Received: 1 November 2017 | Revised: 30 July 2018 | Accepted: 16 October 2018

DOI: 10.1002/dys.1604

RESEARCH ARTICLE

WILEY

N1 lateralization and dyslexia: An event-related potential study in children with a familial risk of dyslexia

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Funding information
Netherlands Organisation for Scientific Research (NWO), Grant/Award Number: 360-89-040

The rapid automatic specialized processing of printed words is signalled by the left-lateralization of the N1 component in the visual event-related potential (ERP). In the present study, we have investigated whether differences in N1 lateralization can be observed between Dutch children with and without (a familial risk of) dyslexia around the age of 12 years using a linguistic judgement task. Forty-five participants were included in the ERP analysis, 18 in the low familial risk group without dyslexia, 15 in the high familial risk group without dyslexia, and 12 in the high familial risk group with dyslexia. The results showed that although the N1 peaked slightly earlier in the left hemisphere, the N1 amplitude was right-lateralized in all groups. Moreover, there were no group differences in N1 amplitude or latency, and there was no relationship between reading (related) test scores and N1 characteristics. The results of the present study and our previous findings in adults suggest that print-tuning lateralization is a process that is still developing in adolescence. Because other studies did find N1 lateralization in younger readers with a print versus nonprint contrast, the current results seem to indicate that differences in N1 lateralization also depend on the experimental paradigm.

KEYWORDS

children, dyslexia, familial risk, lateralization, N1, neuroimaging

1 | INTRODUCTION

Dyslexia is a specific learning disorder that is characterized by deficits in accurate and/or fluent word recognition, decoding, and spelling (American Psychiatric Association, 2013, p. 67). Dyslexia affects about 3–10% of the normal population (Miles, 2004), depending among others on the exact criteria used; because dyslexia is not a discrete disorder, there are no natural cut-off points (Shaywitz, Escobar, Shaywitz, Fletcher, & Makuch, 1992). The prevalence of dyslexia among children with a parent with dyslexia is much higher, on average 45% (Snowling & Melby-Lervåg, 2016). In transparent languages like Dutch, with a regular letter-to-sound relationship, dyslexia is mainly characterized by speed deficiencies (Serrano & Defior, 2008; Wimmer, 1993). An explanation for the slow and effortful reading can be deficient visual processing of print. The present study aims to investigate if there are differences in brain activity during visual print processing between Dutch children around the age of 12 years with and without (a familial risk [FR] of) dyslexia.

1.1 | The development of N1 lateralization

To process written information successfully, the human brain develops perceptual expertise for print to recognize graphemes successfully and activate the corresponding phonemes. Neuroimaging studies have revealed that the visual word form area in the fusiform gyrus in the left hemisphere is particularly activated during the early processing of print (Dehaene, Clec'H, Poline, Bihan, & Cohen, 2002; Moscoso del Prado Martín, Hauk, & Pulvermüller, 2006; Nobre, Allison, & McCarthy, 1994). From this area, the N1 or N170 component is thought to arise. This early negative event-related potential (ERP) component is thought to be sensitive to category-specific visual information, such as to words or faces (Schendan, Ganis, & Kutas, 1998). In response to print, it peaks in normal reading adults around 150–200 ms after stimulus presentation in the parietal-occipital region. It is typically left-lateralized, as the amplitude is larger and the peak occurs earlier in the left compared with the right hemisphere (Bentin, Mouchetant-Rostaing, Giard, Echallier, & Pernier, 1999). The left-lateralized N1 response to print is not specific to alphabetic scripts but has also been found in Japanese readers of the logographic Kanji script (Maurer, Zevin, and McCandliss (2008). By studying the adaptation response using independent component analysis (ICA) in a visual oddball paradigm with the letters “g” and “s,” it was found that the N1 component probably consists of multiple subcomponents (Korinth, Sommer, & Breznitz, 2013); the earlier part has a lower neural response specificity and seems to be sensitive to more broad stimulus properties than the later part of the N1, which is more finely tuned.

Many studies have used a paradigm involving a contrast between letter strings or words and symbol strings or false font strings to investigate coarse print tuning, the specific visual expertise for the processing of print versus nonprint. The N1 print-tuning effect becomes more lateralized with age. Maurer, Brem, Bucher, and Brandeis (2005) found no signs of N1 lateralization in an electroencephalography (EEG) study in prereading children using a repetition detection task. By Grade 2, Maurer et al. (2007) found lateralized print tuning in children without reading problems, but lateralized print tuning could not be observed in children with dyslexia. In another study, a clear print-tuning effect could be observed in first grade students; not only at the group level but also at the individual level for almost 90% of the children (Eberhard-Moscicka, Jost, Raith, & Maurer, 2015). Brem et al. (2010) showed that N1 tuning for print can be found after a short training of grapheme-phoneme correspondences in prereading children, although the effect disappeared after a few weeks. Finally, in a more recent study, using letter strings presented in rapid streams of pseudo fonts, it was found that the brain's response to print for prereading 5-year-old children already correlated with letter knowledge, which is an important predictor of later reading (Lochy, Reybroeck, & Rossion, 2016). Thus, in typical readers, course print tuning develops quickly after a short exposure to print.

Evidence for reduced N1 print-tuning lateralization has been found in preadolescent children with dyslexia in contrast to typical reading controls using a lexical decision task (Kast, Elmer, Jancke, & Meyer, 2010) and using an implicit reading task (Araújo, Bramão, Faísca, Petersson, & Reis, 2012). In the EEG study by Maurer, Schulz, Brem,

van der Mark, Bucher, Martin, and Brandeis (2011), using a repetition detection task, the difference between readers with dyslexia and typically reading controls almost completely disappeared by Grade 5. However, the accompanying functional magnetic resonance imaging measurement did reveal differences in brain activation between the dyslexic and nondyslexic groups in the visual word form area. For adults with dyslexia, Helenius, Tarkiainen, Cornelissen, Hansen, and Salmelin (1999) found reduced N1 print-tuning lateralization with a repetition-detection task using magnetoencephalography. Furthermore, in an EEG study with a lexical decision task reduced N1 lateralization was also found among French adults with dyslexia (Mahé, Bonnefond, Gavens, Dufour, & Doignon-Camus, 2012). These findings seem to suggest that there are still differences in coarse print-tuning lateralization between older readers with and without dyslexia.

Some studies have found that the N1 is also sensitive to lexicality effects, as the N1 was found to be more negative in response to words in contrast to pseudowords. The development of this more fine-grained tuning of the N1 to word-specific characteristics seems to develop in adolescence as it was not found in late-elementary school children, but it was present in adults (Coch & Meade, 2016). The lexicality effect was also not found in the study by Eberhard-Moscicka et al. (2015) with first grade children nor in the studies by Araújo et al. (2012) and Kast et al. (2010) with preadolescent children. Xue, Jiang, Chen, and Dong (2008) showed that the N1 lexicality effect is also modulated by factors such as familiarity of the script and stimulus length. Recently, Eberhard-Moscicka, Jost, Fehlbaum, Pfenninger, and Maurer (2016) found that the first and the second subcomponent of the N1 are sensitive to course print tuning in children, whereas in adults only the first subcomponent is sensitive to course print tuning and the second subcomponent is sensitive to the lexicality effect, but only in the participants' native language German and not in the second language English. Zhao et al. (2014) found that the N1 was larger in response to words than consonant strings among 7-year-old readers with a high reading ability in contrast to readers with a low reading ability. Another study showed that the N1 may not only be sensitive to lexicality but may also be influenced by orthographic processing as the N1 for orthographically legal pseudowords was larger than for orthographically illegal nonwords for typically reading adults (Araújo, Faísca, Bramão, Reis, & Petersson, 2015); for readers with dyslexia, this effect of orthographic effect was absent. Together, these studies suggest that the more fine-grained early processing of words develops after course print tuning can be observed. The development of this more fine-grained processing of words in the N1 time window depends among other factors upon reading experience and reading skill level, but methodological factors may also play a role.

A few studies have also studied the N1 response related to reading or dyslexia without a print versus nonprint contrast or word versus pseudoword contrast. Using a linguistic judgement task, Spironelli and Angrilli (2009) found N1 lateralization in the right hemisphere in 10-year-old normal-reading children in contrast to both students and older adults where the N1 was left-lateralized. In this study, participants had to judge whether consecutively presented word pairs rhymed, were semantically related, or matched visually. The N1 response was measured during the presentation of the first word. Because all stimuli were words, it is likely that the N1 response contains both coarse print tuning and lexicality-related subcomponents. Using a similar methodology, van Setten, Martinez-Ferreiro, Maurits, and Maassen (2016) found N1 lateralization differences in the ERPs of right-handed higher education students with and without dyslexia. Moreover, there were correlations between the N1 amplitude in the left hemisphere, reading fluency and scores on a visual attention span (VAS) test. In the present study, we used the exact same ERP experiment as van Setten et al. (2016) to investigate whether N1 lateralization differences between readers with and without (an FR of) dyslexia are present around the age of 12.

1.2 | The role of FR

As we mentioned above, there is an FR of dyslexia, as children of parents with dyslexia are more likely to develop dyslexia than children of parents without dyslexia. Genetic factors play a role in the development of dyslexia, as the concordance rate is higher among identical twins than among fraternal twins (DeFries & Alarcón, 1996), and

several genes have been linked to dyslexia (Carrion-Castillo, Franke, & Fisher, 2013;e.g., Carrion-Castillo et al., 2017; Fisher & Francks, 2006; Mascheretti et al., 2017). Dyslexia has a multifactorial origin, as there is not a single underlying cause or cognitive deficit (Pennington, 2006; Pennington et al., 2012). Therefore, children with a high FR without dyslexia (HRnonDys) may still have inherited or been exposed to some of the same risk factors as children with a high FR with dyslexia (HRDys). As a result, they show some of the same cognitive and reading deficits, though usually in a milder form, as children with dyslexia. In several studies with children with an FR, this has resulted in a three-step pattern, where the scores of the HRnonDys group are in between the scores of the HRDys group and a group with a low FR without dyslexia (LRnonDys;e.g., Elbro, Borstrøm, & Petersen, 1998; Pennington & Lefly, 2001; Snowling, Gallagher, & Frith, 2003; van Bergen, de Jong, Plakas, Maassen, & van der Leij, 2012). Thus, like dyslexia itself, the FR of dyslexia is a continuous measure (see, for a more in-depth discussion, van Bergen, van der Leij, & de Jong, 2014). Differences between the LRnonDys and HRnonDys groups tend to be more pronounced in young beginning readers compared with older more advanced readers where differences are often not significant (Dandache, Wouters, & Ghesquière, 2014; Eklund, Torppa, Aro, Leppänen, & Lyytinen, 2014).

1.3 | Hypotheses

In this study, we investigated the N1 lateralization related to print processing in three groups of participants: HRDys, HRnonDys, and LRnonDys. Because the children in our study were older than the children in the study by Spironelli and Angrilli (2009), we expected that at least for the LRnonDys group, the N1 would be somewhat left-lateralized. Furthermore, we expected that the N1 would be less left-lateralized in the HRDys group compared with the two nondyslexic groups. In addition, we anticipated that the left-lateralization of the N1 would be more pronounced in the LRnonDys group compared with the HRnonDys group, as previous studies have also found that the HRnonDys group sometimes scores in between the other two groups because dyslexia and the FR for dyslexia are continuous constructs. We also conducted behavioural tests to asses reading fluency and reading-related skills. Based on van Setten et al. (2016), we expected that especially reading fluency and VAS are related to N1 lateralization.

2 | METHODS

2.1 | Participants

All participants in this study were Dutch children, around the age of 12 years, who participated in the Dutch dyslexia program (DDP; see,e.g., van Bergen et al., 2012; van der Leij et al., 2013) in Groningen. Initially, 68 children were included in the study. Seven of those started the experiment but did not complete it because of discomfort, and one participant with severe behavioural problems during the behavioural testing was excluded before the EEG measurement, leaving 60 children for further analysis.

Children were subsequently divided into three groups based on their dyslexia and FR status. Risk status was based on parental word reading fluency (WRF) and pseudoword reading fluency (PWRF) scores, using the same tests used in this study for the children described later. A child was categorized in the high-FR group if at least one parent read on one test in the lowest 20th percentile and on the other test below average, based on the norms by Kuijpers et al. (2003). Furthermore, the parent had to have self-reported dyslexia and a self-reported family history of dyslexia. Children were categorized in the low-FR group if both parents did not meet these criteria. Dyslexia status of the children was based on the WRF and PWRF measurements of Grades 2, 3, and 6. If a child scored, on at least two out of three occasions, in the lowest 10th percentile on either WRF or PWRF and on the other test at least below average, the child was categorized in the group with dyslexia. When a child had a missing value for one measurement, he or she was still included if the outcome of the two remaining measurements corresponded.

Of the 60 participants who completed the EEG experiment, five participants were excluded because their risk or dyslexia status could not be determined because only one nondyslexic parent was tested or due to too many missing values of the child. Three participants with dyslexia in the low-FR group were excluded because this group was too small to include as a separate group in the study. Two participants with an IQ below 80, as determined during a previous DDP measurement, and one participant with severe medical problems were excluded because reading difficulties could be caused by other factors than dyslexia in these cases. Children with comorbid disorders were not excluded from the study as comorbidity between dyslexia and other developmental disorders is common and excluding these participants would introduce a bias and result in a lower power in the analyses. The EEG of four participants (two in the LRnonDys group and one in each HR group) could not be used for the analysis because of technical reasons that will be described below in the EEG recording and analyses section; thus, 45 participants were included in the EEG analyses. However, because these latter four participants (one right-handed boy and three girls, of whom one girl was left-handed) did complete the whole task and met all other inclusion criteria, they have been included in the analysis of the behavioural tests and the analysis of the reaction times and accuracy of the EEG tasks. Of the 49 children included in the behavioural analyses, there were 21 boys (nine in the LRnonDys group, six in the HRnonDys group, and six in the HRDysGroup). Ten children were left-handed (four in the LRnonDys group, three in the HRnonDys group, and three in the HRDys group). Most children were in Grade 6, but one was in Grade 5, and 14 were in Grade 7. Further demographic information per group can be found in Table 1.

2.2 | Experimental design

The exact same experimental procedure and stimuli as used by van Setten et al. (2016) were used for the present EEG experiment. This design was based on the study by Spironelli and Angrilli (2009). Participants had to perform a judgement task with word pairs. They performed three tasks with the same 100 word pairs; thus, there were 300 trials in total. The first task was a visual judgement task where the participants had to decide whether both words were written in capitals. The second task was a phonological judgement task where the participant had to decide whether the words rhymed. The third task was a semantic task where the participant had to decide whether the word meanings were related. Participants had to press a button with a green happy smiley with their left or right index finger when there was a match, and they had to press a button with a red sad smiley when there was no match. The locations of the match and no-match buttons were balanced across participants such that for half of the participants, the match button was on the right and the no-match button on the left, and for the other half vice versa. Twenty-five percent of the trials were match trials. Although task differences were not expected for the N1 analysis, they are of interest for the analysis of the task accuracy and reaction times.

There were four types of word pairs, 25 visual matches, 25 phonological matches, 25 semantic matches, and 25 pairs that did not match in any of these three ways. All words were nouns. They consisted of one or two syllables and had a length varying between three and eight letters. They were all high-frequency nouns with a frequency above 10 per million according to the CELEX database (Baayen, Piepenbrock, & Gulikers, 1995). Words with multiple listed meanings were avoided. The words of a pair were presented successively. They were presented in white in the centre of a black screen in the font Courier New at size 18. A trial started with the presentation of the first word for 1.5 s. During the interstimulus interval of 1 s, a fixation cross was presented in the centre of the screen. The second word was presented for a maximum duration of 5 s, during which the participant had to respond. After the response or after 5 s, the screen was black for 0.5 s. Finally, there was an intertrial interval that varied in length between 1.5 and 2.5 s during which a fixation cross was presented to prepare the participant for the next trial. E-prime 2.0.8.90 (Psychology Software Tools, Pittsburgh, PA, USA) was used to present the stimuli and record the behavioural responses.

Blocks of 50 trials of the same task were created. Half-way a block participants could take a small break if they wished, or they could continue with the second half of the block. In-between blocks, a short entertaining movie was

TABLE 1 Participant characteristics and behavioural test results per group

Variable	LRnonDys (*n* = 20)			HRnonDys (*n* = 16)			HRDys (*n* = 13)			Effect size *r*		
	M	*Mdn*	*SD*	*M*	*Mdn*	*SD*	*M*	*Mdn*	*SD*	LRnonDys – HRDys	HRnonDys – HRDys	LRnonDys – HRnonDys
Demographics												
Handedness score (−10 is extremely left-handed, 10 is extremely right-handed)	5.4	8.0	6.7	6.3	8.5	6.1	5.2	8.0	6.6	0.02	0.05	0.02
Age in months	146.2	146.5	2.9	145.6	146.0	4.3	149.1	149.0	3.9	0.40	0.40	0.09
Grade	6.4	6.0	0.5	6.2	6.0	0.4	6.2	6.0	0.6	0.21	0.02	0.23
Reading												
Word reading fluency (Wechsler-score)	10.1	10.0	2.8	11.0	11.0	2.6	2.8	1.0	2.4	0.82	0.85	0.23
Pseudoword reading fluency (Wechsler-score)	10.6	10.0	2.5	10.8	11.0	3.0	5.0	5.0	2.3	0.79	0.76	0.03
Reading-related skills												
RAN (item/min)	136.6	136.4	19.4	141.3	142.9	31.1	116.3	115.4	12.1	0.52	0.46	0.09
Orthographic knowledge (accuracy, max = 70)	65.1	66.5	4.3	64.6	65.5	3.6	56.6	56.0	6.9	0.61	0.61	0.05
Visual attention span (accuracy, max = 100)	77.5	82.0	14.9	76.0	71.0	14.4	66.5	63.0	14.3	0.35	0.32	0.05
PA accuracy (max = 12)	9.9	10.0	1.6	9.9	10.0	2.1	8.5	9.0	1.8	0.42	0.44	0.05
PA reaction times (ms)	2,733	2,640	904	3,303	3,179	911	5,723	5,069	3,119	0.60	0.50	0.33

Note. LRnonDys: low familial risk without dyslexia; HRnonDys: high familial risk without dyslexia; HRDys: high familial risk with dyslexia; RAN: rapid automatized naming; PA: phonological awareness.

played for 1.5–3 min to help the participants switch between tasks and to force them to take a break. After the participants had performed all tasks once, there was a longer break during which they were offered a drink. The task order was balanced across participants. During the second half of the experiment, participants performed all tasks again in the same order as during the first half. Participants were seated in a dimly lit electronically and sound-isolated room. The approximate distance to the 16-inch computer screen was 50 cm. The stimuli were approximately 2–5.5 cm wide depending on the number of letters. Therefore, the visual angle varied between 1.15 and 3.15 degrees. Before the real experiment, participants were given the opportunity to practice each task with different words than the ones used in the real experiment. Unlike during the real experiment, participants automatically received feedback about their performance during the practice experiment.

2.3 | Behavioural tests

The data collection was spread over two sessions, an EEG session and a behavioural session, with at least a 2-hr break in between, but sometimes also on separate days. The behavioural measures in this experiment were part of a longer behavioural testing session that took approximately 1.5 hr including a break. A full report of all measures is, however, beyond the scope of this paper; therefore, we only describe the measures relevant for the present study.

Like in the study by van Setten et al. (2016), WRF and PWRF were measured using a fluency test where the participant had to read as many (pseudo)words as possible correctly within the allotted time. WRF was measured with the 1-min reading test ("Eén-minuut-test"; Brus & Voeten, 1973), and PWRF was measured with the "Klepel" test (van den Bos, Lutje Spelberg, Scheepstra, & de Vries, 1994) where the allotted time was 2 min. Rapid automatized naming (RAN) and VAS were also included. RAN was measured using a digit naming test (van den Bos & Lutje Spelberg, 2007) where 50 digits had to be named correctly as fast as possible. Based on the time and errors, it was calculated how many items could be named correctly within 1 min. VAS was measured using a task based on the study by Valdois et al. (2003). During this test, the child would see letter strings consisting of five letters for 200 ms on a computer screen. The following capital letters were used: B, D, F, H, L, M, P, R, S, and T. The child had to verbally report the letters presented on the screen in the right order. There were 20 trials, so the maximum score was 100 letters reported correctly. An adapted version, of the Dutch handedness inventory (van Strien, 1992), appropriate for children, was used to measure handedness. Like in the original Edinburgh Handedness Inventory (Oldfield, 1971), participants had to indicate which hand they used for actions. The final score ranged from −10 to 10, where 10 signifies completely right-handed and −10 completely left-handed.

As deficits in phonological awareness (PA) and orthographic knowledge are frequently observed among children with dyslexia (e.g., Georgiou, Papadopoulos, Zarouna, & Parrila, 2012; Ramus et al., 2003; Rothe, Cornell, Ise, & Schulte-Körne, 2015; Shaywitz & Shaywitz, 2005), we also included measures of these cognitive processes in the study. PA was measured with a phoneme deletion task (van Bergen, Bishop, van Zuijen, & de Jong, 2015). During this test, the child heard a pseudoword that it had to change into a different pseudoword by deleting a specific sound. There were 12 items, consisting of one or two syllables, and the same sound had to be deleted once or twice. The task was administered using a computer such that both accuracy and reaction times could be recorded. Orthographic knowledge was tested, using an orthographic choice task (Horsely, 2005). During this test, the child had to pick the correctly written word out of three orthographically related options. There were 70 items, and the test was terminated after 10 min. The score is the number of correctly identified words within the allotted time.

2.4 | EEG recording and analyses

For the EEG recording, a 64-channel EEG system was used with an elastic electro-cap with tin electrodes arranged in accordance with the 10–20 system (Sharbrough et al., 1991). In addition, four tin electrodes were used to measure the horizontal and vertical electro-oculogram, two electrodes were located at the mastoids, and one electrode

located at the sternum served as the ground electrode. The EEG was recorded at a sampling rate of 500 Hz with a Refa 8–64 average reference amplifier (TMSi, Oldenzaal, the Netherlands). There were no online filters. For data acquisition, Brain Vision Recorder 1.10 (Brain Products GmbH, Munich, Germany) was used. For one participant in the LRnonDys group, the EEG could not be recorded because the impedance was extremely high and could not be lowered successfully; for this participant only reaction times and accuracy were recorded.

For data preprocessing and analysis, Brain Vision Analyzer 2.0.3.6367 (Brain Products GmbH, Munich, Germany) was used. First, a low-pass filter of 30 Hz and a high-pass filter of 0.5 Hz, both with a slope of 24 dB/Oct, were applied to the data. In the next step, we manually removed large artefacts and breaks using visual inspection such that these would not interfere with the ICA ocular correction that we applied in the following step to remove the influence of eye blinks and saccades on the signal. One participant in the LRnonDys group and one participant in the HRnonDys group had to be excluded from the EEG analyses because there were too many large artefacts that disturbed the ICA. The ICA was followed by re-referencing the signal to an average reference without the eye and mastoid electrodes and without any electrodes that exhibited a lot of noise. Because of bad contact above the ear, T7 and T8 were always excluded from the average. For the other electrodes, it depended on the automatic artefact rejection whether they would be excluded from the average and the analysis. When one of the following criteria was met, an artefact would be detected: an absolute amplitude larger than 100 μV, a difference of 200 μV within 200 ms, or a gradient larger than 50 μV/ms. For four participants, one or more channels were excluded from the average and from the analysis, because more than 10% of the usable EEG was rejected during the artefact rejection. If a channel of interest (P3, P5, P7, PO3, PO7, P4, P6, P8, PO4, and PO8) showed artefacts, a stricter exclusion criterion of more than 5% rejection was used; this applied to three participants. An epoch length of 1200 ms was used. The epoch started 200 ms before the onset of Word 1 such that the first 200 ms before the word onset could be used for baseline correction. The number of trials kept in the analysis varied between 47 and 100 per participant per task, with the mean number of trials varying between 91.22 (semantic task) and 92.71 (phonological task; *SD* between 7.31 and 9.58). The number of trials left in the analysis, as tested by a repeated measures analysis, did not differ significantly between groups or tasks, nor was there a group × task interaction.

For the statistical analysis, two electrode clusters of interest were created: posterior left, consisting of P3, P5, P7, PO3, and PO7; and posterior right, consisting of P4, P6, P8, PO4, and PO8. For the three participants with a noisy channel among the channels of interest, a cluster of four electrodes was created. The signals were first averaged across channels before peaks were identified using semi-automatic peak detection. A search window of 100 ms symmetrically around the average N1 peak latency for all participants in all tasks was applied. One participant in the HRDys group was excluded because the N1 peak could not be identified, and including this participant would only add noise. This decision was based on visual inspection of the waveform and the ERP distribution in the topographic maps for the N1 time window. For the statistical analysis, the mean peak latency and mean peak amplitude, averaged over a time window of 10 ms symmetrically around the peak, were exported for each participant per cluster and per task.

2.5 | Statistical analyses

A similar analysis strategy as in van Setten et al. (2016) was used. First group differences (LRnonDys vs. HRnonDys vs. HRDys) on behavioural tests were analysed using, depending on normality of the distribution, either ANOVA or Kruskal–Wallis tests with post hoc tests if needed. Next, group differences in the reaction times and accuracy were analysed using 3 × 3 repeated measures analyses with Task (visual vs. phonological vs. semantic) as within-subject factor and Group as between-subject factor. Finally, 3 × 2 × 3 repeated measures analyses, with Task and Hemisphere (Left vs. Right) as within-subject factors and Group as between-subject factor, were used to analyse the N1 latency and amplitude data. Correlation analyses, Pearson or Spearman depending on the distribution of the variables involved, were used to investigate a possible relationship between the behavioural measures and the EEG. Like

van Setten et al. (2016), we also repeated the analysis for strongly right-handed participants only, although we used a more lenient criterion, a handedness score above 7 instead of 8, because of the small sample size. Finally, we statistically compared the results of van Setten et al. (2016) for the strongly right-handed adults (Handedness score > 8, n = 24, mean age = 21;10 years; months, see original study for more details about the participants) and the right-handed children in the HRDys and LRnonDys groups of the present study.

3 | RESULTS

3.1 | Behavioural tests

Descriptive statistics for all behavioural measures and demographic characteristics can be found in Table 1. According to the Kolmogorov–Smirnov test, only age in months, RAN, orthographic knowledge, and VAS were normally distributed. There was homogeneity of variance between the groups for most measures, except for orthographic knowledge and the PA test. Handedness and grade did not differ between the groups, but age in months did, $F(2, 48) = 3.67$, $p = 0.033$. The HRDys group was significantly older than the LRnonDys group, $t(31) = -2.42$, $p = 0.021$, and the HRnonDys group, $t(27) = -2.28$, $p = 0.030$.

There was a significant difference between the groups in WRF, $H(2) = 28.29$, $p < 0.001$; PWRF, $H(2) = 24.22$, $p < 0.001$; RAN, $F(2, 48) = 4.89$, $p = 0.012$; orthographic knowledge, $F(2, 48) = 13.25$, $p < 0.001$; PA accuracy, $H(2) = 7.29$, $p = 0.026$; and PA reaction times, $H(2) = 15.01$, $p = 0.001$. VAS did not differ between the groups, $F(2, 48) = 2.42$, $p = 0.100$. The HRDys group scored significantly lower than the LRnonDys group on WRF ($U = 4.0$, $p < 0.001$); PWRF ($U = 7.0$, $p < 0.001$); RAN, $t(31) = 3.36$, $p = 0.002$; orthographic knowledge, $t(31) = 4.32$, $p < 0.001$; PA accuracy ($U = 66.5$, $p = 0.017$); and PA reaction times ($U = 36.0$, $p = 0.001$). The HRDys group also scored lower than the HRnonDys group on WRF ($U = 1.0$, $p < 0.001$); PWRF ($U = 11.0$, $p < 0.001$); RAN, $t(27) = 2.73$ $p = 0.011$; orthographic knowledge, $t(27) = 4.01$, $p < 0.001$; PA accuracy ($U = 51.5$, $p = 0.18$); and PA reaction times ($U = 43.0$, $p = 0.007$). The HRnonDys group had longer PA reaction times than the LRnonDys group ($U = 98.0$, $p = 0.048$); all other measures did not differ between the nondyslexic groups ($p > 0.05$).

3.2 | Reaction times and accuracy

A 3 × 3 repeated measures ANOVA with Task (visual vs. phonological vs. semantic) as within-subject factor and Group (LRnonDys vs. HRnonDys vs. HRDys) as between subject factor was used to analyse the reaction times and accuracy. Mean reaction times per group can be found in Table 2 and Figure 1. After log-transformation, there was homogeneity of (error) variances, a normal distribution in the groups, and the assumption of sphericity was met for the reaction times. There was a significant main effect of Task, $F(2, 92) = 36.64$, $p < 0.001$, $\eta_p^2 = 0.44$. Reaction times were faster during the visual task (M = 973, SD = 326) compared with the phonological task (M = 1055, SD = 358,

TABLE 2 Means and standard deviations of the untransformed reaction times in milliseconds per task for all dyslexic and control participants

	LRnonDys (n = 20)		HRnonDys (n = 16)		HRDys (n = 13)	
Task	*M*	*SD*	*M*	*SD*	*M*	*SD*
Visual	907	346	908	297	1,157	276
Phonological	903	283	979	282	1,386	348
Semantic	1,032	293	1,062	307	1,579	324

Note. LRnonDys: low familial risk without dyslexia; HRnonDys: high familial risk without dyslexia; HRDys: high familial risk with dyslexia.

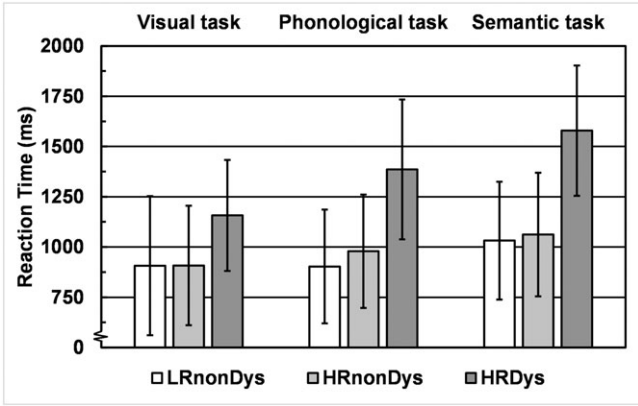

FIGURE 1 Mean reaction time in milliseconds per group and task. Error bars represent standard deviations. LRnonDys: low familial risk without dyslexia; HRnonDys: high familial risk without dyslexia; HRDys: high familial risk with dyslexia

$p = 0.001$) and compared with the semantic task ($M = 1186$, $SD = 0.383$, $p < 0.001$). Furthermore, reaction times during the phonological task were faster than during the semantic task ($p < 0.001$). There was also a significant main effect of Group, $F(2, 46) = 8.94$, $p = 0.001$, $\eta_p^2 = 0.28$. Pairwise comparisons showed that the HRDys group ($M = 1374$, $SD = 276$) reacted slower than the HRnonDys group ($M = 983$, $SD = 279$, $p = 0.001$) and the LRnonDys group ($M = 947$, $SD = 293$, $p < 0.001$). Finally, there was a significant interaction between Group and Task, $F(4, 92) = 2.95$, $p = 0.024$, $\eta_p^2 = 0.11$. Post hoc t-tests revealed that the difference in reaction times between the phonological and visual tasks was larger for the HRDys group ($M = 229$, $SD = 299$) than for the LRnonDys group, $M = -4$, $SD = 142$, $t(31) = -2.62$, $p = 0.014$, $r = 0.43$, but that this difference was similar for the HRDys and HRnonDys groups, $M = 71$, $SD = 180$, $t(27) = 1.33$, $p = 0.196$, $r = 0.25$. The difference in reaction times between the semantic and visual tasks was also larger for the HRDys group ($M = 422$, $SD = 276$) compared with the LRnonDys group, $M = 125$, $SD = 214$, $t(31) = -2.46$, $p = 0.020$, $r = 0.40$, and for the HRDys group compared with the HRnonDys group, $M = 154$, $SD = 184$, $t(27) = 2.23$, $p = 0.034$, $r = 0.40$. The difference in reaction times between the semantic and phonological tasks did not differ between any of the groups.

Mean accuracy per group can be found in Table 3. For accuracy, there was also homogeneity of (error) variances and sphericity could be assumed. However, accuracy was not normally distributed within groups except for the HRDys group during the visual and semantic tasks. Because of the high accuracy, the data were severely skewed, which could not be resolved with a transformation; therefore, one should be careful when interpreting these results. There was a significant main effect of Task, $F(2, 92) = 3.47$, $p = 0.035$, $\eta_p^2 = 0.70$. The accuracy was higher during the phonological task ($M = 0.95$, $SD = 0.08$) compared with the semantic task ($M = 0.93$, $SD = 0.06$, $p = 0.006$). Other task

TABLE 3 Means and standard deviations of the accuracy percentages per task for all dyslexic and control participants

	LRnonDys ($n = 20$)		HRnonDys ($n = 16$)		HRDys ($n = 13$)	
Task	*M*	*SD*	*M*	*SD*	*M*	*SD*
Visual	93.8	9.0	95.9	6.1	91.2	5.7
Phonological	94.8	10.0	97.0	3.5	94.0	9.3
Semantic	93.6	4.7	93.1	7.5	90.4	6.8

Note. LRnonDys: low familial risk without dyslexia; HRnonDys: high familial risk without dyslexia; HRDys: high familial risk with dyslexia.

differences were not significant ($p > 0.05$). The effect of Group and the interaction between Group and Task were not significant either ($p > 0.05$).

3.3 | EEG analysis

Forty-five participants were included in the EEG analyses: 18 participants in the LRnonDys group, 15 participants in the HRnonDys group, and 12 participants in the HRDys group. The analyses of both N1 latency and amplitude included Hemisphere (left vs. right) and Task (visual vs. phonological vs. semantic) as within-subject factors, and Group as between-subject factor. The assumption of sphericity was met in the analysis of the N1 amplitude but not for Task in the analysis of the N1 latency; a Greenhouse–Geisser correction has therefore been used for the latter analysis. All within-subject variables were normally distributed except for latency in the posterior left hemisphere for the HRDys group during the phonological task, and there was homogeneity of (error) variances across groups. Grand average ERP waveforms are displayed per hemisphere and group in Figure 2, and topographical maps for the N1 time window can be found in Figure 3. Mean N1 amplitudes and latencies per hemisphere and group can be found in Table 4.

A significant effect of Hemisphere was found for N1 latency; the N1 peaked earlier in the left hemisphere ($M = 201$, $SD = 2$) compared with the right hemisphere, $M = 210$, $SD = 11$, $F(1, 42) = 18.97$, $p < 0.001$, $\eta_p^2 = 0.31$. No significant main effects of Group or Task, or interactions, were found. When the analysis was repeated with strongly right-handed participants only (Handedness score > 7; $N = 30$, LRnonDys: $n = 13$, HRnonDys: $n = 9$, and HRDys: $n = 8$), the results were similar.

The N1 amplitude was more negative in the right hemisphere ($M = -6.81$, $SD = 0.3.05$) than in the left hemisphere, $M = -5.28$, $SD = 2.80$, $F(1, 22) = 9.07$, $p = 0.006$, $\eta_p^2 = 0.29$. No (marginally) significant main effects

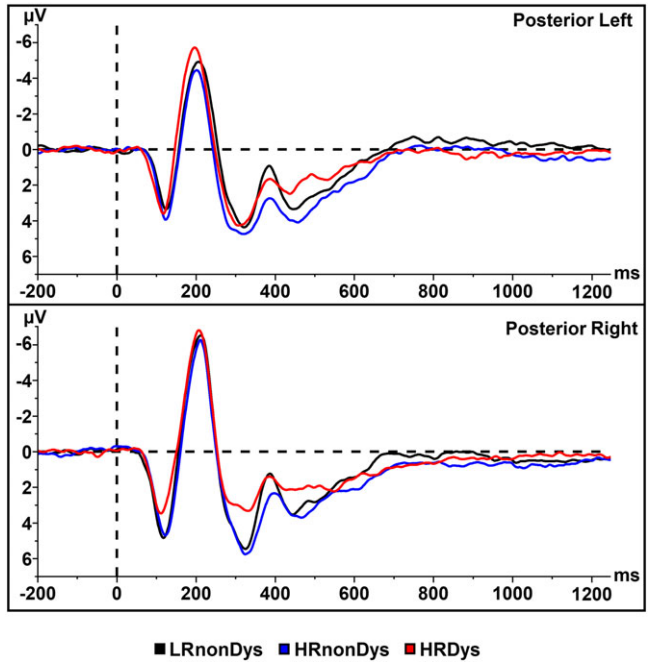

FIGURE 2 Grand average event-related potential response in the left and right hemispheres per group. LRnonDys: low familial risk without dyslexia; HRnonDys: high familial risk without dyslexia; HRDys: high familial risk with dyslexia [Colour figure can be viewed at wileyonlinelibrary.com]

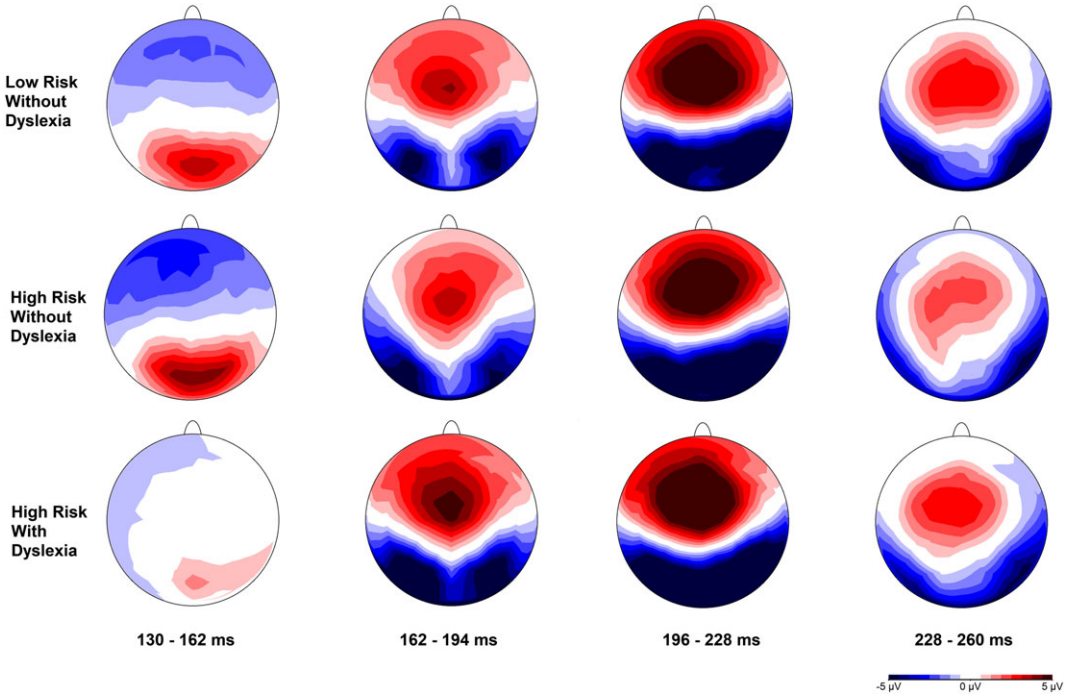

FIGURE 3 Topographical mapping of the N1 time window per group [Colour figure can be viewed at wileyonlinelibrary.com]

TABLE 4 Mean amplitude and latency of N1 per hemisphere and group

Measure and group	Left hemisphere		Right hemisphere	
	M	*SD*	*M*	*SD*
Amplitude (µV):				
LRnonDys	−5.4	2.5	−6.8	3.5
HRnonDys	−4.5	2.3	−6.5	2.4
HRDys	−6.1	3.6	−7.2	3.3
Latency (ms):				
LRnonDys	206	14	211	11
HRnonDys	198	13	211	9
HRDys	199	16	208	14

Note. LRnonDys: low familial risk without dyslexia; HRnonDys: high familial risk without dyslexia; HRDys: high familial risk with dyslexia. $N = 45$, LRnonDys: $n = 18$, HRnonDys: $n = 15$, HRDys: $n = 12$.

of Task, Group, or interactions were found. When the analysis was repeated with strongly right-handed participants only, the results were also similar.

As there was no significant effect of Task, the N1 amplitude and latency were averaged across tasks for the correlation analysis. There were no significant Pearson or Spearman correlations between the N1 amplitude or latency in the left or right hemisphere and any of the behavioural measures, reaction times, or the handedness score. The lateralization index (left minus right) for the N1 amplitude did also not correlate with any of these measures. For latency, the lateralization index correlated with orthographic knowledge ($r = 0.388$, $p = 0.008$): Better orthographic

knowledge was associated with an earlier N1 in the right compared with the left hemisphere. In addition, this lateralization index correlated with the handedness score (r_s = −0.338, p = 0.023): More right-handedness was associated with an earlier response in the left compared with the right hemisphere.

3.4 | Statistical comparison adults and children

In order to investigate the effect of Age, a statistical comparison was made between the children of the current study and the strongly right-handed higher education adult students of the study by van Setten et al. (2016) for whom the N1 was generally left-lateralized, and reduced left-lateralization was found in the students with dyslexia. Using a repeated measures ANOVA, we compared the results of the right-handed participants in the HRDys (n = 10) and LRnonDys (n = 14) groups from the present study with the strongly right-handed students with dyslexia (n = 12) and without dyslexia (n = 12). In this analysis, Hemisphere (Left vs. Right) was used as a within-subject factor, and Age group (Adult vs. Child) and Diagnosis (Dyslexia vs. Control) were used as between-subject factors. Because the effect of Task was not significant in either study, this factor was not included in the analysis. For the N1 amplitude, a significant main effect of Age group was found, $F(1, 44) = 41.77$, $p < 0.001$, $\eta_p^2 = 0.49$; the N1 was significantly more negative for children (M = −6.34, SD = 2.78) compared with adults (M = −2.21, SD = 1.36). Furthermore, there was a significant interaction between Hemisphere and Age group, $F(1, 44) = 16.36$, $p < 0.001$, $\eta_p^2 = 0.27$. A follow-up independent t-test of the difference in the N1 voltage in the left hemisphere and the N1 voltage in the right hemisphere revealed that for adults, the N1 amplitude was more negative in the left hemisphere (M = −1.12, SD = 1.96), whereas for children, it was more right-lateralized (M = 1.76, SD = 2.88); this difference was significant, $t(46) = 4.05$, $p < 0.001$. This interaction can also be seen in Figure 4. A main effect of Diagnosis or interactions with Diagnosis were not found.

The analysis for N1 latency revealed a main effect of Age group, $F(1, 44) = 32.92$, $p < 0.001$, $\eta_p^2 = 0.43$; the N1 peaked earlier for adults (M = 181, SD = 18) compared with children (M = 207, SD = 11). Furthermore, a main effect of Hemisphere was found, $F(1, 44) = 13.97$, $p = 0.001$, $\eta_p^2 = 0.24$. The N1 occurred earlier in the left (M = 187.986, SD = 26.715) compared with the right hemisphere (M = 201, SD = 21). Finally, there was a marginally significant interaction of Hemisphere with Age group, $F(1, 44) = 3.58$, $p = 0.065$, $\eta_p^2 = 0.08$; the difference between the N1 latency in the left compared with the right hemisphere seemed slightly larger for adults, M = 21, SD = 33, $t(31.36) = 1.99$, $p = 0.056$, compared with children (M = 7, SD = 14). We found no main effect of Diagnosis or interaction with Diagnosis.

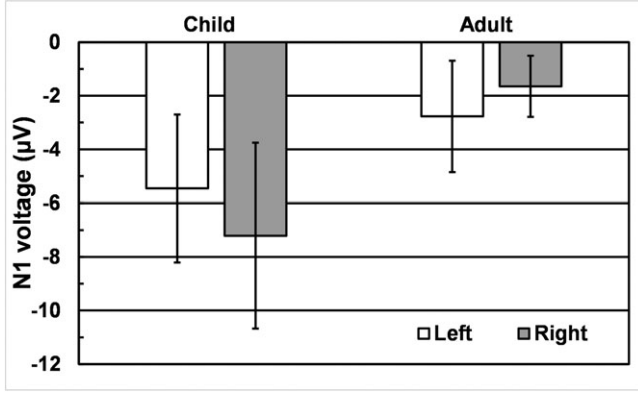

FIGURE 4 Mean N1 amplitude in the left and right hemispheres for adults and children. Error bars represent standard deviations

4 | DISCUSSION

In the present study, we investigated N1 lateralization in children around the age of 12 years, with and without (an FR of) dyslexia. In contrast to our expectations, the N1 amplitude was not left-lateralized for any of the groups, as it was generally stronger in the right hemisphere. There was a slight left-lateralization in latency, but this did not differ between the groups. The effect of handedness was also checked, but this did not change the results regarding N1 lateralization. However, it should be mentioned that the groups were very small when only strongly right-handed participants were included, so it is likely that there was not enough power to detect an effect of handedness in these analyses. No significant relationships between the N1 amplitude or latency in the left or right hemisphere and any of the behavioural measures were found. A moderate positive correlation was found between the latency lateralization index and orthographic knowledge, as well as a moderate negative correlation between the latency lateralization index and the handedness score. These relationships, however, are difficult to interpret in the absence of an effect of the amplitude lateralization index where N1 lateralization is usually observed. As these effects were still quite small and no corrections for multiple comparisons were made, future research should follow up on these findings before firm conclusions can be drawn about this. The comparison between the results of adults and children revealed that the N1 amplitude was more right-lateralized in children compared with adults and that the N1 amplitude was generally larger in children. The N1 peaked earlier in adults compared with children. For both groups, the N1 peaked earlier in the left hemisphere, but the latency difference between the left and right hemispheres seemed larger for adults.

The results of this experiment contradict the results of studies that found evidence of left-lateralized coarse print tuning in typically reading children (e.g., Araújo et al., 2012; Eberhard-Moscicka et al., 2015; Kast et al., 2010; Maurer et al., 2007). However, they used a different experimental approach with a print versus nonprint contrast. In the earlier study by Spironelli and Angrilli (2009), who used a similar linguistic judgement task as used in the present study, the N1 was right-lateralized in children at the age of 10, compared with both young and older adults where the N1 was left-lateralized. Moreover, the N1 latency in children was both in this Dutch study and in their Italian study longer for children than for adults. This seems to suggest that although early coarse print-tuning development can be observed among young typically reading children, the full maturation of the N1 response to written words, which was tested using the current paradigm, takes much longer and happens in normal readers in adolescence, somewhere between the ages of 12 years, the age of the participants in this study, and 22 years, the age of the young adults in the study by van Setten et al. (2016). This idea seems to be supported by the absence of a lexicality effect obtained with a word versus pseudoword contrast in children in contrast to adults (e.g., Coch & Meade, 2016). A question that can be raised on the basis of the current study is "when does N1 lateralization, as measured with a linguistic judgement task, shift from right to left?" It would be interesting to study this question in a study with normal reading participants of different ages between adolescence and young adulthood.

Because N1 lateralization was not observed in the low-risk control group, we can make no claims about the influence of FR on print-tuning lateralization. Based on the literature reviewed in the introduction, it seems that in people with dyslexia, both lateralized coarse print tuning and the more fine-grained processing of lexical and orthographic information in the N1 time window is reduced (e.g., Araújo et al., 2015; Helenius et al., 1999; Kast et al., 2010; Mahé et al., 2012; van Setten et al., 2016). The absence of a significant three-way interaction between Age group, Hemisphere, and Dyslexia diagnosis in the present study is probably a result of the low power in the analysis, as the study by van Setten et al. (2016) showed that for right-handed participants, the N1 left lateralization was reduced for people with dyslexia. It is still unclear whether lateralized course print tuning and fine-grained word processing in the N1 time window can be found in people with a high FR of dyslexia who have not developed dyslexia themselves. To investigate this question, future studies should either include older participants when focussing on lexical effects or include younger participants and use a different experimental paradigm with a print versus nonprint contrast when focussing on coarse print tuning. Furthermore, it would also be interesting to investigate at the individual level whether N1 lateralization is more an all-or-none phenomenon or whether there is a continuum just like for reading fluency.

Like in the study by van Setten et al. (2016) in adults, reaction times in the children were generally fastest during the visual task and slowest during the semantic task. Reaction times also differed between the groups. The HRDys group performed generally slower than the two nondyslexic groups, and this difference was larger during the phonological and semantic tasks than during the visual task. It could be that this pattern reflects the involvement of reading, which was not required for the visual task. Accuracy was generally high, exhibiting a ceiling effect, and did not differ between the groups. These results are in line with the fact that speed but not accuracy deficits mostly mark dyslexia in transparent languages and in older readers.

The behavioural results clearly showed that the participants in the HRDys group did not only have difficulties with reading but also scored lower on RAN, PA, and orthographic knowledge, deficits that are typically associated with dyslexia (e.g., Georgiou et al., 2012; Kirby, Georgiou, Martinussen, & Parrila, 2010; Norton & Wolf, 2012; Ramus et al., 2003; Rothe et al., 2015; van der Leij & Morfidi, 2006). Participants in the HRDys group did not score significantly lower on VAS, which is in contrast to the result in a larger sample of children of the DDP where the effect size for the difference between the dyslexic and nondyslexic groups was larger (0.55 as compared with 0.35 in this study) and was significant (van Setten, Hakvoort, van der Leij, & Maassen, 2018). It should be noted that the participants in the HRDys group were slightly older than the participants in the nondyslexic groups, although the groups did not differ in grade. Thus, even though the dyslexic participants were slightly older, they showed large reading (related) deficits. This age difference may be the result of the fact that more children in the HRDys group repeated a grade (van Setten et al., 2018). The reason why there is no difference in grade is probably that we tried to test as many children as possible in Grade 6.

The scores on the behavioural tests of the HRnonDys group were in between the scores of the LRnonDys group and the HRDys group, but the difference between the non-Dys groups was in general not significant. There was only limited evidence of a three-step pattern in the behavioural data and reaction times, in concordance with the studies by Dandache et al. (2014) and Eklund et al. (2014). Still there were some signs of a slight phonological deficit in the HRnonDys group. Although they performed as accurately as the LRnonDys group on the phoneme deletion task, they were significantly slower. Second, the difference score between the reaction times of the phonological and visual task was similar for the HRDys and HRnonDys groups (effect size = 0.247), whereas the HRDys group showed a significantly larger difference than the LRnonDys group (effect size = 0.426). Because of the small sample size, small differences between the LRnonDys group and HRnonDys group may have been undetectable because of a lack of power. Thus, although we can conclude that there were no large differences between the two non-Dys groups, the HRnonDys group may still have slight phonological difficulties resulting from the continuity of FR.

Future studies should ideally have a larger sample size to increase the power of the study, and handedness should be better balanced across groups such that the role of this factor can be more carefully investigated like in the study by van Setten et al. (2016). Despite the small sample size, most parametric assumptions were not violated, and when they were violated, we used nonparametric tests when possible. Furthermore, the N1 was based on 300 trials (100 per task), which generally resulted in a good signal-to-noise ratio, and makes our estimate of the N1 reliable. We did not consider factors like reading behaviour or reading interventions that the children with dyslexia may have received in our analysis; future studies may perhaps look at these factors to explain individual differences within the groups. It would also be interesting to investigate the role of methodological factors with the current experimental paradigm, such as presentation duration, and stimulus characteristics, such as word length, because the study by Xue et al. (2008) showed that these may influence early lexical processing in the N1 time window. Furthermore, the influence of orthographic transparency on the lexical N1 effects could also be considered in future studies. Although differences in the N1 print-tuning effect between people with and without dyslexia as well as beginning and advanced readers have been found across languages and orthographies, more research could investigate whether orthographic factors influence lexical processing reflected in the N1.

Furthermore, other ERP components elicited by this paradigm, like the P2, P3, and N400, could also be studied. Because there seemed to be group differences in the P2 time window around 325 ms in the right hemisphere, based on visual inspection of Figure 2, we have also analysed differences in this component in the posterior left and right

hemispheres, but group differences were not significant, possibly as a result of large interindividual differences; therefore, we have not further reported these analyses in this paper. Although we did not expect any task-related effects in the present study, there may be task-related effects and interactions with group in later components, and it would also be interesting to look at the ERP response after the second presented word, because the correct response had to be selected when processing this word.

In conclusion, this study found no signs of N1 lateralization in the left hemisphere in children around the age of 12 years using a linguistic judgement task. This is in contrast with other studies, with a print versus nonprint contrast, that have found course print-tuning lateralization in young typical readers. The current results seem to suggest that the lateralization of the N1 in children depends on the experimental paradigm and contrast used. Additionally, because left-lateralized print tuning has been found with the present paradigm among adult readers, it seems that the full maturation of N1 lateralization in response to written words is still taking place in adolescence and is not something that can and should only be studied during the first years of reading development.

ACKNOWLEDGMENTS

This work is part of the research programme 360-89-040, which is financed by the Netherlands Organisation for Scientific Research (NWO). We thank the master students who helped with the data collection. We are also thankful for the participation of the children and the commitment of their parents to this study.

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How to cite this article: van Setten ERH, Maurits NM, Maassen BAM. N1 lateralization and dyslexia: An event-related potential study in children with a familial risk of dyslexia. *Dyslexia*. 2019;25:84–102. https://doi.org/10.1002/dys.1604