienced reading difficulties was assessed by presenting them with Dutch norm-referenced tests for word- and pseudoword reading ([van den Bos, Lutje Spelberg, Scheepstra, & de Vries, 1994](#); [Brus & Voeten, 1973](#); see [Materials](#)). If parents scored below the 15th percentile on either test and not higher than the 50th on the other, or below the 20th percentile on both tests, their children were assigned to the familial risk group. Children were assigned to the control group if their parents scored above the 50th percentile on both the word- and pseudoword reading tests.

In order to be assigned to the familial risk group of children who develop dyslexia (FRD) group, children from the familial risk group had to perform poorly on a word- and pseudoword reading test the last time that these tasks were administered in grade 5 or 6 and at least one out of the two times these tasks were administered earlier: at the end of 2nd grade and in grade 3. A poor performance was defined as a score below the 10th and 40th percentile on either the word or the pseudoword reading test, or below the 25th percentile on both tests.

ERP data from one child had to be omitted due to technical problems while recording the EEG. Five children (1 control, 1 FRND, and 3 FRD) had an ADD diagnosis, for which they used medication. Exclusion of these children did not influence the results. In total, data from 54 children were included in the analysis (Table 1).

2.2. Materials

2.2.1. Word reading fluency

To measure and assess word reading fluency (WRF), the “Een-minuut-test” (1 min test; Brus & Voeten, 1973) was used in grade 3 and in grade 5/6. In grade 2, the second list of the “Drie Minuten Toets” was used (3 min test; Verhoeven, 1995). The 1 min test consists of a list of 116 mono- and polysyllabic words, increasing in difficulty. The administered list of the 3 min test consists of 150 monosyllabic words. For both tests, the score was the number of words read correctly in 1 min.

2.2.2. Pseudoword-reading fluency

Pseudoword-reading fluency (PWF) was measured with the Dutch norm-referenced task De Klepel (van den Bos et al., 1994). It consists of a list of 116 mono- and polysyllabic pseudowords. The score was the number of words read correctly within 2 min.

2.2.3. Phonological awareness

PA was measured by a computerized version of the phoneme deletion task (de Jong & van der Leij, 2003). The test comprised three parts. First, participants were presented with four monosyllabic pseudowords and were asked to delete one consonant phoneme, resulting in another pseudoword. Subsequently, they were presented with four bisyllabic

pseudowords of which they also had to delete one consonant. Next, they were presented with four bisyllabic pseudowords and asked to delete one consonant phoneme twice, again resulting in a new pseudoword. The first and third parts of the test were preceded by two practice items. The score on this task was the total number of items correct.

2.2.4. Non-verbal IQ

The Block Design subtest of the WISC (Wechsler, 1992) was used to measure non-verbal IQ in grade 3. Children were asked to complete block designs using coloured blocks, using an example presented to them on a card. The experimenter first demonstrated the task, after which the participant was asked to complete the design according to the card. Each trial had a time limit of 45 sec. The number of blocks that had to be used per trial increased. The maximum number of trials was 15. If the child failed or exceeded the time limit on two consecutive trials, the task ended.

2.3. Stimuli

Stimuli were offered using a Multi-Feature paradigm (Pakarinen et al., 2007). Stimuli were tones with a duration of 400 msec and an inter stimulus interval of 250 msec, synthesized using Audacity for Windows (Audacity, Pittsburgh, USA) and edited using Adobe Audition (Adobe Systems Inc., San Jose, USA). The standard stimulus had a rise time of 15 msec and a fall time of 50 msec, a frequency of 523 Hz and an intensity of 80 dB. The deviant stimuli deviated on the features ART, FREQ and INT. Each deviant type had 3 sublevels; resulting in a total of 9 deviants. The three ART deviants had rise times of 90, 180 and 270 msec, respectively. The FREQ deviants had a frequency of 554, 587 and 622 Hz, and the INT deviants had an intensity of -2.5 , -5 and -7.5 dB compared to the standard stimulus. One experimental block contained 612 stimuli. Each participant was offered 3 blocks of stimuli. The beginning of each experimental block was marked by a sequence of 4 standard stimuli, after which standards and deviants were presented in an alternating pattern with the constraint that no deviant of the same type occurred twice in a row. In total, the standard stimulus occurred 308 times per block. Deviant features had a probability of 50% (rise time 16.67%, frequency 16.67% and intensity 16.67%, each type therefore being represented 100 times per block). Each feature deviant's levels had a probability of 5.5%, totaling approximately presentations of each deviant level per block. Fig. 1 depicts a schematic overview of the paradigm.

2.4. Procedure

2.4.1. Data collection

The EEG recording took about twenty minutes and was part of a longer recording session of approximately 3 h. After they were familiarized with the procedure, children were seated in a comfortable chair and watched a silent movie with subtitles. During the recording, the experimenter monitored the child in an adjacent room and attended to the child between blocks. Breaks were taken when necessary. Behavioral tasks were administered in a separate session in a quiet room. This session took approximately 2 h. Our research procedures were

Table 1 – WRF: number of words read accurately within 1 min, PWF: number of pseudowords read accurately within 2 min. PA: Phonological awareness, measured by a phoneme deletion task and displayed in items correct. Non-verbal IQ was measured in grade 3 by the block design subtest of the WISC. For a description of these tasks, see Materials. All values are given as mean (SD). Group differences were attested using ANOVAs. Shared subscripts are indicative of no significant difference. Significant differences are all $p < .01$.

	Controls (N = 15)	FR no dyslexia (N = 24)	FR dyslexia (N = 15)
Age (months)	143.60 (7.18) _a	142.87 (7.64) _a	142.06 (6.18) _a
WRF	76.33 (11.06) _a	69.42 (9.38) _a	48.40 (8.03) _b
PWF	63.87 (18.05) _a	48.58 (14.49) _b	34.53 (9.79) _c
PA	11.13 (1.12) _a	9.33 (3.14) _a	9.06 (2.60) _a
Non-verbal IQ	43.06 (10.83) _a	44.16 (11.77) _a	43.06 (10.87) _a

Fig. 1 – A simplified presentation of the Multi Feature paradigm. Shapes represent standard and deviant tones with certain features. Deviant levels of each type are not represented in this image.

approved by the Ethics Committee of the Child Development and Education Department, Faculty of Social and Behavioural Sciences, of the University of Amsterdam.

2.4.2. EEG recording & analysis

The EEG was recorded at a sampling rate of 1024 Hz/channel applying an online band pass filter of 0.01–100 Hz using ActiView (BioSemi, Amsterdam, The Netherlands). Children were wearing a 64-electrode EEG cap. The electrodes were positioned according to the international 10–20 system (Jasper, 1958). A total of four electro-oculogram (EOG) electrodes were used to register eye blinks and eye-movements. Additionally, electrodes were attached to the mastoids and nose. The latter was used as a reference.

Data were analyzed using Brain Vision Analyzer (Brain Vision Analyzer software, Brain Products GmbH, Munich). The EEG was bandpass filtered offline between 1 Hz (12 dB/oct) and 30 Hz (12 dB/oct). Independent Component Analysis (ICA) was used to identify and remove eye-blink artifacts. The signal was segmented between –150 and 650 msec relative to stimulus onset and baseline corrected (–150 to 0 msec relative to stimulus onset). Any trial with amplitudes exceeding $\pm 150 \mu V$ was seen as containing artefacts and not included for further analysis. Next, averages were calculated for the standard stimulus and for each deviant type. The minimum number of deviants of combined difficulty levels included per participant was 137 for ART ($M = 235.40$), 133 for FREQ ($M = 238.35$) and 139 for INT ($M = 238.16$). Additionally, difference waves (deviant minus standard) were calculated for each deviant ERP and difference waves of the control group were examined to determine MMN and LDN peak latency, i.e., the moment in time at which the average difference in amplitude between standard and deviant stimuli was largest. Around this grand-average peak latency a symmetric window of 40 msec was taken to calculate MMN and LDN amplitude and compare the response to differences in ART, FREQ and INT between participants.

3. Results

Grand average waveforms for standard and deviants for all groups are displayed in Fig. 2. All groups showed a positive deflection around 100 msec in response to the standard and all three deviants (P1), followed by a negative deflection peaking around 260 msec (MMN). The second negative deflection seen

in the waveforms of the deviant stimuli was identified as the LDN, peaking around 420 msec.

3.1. MMN

To establish whether an MMN was elicited for each deviant type in each group, mixed analyses of variances (ANOVAs) were run per deviant type (ART, FREQ, INT) with factors stimulus type (standard, deviant), electrode (F3, F1, Fz, F2, F4, inverted P9, inverted P10, inverted left mastoid [LM], inverted right mastoid [RM] [the signal from the mastoids and P9 and P10 was inverted because of a polarity reversal]) and between factor groups (FRND, FRD, C). Prior to further analysis, the effect of deviance level on MMN amplitude was addressed. No effects of deviance level were found for either of the three deviant types, possibly due to too few collected deviants per level. To improve signal-to-noise ratio for our further analyses, we averaged across the levels of each type of deviant.

A main effect of stimulus type [$F(1,51) = 7.99, p = .003$] was found for ART. No Group $\times$ Stimtype interactions were found. Looking at the standard and deviant waveforms, it can be observed that the ART deviant was more positive than the standard for all groups. For FREQ, a main effect of Stimtype [$F(1,51) = 44.37, p < .001$] was also found, as well as a Group $\times$ Stimtype interaction [$F(2,51) = 4.57, p = .015$]. Planned post-hoc tests on the MMN amplitude (deviant – standard) revealed a significant difference between controls and the FRND group ($p = .016$) and a marginal difference between controls and the FRD group ($p = .076$). For INT, no main effects of stimulus type were found. We found main effects for electrode for ART [$F(1.58,80.92) = 59.49, p < .001$], FREQ [$F(1.53,78.10) = 68.60, p < .001$] and INT [$F(1.44,73.55) = 59.34, p < .001$]. Post-hoc t-tests were administered to identify electrodes at which MMN amplitude was significantly different from zero, per group. Results are displayed in Table 2.

Scalp distributions between 240 and 280 msec per condition and participant group are presented in Fig. 3. The scalp activity underlying the ART and FREQ MMN looks similar in all three groups, with a negative polarity on frontal electrodes and a bilateral area of positive polarity around the mastoids. All three groups exhibit a negative frontal polarity. We addressed group differences in scalp lateralization of MMN activity in two mixed ANOVAs by comparing right hemisphere (inverted RM, inverted P10, F4) and left hemisphere (inverted LM, inverted P9, F3) electrodes across three groups for ART and FREQ, because an MMN was found in all three groups for these

Fig. 2 – ERP responses on electrodes F1, Fz and F2. Lines represent elicited ERPS for the standard (gray), ART deviant (red), FREQ deviant (blue) and INT deviant (green) for (A) control children ($N = 15$), (B) the FRND group ($N = 24$) and (C) the FRD group ($N = 15$).

Table 2 – Mean amplitude per electrode, per condition, per group. Asterisks reflect MMN amplitudes to be significantly different from zero. Note: $p < .05^*$, $p < .01^{}$, $p < .001^{***}$.**

Electrode	Controls (N = 15)			FR no dyslexia (N = 24)			FR dyslexia (N = 15)		
	ART	FREQ	INT	ART	FREQ	INT	ART	FREQ	INT
Fz	.47 (1.98)	–1.64 (1.53)**	–.68 (1.63)	.47 (1.28)	–.34 (1.93)	.23 (1.70)	.49 (1.26)	–.60 (1.61)	.71 (1.28)*
F1	.34 (2.24)	–1.38 (1.54)**	–.61 (1.62)	.38 (1.21)	–.45 (1.70)	.15 (1.50)	.31 (1.21)	–.50 (1.55)	.64 (1.21)
F2	.51 (2.01)	–1.71 (1.40)**	–.77 (1.66)	.61 (1.28)*	–.47 (1.95)	.01 (1.57)	.54 (1.26)	–.74 (1.47)	.69 (1.27)
F3	.46 (2.39)	–1.72 (2.02)**	–.79 (1.64)	.29 (1.08)	–.49 (1.74)	.17 (1.61)	.11 (1.17)	–.72 (1.62)	.43 (1.27)
F4	.48 (1.80)	–1.82 (1.46)**	–.99 (1.70)*	.68 (1.29)*	–.48 (1.43)	.02 (1.57)	.30 (1.27)	–.84 (1.32)*	.60 (1.11)
P9	.25 (1.77)	–.64 (1.82)	.55 (1.66)	.27 (1.49)	–.44 (1.48)	.17 (1.87)	.36 (1.60)	–.43 (1.13)	.01 (1.67)
P10	.12 (1.52)	–.64 (1.67)	.53 (1.03)	.12 (1.39)	–.66 (1.37)*	.26 (1.89)	.04 (1.62)	–.37 (1.17)	–.09 (1.23)
LM	.08 (1.40)	–.93 (1.52)*	.29 (1.02)	.23 (1.52)	–.17 (1.73)	.31 (2.15)	–.06 (1.42)	–.44 (1.05)	–.34 (1.39)
RM	–.02 (1.33)	–.36 (1.84)	.43 (1.12)	.25 (1.15)	–.51 (1.35)	.19 (1.74)	–.07 (1.53)	–.17 (1.01)	–.26 (1.18)

two conditions. There were no main effects of hemisphere, suggesting bilateral processing. Furthermore, no significant differences between the groups were found in hemispheric activity for either ART or FREQ, suggesting no differences in lateralization across groups.

3.2. LDN

To assess whether an LDN was present in all groups, mixed ANOVAs were run for each deviant type (ART, FREQ, INT) with factors stimulus type (standard, deviant), electrode (F3, F1, Fz, F2, F4, inverted P9, inverted P10, inverted LM, inverted RM [the signal from the mastoids and P9 and P10 was inverted because of a polarity reversal]) and between factor groups. Prior to further analysis, we investigated the effect of deviance level on LDN amplitude. No effects of deviance level were found for all three deviant types, presumably due to too few collected deviants per level. Hence, to improve signal-to-noise ratio for our further analyses, we averaged across the levels of each type of deviant.

Main effects of stimulus type were found for ART [$F(1,51) = 39.16$, $p < .001$] and FREQ [$F(1,51) = 106.51$, $p < .001$]. No Group $\times$ Stimulus type interactions were found, indicating that an MMN was elicited for ART and FREQ in all three groups. For INT, we found a main effect for Stimulus type [$F(1,51) = 12.85$, $p = .001$] and a Group $\times$ Stimtype interaction [$F(2,51) = 3.78$, $p = .029$]. Planned post-hoc tests showed that an LDN was only elicited in the control group [$F(1,14) = 10.47$, $p = .006$] but not in the FR groups. We also found main effects for electrode for ART [$F(1.65,84.14) = 66.54$, $p < .001$], FREQ [$F(1.50,76.47) = 64.17$, $p < .001$] and INT [$F(1.60,81.69) = 57.25$, $p < .001$]. Post-hoc t-tests were administered to identify electrodes at which LDN amplitude was significantly different from zero, per group. Results are displayed in Table 3.

To assess whether LDN amplitude differed in size between groups, a mixed ANOVA with factors Deviant type (ART, FREQ, INT), electrode (F1, F3, Fz, F2, F4) and group (C, FRD, FRND) was run. There was a main effect for Deviant type [$F(2,102) = 6.30$, $p = .003$] and a marginal interaction effect for Group $\times$ Deviant type [$F(4,102) = 2.15$, $p = .080$]. Subsequently, we pooled over the two at-risk groups to assess amplitude differences in controls versus children at risk of dyslexia regardless of their reading level. There was a main effect for Deviant Type [$F(4,102) = 3.50$, $p = .034$] and a Group $\times$ Deviant type interaction was found [$F(2,104) = 3.29$, $p = .023$]. It appears that the

INT LDN is larger in control children, and absent in both groups of at-risk children. There are no group differences in LDN amplitude for ART and FREQ, indicating that the elicited LDNs are not different in size.

Scalp distributions between 400 and 440 msec per condition and participant group are presented in Fig. 4. The scalp activity underlying the ART LDN looks similar in all three groups, with a negative polarity on frontal electrodes and a bilateral area of positive polarity around the mastoids. For FREQ, a positive potential near the LM can be observed in the control group. In both FR groups, a bilateral scalp distribution around mastoid sites is seen. All three groups exhibit a negative frontal polarity. We addressed group differences in scalp lateralization of activity in two mixed ANOVAs by comparing right hemisphere (inverted RM, inverted P10, F4) and left hemisphere (inverted LM, inverted P9, F3) electrodes across three groups for ART and FREQ, because an LDN was found in all three groups for these two conditions. No significant differences were found between the groups in hemispheric activity for ART, suggesting no differences in lateralization across groups. We found a significant Laterality $\times$ Group interaction for FREQ [$F(2,51) = 4.60$, $p = .015$]. A within-subjects post-hoc mixed ANOVA yielded a main effect of laterality for control children only [$F(1,14) = 6.52$, $p = .023$]. This suggests that although all groups show an MMN in this condition, the scalp distribution of the response is different. Bilateral activation patterns are found in both at risk groups, whereas a left lateralized scalp distribution is seen in typically reading controls (see Fig. 3).

Additionally, Pearson correlations were used to investigate the relationship between MMN and LDN amplitude, reading fluency (PWF, WRF) and PA. Correlation analyses examining the relation between MMN and LDN amplitude and reading fluency yielded no significant results. No significant relations were found between MMN and LDN amplitude and PA either. We found, however, significant correlations between PA and WRF ($r = .30$, $p = .024$) and PWF ($r = .71$, $p < .001$).

4. Discussion

We investigated sensitivity to changes in ART in typically developing control children versus children at-risk of dyslexia who did or did not become fluent readers. We found that all three groups showed a sensitivity to ART and frequency

Fig. 3 – Top, left, and right scalp distributions of the mismatch response per deviant type displayed in voltage maps. (A) represents the scalp distributions of the ART MMN, (B) shows the scalp distribution of the FREQ MMN and (C) represents the scalp distribution of the INT MMN. Scalp distributions of control children are displayed in the left column, of the FRND children in the middle column and of the FRD children in the right column. The time window represented is 240–280 msec.

changes as indicated by an MMN. For ART, the deviant stimulus unexpectedly had a more positive polarity compared to the standard, similar to results of Hämäläinen et al., 2008. For frequency, differences in amplitude could be observed

between controls and FRND children. For intensity, none of the groups showed an MMN. With regard to LDN elicitation, all groups were sensitive to changes in ART and frequency. No group differences were found in LDN amplitude for ART and

Table 3 – Mean amplitude per electrode, per condition, per group. Asterisks reflect LDN amplitudes to be significantly different from zero. Note: $p < .05^*$, $p < .01^{}$, $p < .001^{***}$.**

Electrode	Controls (N = 15)			FR no dyslexia (N = 24)			FR dyslexia (N = 15)		
	ART	FREQ	INT	ART	FREQ	INT	ART	FREQ	INT
Fz	-.80 (1.16)*	-1.41 (2.18)*	-1.39 (2.05)*	-.75 (1.47)*	-1.23 (1.44)***	.11 (1.43)	-1.29 (2.02)*	-1.45 (1.00)***	-.07 (1.54)
F1	-.97 (1.56)*	-1.33 (2.38)*	-1.27 (2.29)*	-.72 (1.33)*	-1.12 (1.49)***	.12 (1.34)	-1.47 (1.74)**	-1.31 (1.04)***	-.04 (1.63)
F2	-.73 (1.11)*	-1.45 (2.38)*	-1.44 (2.05)*	-.71 (1.59)*	-1.25 (1.68)***	-.08 (1.40)	-1.31 (1.83)*	-1.54 (1.11)***	-.10 (1.59)
F3	-.45 (1.41)	-1.42 (2.20)*	-.79 (2.91)	-.68 (1.38)*	-1.05 (1.27)***	.14 (1.32)	-1.51 (1.58)**	-1.55 (1.85)***	-.14 (1.50)
F4	-.53 (1.00)	-1.62 (2.52)*	-1.51 (2.04)*	-.75 (1.63)*	-1.33 (1.61)***	-.15 (1.48)	-1.42 (1.61)**	-1.71 (1.19)***	.01 (1.54)
P9	-1.06 (1.99)	-.81 (1.89)	.22 (2.16)	-.47 (1.19)	-.79 (1.55)*	-.61 (1.67)	-.32 (1.53)	-.79 (1.69)	-.18 (1.92)
P10	-.66 (1.93)	-.08 (1.66)	-.04 (1.71)	-.52 (1.24)*	-.89 (1.02)***	-.20 (1.43)	-.31 (1.57)	-.82 (1.57)	-.44 (1.63)
LM	-1.27 (1.87)*	-1.19 (1.51)**	-.43 (1.61)	-.31 (.99)	-.61 (1.56)	-.19 (1.52)	-.57 (1.16)**	-.93 (1.18)	-.64 (1.56)
RM	-.57 (1.76)	-.12 (1.63)	.14 (1.64)	-.29 (1.25)	-.78 (1.30)*	-.17 (1.35)	-.66 (1.37)	-.61 (1.30)	-.68 (1.41)

frequency, though frequency processing appeared less lateralized in the LDN window in both groups of at-risk children. Interestingly, in the LDN window neither good nor poor reading at-risk children discriminated changes in intensity. Only control children showed an LDN for the intensity deviant. Taken together, these results suggest that proficiency of processing of ART and frequency is not related to reading at age 11, whereas deficits in intensity processing as reflected by an absent LDN, may be related only to being at-risk for dyslexia. Differential lateralization of the LDN of frequency processing also seems related to being at-risk of dyslexia.

Looking at the pattern of results regarding MMN and LDN, it must be noted that the component we labeled MMN seems to displays functional properties of an adult auditory N1 wave, which emerges around age 10 (Csépe, Dieckmann, Hoke, & Ross, 1992; Kurzberg, Vaughan, Kreuzer, & Fliegel, 1995). Support for this interpretation especially comes from the observation that the ART and intensity deviants are more positive compared to the standard at this latency. This could be explained by a lack of afferent stimulation, because the ART and intensity stimuli overall sounded softer. In contrast, a more negative peak for the frequency deviant can be seen, reflecting more afferent stimulation resulting from the higher frequency of the deviant compared to the standard. In this light, it may be inferred that what we call MMN reflects the characteristics of adult obligatory component N1, and what we call LDN is actually reflecting a change discrimination similar to adult MMN functionality. However, an interpretation where the first peak is labeled an MMN and the second LDN is in concordance with the literature (e.g., Cheour et al., 2001; Hämäläinen et al., 2008; Neuhoff et al., 2012; Schulte-Körne et al., 2001) and has been adopted here.

Our findings regarding ART-processing are interesting in light of the previous DDP-study of Plakas et al. (2013). It was found that 41-month-old children with a familial risk for dyslexia were less proficient in processing differences in ART compared to controls, suggesting that at younger age, poor ART processing is a characteristic of children who have a familial risk for dyslexia. There was, however, no relation with differences in reading within the at-risk group. The present study investigated ART processing at age 11 (with a different subgroup of DDP children) and we found that all three groups were equally proficient processing ART, both in an early and later stage. Our results suggest that at age 11, ART processing does not relate to reading skill and—in contrast to Plakas et al.—it does not relate to being at familial risk of dyslexia. Possibly, previous impairments in ART processing in at risk children have been overcome during the years of reading instruction.

Our results are in contrast with other studies with school-aged children between 9 and 11 years old, which do report differences between good and poor readers in ART processing (e.g., Goswami et al., 2002; Richardson et al., 2004; Surányi et al., 2009). However, as has been suggested in the introduction, these outcomes may have been confounded by not controlling for two factors. First, in contrast to the tasks used in the behavioral studies, MMN paradigms do not require attention from participants which may explain our diverging results, showing that when attention is not crucial, proficiency of ART processing is not related to reading fluency.

Fig. 4 – Top, left, and right scalp distributions of the mismatch response per deviant type displayed in voltage maps. (A) represents the scalp distributions of the ART MMN, (B) shows the scalp distribution of the FREQ MMN and (C) represents the scalp distribution of the INT MMN. Scalp distributions of control children are displayed in the left column, of the FRND children in the middle column and of the FRD children in the right column. The time window represented is 400–440 msec.

Second, in contrast to our study, the possibility that ART processing level in these behavioral studies relates to family risk status of the compared groups and not to differences in reading, was not addressed.

To be able to investigate whether ART processing specifically relates to reading, the present study also included a frequency deviant in the paradigm. The results show that all three groups process frequency adequately in the LDN

window, suggesting that frequency processing does not relate to reading fluency at all. This is in line with other studies investigating pre-attentive responses to frequency changes in dyslexia (e.g., Heim et al., 2000; Schulte-Körne, Deimel, Bartling, & Remschmidt, 1998). Regarding the MMN window, we found a slight attenuation in MMN amplitude in at-risk children compared with controls despite significant MMN elicitation in all groups. Yet, no correlates with reading measures were found. There are studies that find an attenuated MMN to frequency changes in dyslexia, especially when the deviation is less than 10% and when the stimulus onset asynchrony (SOA) is short (e.g., Baldeweg, Richardson, Watkins, Foale & Gruzelier, 1999; for an overview, see Bishop, 2007). It is possible that a deficit in frequency processing thus only becomes apparent when differences are small.

Though our groups were all able to process changes in frequency, a differential scalp distribution in reaction to frequency deviants was found in our at risk groups compared to our control group in the LDN window. No difference in laterality of the scalp activation was observed in at-risk children whereas control children showed left lateralized scalp activations. This finding is in line with previous studies that have reported differential processing circuits for language and reading in dyslexics (Helenius, Tarkiainen, Cornelissen, Hansen, & Salmelin, 1999; for a review, see Pugh et al., 2000) and differential hemispheric activation in dyslexic participants of various ages for tone- and speech processing (Kujala, Belitz, Tervaniemi, & Näätänen, 2003; Lovio, Näätänen, & Kujala, 2010; Lyytinen et al., 2005; van Herten et al., 2008; van Zuijen, Plakas, Maassen, Maurits, & van der Leij, 2013). However, it was unexpected that our control group showed left lateralized scalp activation when processing frequency, as previous results suggest a right lateralized scalp activation to changes in pitch in newborns that later turned out to be fluent readers (Leppänen et al., 2010). In our study, FR children show a bilateral scalp pattern compared to controls. It is possible that a different frequency processing network underlies these differences, or perhaps that the lateralization of processing of frequency information follows a different developmental trajectory in FR children compared to controls.

Our study yielded a novel finding regarding intensity processing. We included an intensity deviant to control for intensity confounds, as ART deviants can in general be perceived as having a decreased loudness. Including an intensity deviant allowed us to distinguish between effects caused by intensity versus ART. Although we did not find poor ART processing in any of the groups and no indications of an intensity MMN, the intensity LDN was impaired in both groups of at risk children, but not in controls. Hence, these results provide support for the idea that ART and intensity processing do not tap the same processing mechanisms. Additionally, this suggests that a deficit in intensity processing may be a characteristic of being at familial risk for dyslexia. Several studies have investigated intensity processing on a behavioral level. Contrary to our results, the larger part of these studies have not found any differences in intensity processing between dyslexic participants and controls, both in adult and child populations (for a review, see Hämäläinen et al., 2013). Good and poor readers did not differ in their intensity discrimination threshold. Only 3 out of 16

reviewed studies by Hämäläinen et al. found differences in intensity processing. Goswami et al. (2010) investigated intensity processing in multiple languages, but only found impaired intensity processing for English dyslexic participants and not for Spanish and Chinese. Thomson, Fryer, Maltby, and Goswami (2006) found a significant difference in intensity discrimination between dyslexic participants and controls. Poor readers had a higher perceptual threshold than fluent readers. Results from a study by Amitay, Ben-Yehudah, Banai, and Ahissar (2002) partly support our findings. They found that a subgroup of adults with dyslexia performed poorer on an intensity discrimination test compared to controls. Taken together, evidence suggests that in general, good and poor readers are equally able to discriminate intensity differences on a behavioral level. To our knowledge, only a few studies investigated pre-attentive intensity processing. In a study with typically developing children, Sussman and Steinschneider (2011) found that the intensity MMN was dependent on active attention. Children only discriminated intensity differences when aided by behavioral cues. Kujala et al. (2006) investigated pre-attentive intensity processing without behavioral cues in adults. They found no significant differences in MMN amplitude for intensity between poor readers and controls. Children in our study did not receive any behavioral cues. The MMN results obtained are thus in concordance with Sussman and Steinschneider (2011) and Kujala et al. (2006). However, the intensity deviant yielded a clear LDN difference in the at-risk children. Though we found differences in pre-attentive intensity processing at age 11, it is possible that intensity processing normalizes as children mature as the LDN gradually diminishes throughout development (e.g., Čeponiene et al., 2004). It is unlikely that our results regarding intensity can be attributed to hearing deficits. None of the participating children reported hearing problems and if there were slight differences in hearing thresholds, we assume these are randomly divided over groups.

An alternative explanation for the pattern of results described, is that the FRND group had slight subclinical reading deficits because they scored poorer on pseudoword reading than controls. In this light, results could be interpreted as being a consequence of the pseudoword reading deficit and thus, impairments in pre-attentive processing could be related to reading skill, instead of family risk. Nonetheless, the pseudoword deficit of the FRND group is merely subclinical (scores still fall within the average range) and WRF was not affected in this group. Moreover, the absence of correlations between reading and ERP measures (both MMN and LDN) provide little support for this interpretation.

The fact that both good and poor readers have proficient ART processing questions the relationship between ART processing, PA and reading. If it were true that unimpaired ART processing relates to the development of PA, which in turn predicts reading skill, we would expect to find a relation between ART and PA and ART and reading fluency. However, results from Plakas et al. (2013) and our own study do not indicate such a relation. Combining the results from these DDP studies suggests that impaired ART processing is a characteristic of FR children in early childhood, which

normalizes by the time they reach puberty. In addition, both studies have shown that ART processing is not directly related to reading skill, and, therefore, does not qualify as a cause of dyslexia.

5. Conclusion

We conclude that ART processing, when measured independent of attention, is not related to reading as it is unimpaired in both good and poor reading FR children. The same holds for frequency processing. We found group differences in the scalp distribution of frequency processing but the distinction was between at risk children versus controls. We found bilateral frequency processing in FR children versus left lateralized frequency processing in controls. This may indicate that FR children employ different processing networks compared to controls. Intensity processing was impaired in FR children regardless of their reading level. Taken together, our results suggest that differential scalp lateralization when processing frequency and impaired intensity processing are correlates of being at familial risk for dyslexia. Furthermore, abnormal basic auditory processing deficits—ART included—are not associated with reading skill, because we cannot discriminate between FR children who do and do not develop reading problems. Rather, we consider impairments of some basic auditory processing skills to be characteristic of a group of FR children.

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