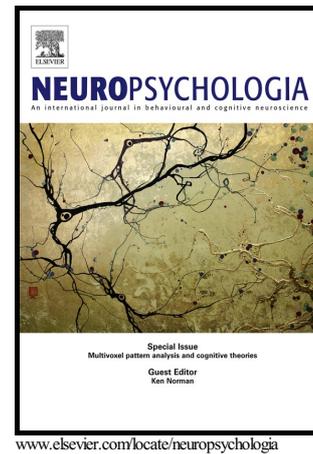


Author's Accepted Manuscript

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PII: S0028-3932(17)30440-2
DOI: <http://dx.doi.org/10.1016/j.neuropsychologia.2017.11.018>
Reference: NSY6574

To appear in: *Neuropsychologia*

Received date: 19 January 2017
Revised date: 6 May 2017
Accepted date: 15 November 2017

Cite this article as: Kaisa Lohvansuu, Jarmo A. Hämäläinen, Leena Ervast, Heikki Lyytinen and Paavo H.T. Leppänen, Longitudinal interactions between brain and cognitive measures on reading development from 6 months to 14 years *Neuropsychologia*, <http://dx.doi.org/10.1016/j.neuropsychologia.2017.11.018>

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Longitudinal interactions between brain and cognitive measures on reading development from 6 months to 14 years

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Abstract

Dyslexia is a neurobiological disorder impairing learning to read. Brain responses of infants at genetic risk for dyslexia are abnormal already at birth, and associations from infant speech perception to preschool cognitive skills and reading in early school years have been documented, but there are no studies showing predicting power until adolescence. Here we show that in at-risk infants, brain activation to pseudowords at left hemisphere predicts 44% of reading speed at 14 years, and even improves the prediction after taking into account neurocognitive preschool measures of letter naming, phonology, and verbal short-term memory. The association between infant brain responses and reading speed is mediated by preschool rapid automatized naming ability. Therefore, we suggest that rapid naming and reading speed could share a similar cognitive process of automatized access to lexicon via phonological representations, and brain activation to speech sounds in infancy probably acts as an index of deficient development of the same process.

Keywords: children, dyslexia, event-related potentials, infants, reading, speech perception

Introduction

The risk of having developmental dyslexia at school age is eight times higher than usual if either of the parents has reading difficulty. By studying infants of dyslexic parents, i.e., at-risk infants, atypical developmental processes related to dyslexia can be observed already at a very early age. Indeed, differences in brain function have been found between infants with and without familial risk for dyslexia (e.g. Leppänen et al., 2012; van Zuijen, Plakas, Maassen, Maurits, & Leij, 2013). Several studies have also demonstrated that both brain functions and structures of dyslexics are abnormal at school age and adulthood (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985; for meta-analyses see Richlan, Kronbichler, & Wimmer, 2011; 2013). For example, a recent functional magnetic resonance imaging (fMRI) study found that the functional and structural connectivity between brain areas hosting phonetic representations (auditory cortices) and area related to, among other things, higher-level phonological processing (the left inferior frontal gyrus) is lower in adult dyslexics which suggest deficient access to phonetic representations (Boets et al., 2013). In addition, school-age reading skills have been shown to be closely associated with and predictable by preschool-age cognitive risk factors for dyslexia, such as deficits in phonological awareness, rapid automatized naming (RAN), letter knowledge, and verbal short-term memory (STM) (Puolakanaho et al., 2008; for review see Vellutino, Fletcher, Snowling, & Scanlon, 2004). Despite these findings, it is still unknown how speech processing problems in infants lead to deficient pre-literacy skills and eventually to reading difficulties. In the current study we investigated brain measures of at-risk children at an early

age and behavioral measures of pre-literacy skills and reading skills in a longitudinal design to shed light on the causal mechanisms behind developmental dyslexia.

In previous studies of infants with familial risk for dyslexia, family risk has been found to be strongly associated with a speech perception deficit (Lyytinen et al., 2008; van der Leij, van Bergen, van Zuijlen, de Jong, Mauritis, & Maassen, 2013). Overall, the predictive power of infant and preschool-age brain responses to speech or auditory stimuli for school-age reading skills ranges from 7–27% of the explained variance (e.g., Leppänen et al., 2010; van Zuijlen et al., 2012; van Zuijlen et al., 2013). These associations have been found in different languages, such as Dutch and Finnish. However, the longitudinal relationships and possible mediation mechanisms from infant speech perception abilities via preschool cognitive skills to later reading performance in adolescence remain unclear.

In the current study, event-related potentials (ERPs) in 26 infants with and 22 infants without familial risk for dyslexia were measured at the age of 6 months. At ages of 8, 10, and 14 years (at grades 1, 3, and 8), their reading skills were evaluated and the relationships were investigated to see whether, and to what extent, brain indexes measured in infancy explain reading performance at school age up to adolescence. Furthermore, preschool cognitive measures – phonology, letter naming, rapid naming, and verbal short-term memory (STM) – were studied as mediators of the association between infant ERPs and adolescent reading.

We hypothesized based on the previous studies that phonological skills are associated more with reading accuracy, whereas rapid naming ability is associated with reading speed (e.g., Puolakanaho et al., 2008). Brain responses to speech sounds were expected to be

associated with phonological skills and reading accuracy (McBride-Chang, 1995; Hämäläinen et al., 2013). Furthermore, our previous report which partly studied the same participants, revealed differences between the ERPs of infants with and without risk for dyslexia (Leppänen et al., 2002), also suggesting a link between early speech perception and reading skills.

Accepted manuscript

Materials and Methods

Participants

ERP data from 48 healthy infants (24 boys), a sub-group of the Jyväskylä Longitudinal Study of Dyslexia (JLD, for a review see Lyytinen et al., 2008) sample, were collected at 6 months (for demographics and behavioral group characteristics, see Table 1). Twenty-six infants (13 boys) had a family background of dyslexia, while twenty-two (11 boys) were from control families (for details on the participant characteristics and selection criteria, see Leinonen, Müller, Leppänen, Aro, Ahonen, & Lyytinen, 2001). All infants that were included from control families were assessed to be typical readers at 9 years while only 4 of the at-risk children fulfilled the criteria for dyslexia; therefore, the at-risk children were examined as one group. For the criterion for dyslexia five reading and spelling tasks were administered (word and non-word list reading, text reading, and word and non-word spelling tasks) and from these eight measures of reading speed and reading/spelling accuracy were calculated. The children were defined as dyslexics if their reading performance outcome fell below the 10th percentile of the performance of the control children in at least three out of four measures of reading/writing accuracy or reading speed, or in two out of four in reading accuracy and two out of four in reading speed measures. Otherwise, a child's reading skills were considered to be typical. For details on the criteria for dyslexia see Eklund, Torppa, Aro, Leppänen, & Lyytinen, 2015. Children with a neurological diagnosis or disorder (N = 5), low non-verbal intelligence quotient (IQ) < 80 (N = 2), bad quality EEG data (high frequency noise, offsets, or slow shifts in data, N = 4), or otherwise with ≤ 40 acceptable EEG epochs per stimuli (N = 8) were excluded. The study was approved by the ethics committee of the University of

Jyväskylä and informed consent was obtained from all parents according to the Declaration of Helsinki. The remaining sample size was comparable with previous studies examining longitudinal relationships from infancy to later childhood (e.g., van Leeuwen et al., 2006; Leppänen et al., 2010; Cantiani et al., 2016).

Table 1. Demographics and behavioral group characteristics. Group means (standard deviations in parentheses) and group comparisons (one-way ANOVA) of cognitive and reading measures.

Variable	At-risk group Mean (SD)	Control group Mean (SD)	ANOVA <i>p</i> -value
Gender (boys/girls)	13/13	11/11	
Age (years)			
Infant ERP	0.52 (0.03)	0.51 (0.01)	.32
Preschool measures	5.50 (0.02)	5.51 (0.03)	.50
Non-verbal IQ	8.38 (0.26)	8.48 (0.23)	.17
Reading, 1 st grade	7.83 (0.24)	8.00 (0.25)	.02
Reading, 3 rd grade	9.77 (0.25)	9.91 (0.27)	.09
Reading, 8 th grade	14.29 (0.26)	14.44 (0.25)	.06
Phonology, preschool	-0.20 (0.90)	0.05 (0.69)	.29
Letter naming, preschool	14.12 (7.89)	16.14 (6.61)	.35
RAN, preschool	48.58 (15.62)	39.73 (9.52)	.03
Verbal STM, preschool	-0.26 (0.83)	0.13 (0.84)	.11

Non-verbal IQ, 8 years	101.19 (12.89)	105.43 (12.88)	.27
Reading accuracy, 8 years	0.06 (0.31)	0.21 (0.30)	.10
Reading speed, 8 years	-0.29 (1.06)	0.30 (0.83)	.04
Reading accuracy, 10 years	-0.10 (0.71)	0.36 (0.42)	.01
Reading speed, 10 years	0.03 (0.70)	0.20 (0.78)	.43
Reading accuracy, 14 years	-0.15 (0.94)	0.24 (0.39)	.07
Reading speed, 14 years	-0.12 (0.95)	0.09 (0.86)	.44

Note. ERP = Event-related potential; IQ = intelligence quotient; RAN = Rapid automatized naming; STM = short-term memory.

Reading and cognitive measures

Phonological skills were evaluated at 5.5 years using five tests: Initial phoneme identification, Initial phoneme production, Phonological processing (NEPSY; Korkman et al. 1998), Phoneme- and syllable level segmentation, and Word-level segmentation. The mean score was used as a measure.

Rapid automatized naming (RAN) task (pictures: ball, car, fish, house, pencil) was assessed at 5.5 years with a reduced 6x5-item matrix (Denckla & Rudel 1976). Total matrix completion time (in seconds) was used as a measure.

Verbal short-term memory was composed of the average of correct answers in digit span and memory for names (NEPSY; Korkman et al. 1998) tests assessed at 5 and 5.5 years, respectively.

Letter naming was measured at 5.5 years by presenting 23 capital letters one by one. The sum of correct answers (the use of a phoneme and the use of a letter name would both be coded as correct responses but all of the responses were given using letter names) was used as a measure.

Non-verbal IQ was tested at 8 years by using four performance quotient subtests (Picture Completion, Block Design, Object Assembly and Coding) of the Wechsler Intelligence Scale for Children-III (Wechsler, 1991).

At the end of 1st grade at the age of 8 years, the scores for *reading accuracy* (the percentage or sum of correctly read words) and *reading speed* (words read/minute or total reading

duration including reaction times) were calculated as averages of three oral reading tasks without time pressure: word list (Lukilasse: standardized reading test; Häyrynen, Serenius-Sirve, & Korkman, 1999), non-word list, and text reading.

At the end of 3rd grade at the age of 10 years, the scores for *reading accuracy* (the percentage or sum of correctly read words) and *reading speed* (words read/minute or total reading duration including reaction times) were calculated as averages of five oral reading tasks: word and non-word list reading without time pressure, text and non-word text, and word list reading with time pressure.

At 8th grade at 14 years, the scores for *reading accuracy* (the percentage of correctly read words) and *reading speed* (letters read/second) were obtained as averages of three oral reading tests: text, pseudo-word text, and word list reading with time pressure.

The *reading accuracy* mean scores were calculated as follows: First, the percentages of correctly read words were calculated from word list reading with time pressure, text reading and non-word text reading tasks, and sums of correctly read words were calculated from word and non-word list reading tasks without time pressure. Second, z-scores were calculated and then the z-scores were averaged. Cronbach's alphas for the mean scores of reading accuracy at 1st, 3rd, and 8th grades were $\alpha = .89$, $\alpha = .83$, and $\alpha = .76$, respectively.

Similarly, the *reading speed* mean scores were calculated from word list reading with time pressure, text reading and non-word text reading tasks (letters read/second), and total reading durations including reaction times were calculated from word and non-word list reading tasks without time pressure. Cronbach's alphas for the mean scores of reading speed at 1st, 3rd, and

8th grades were $\alpha = .92$, $\alpha = .90$, and $\alpha = .90$, respectively.

All reading tasks were audio recorded and correct reading was checked from the recordings.

The measures are presented in detail in Puolakanaho et al., 2008 and Eklund et al., 2015.

Stimuli and procedure

Three versions of a naturally produced pseudo-word differing only in the duration of the silent gap between the syllables (95 ms, 195 ms, or 255 ms, respectively) were used as stimuli. In all of these stimuli, the first syllable was 72 ms and the second syllable 133 ms in duration. The length of the silent gap affects the perception of the phonemic length of consonant /t/ in the middle of the pseudo-word as short or long (Richardson, Leppänen, Leiwo, & Lyytinen, 2003). In the Finnish language phonemic length (either short or long) is semantically differentiating, and therefore essential, feature (Suomi, Toivanen, & Ylitalo, 2008). The stimuli were presented in an oddball paradigm: A short /ata/ (300 ms, 80%) as repeated standard stimulus and shorter and longer variations of /at:a/ as rarely-presented stimuli (400 and 460 ms, 10% each). The stimuli were presented via a loudspeaker at 75 dB sound pressure level with an inter-stimulus interval of 610 ms.

Recording and preprocessing of the EEG data

EEG was recorded with ten Ag/AgCl electrodes (F3, F4, C3, C4, T3, T4 (T7, T8 in 10–5 system), P3, P4, O1, O2) according to the 10–20 electrode system and referred to the ipsilateral mastoid electrodes. Electro-oculograms were recorded with one electrode lateral to and above both eyes and referenced to the left mastoid. The online filtered (passband 0.5–35

Hz, sampling rate 200 Hz) EEG epochs between -50–840 ms were averaged (for the repeated stimulus, three epochs preceding the rare stimuli were included). Epochs with artefactual deflections exceeding ± 200 μV at EOG and EEG channels were excluded from the averaging. The mean numbers (and standard deviations) of accepted EEG epochs within the control group were 365.86 (69.50) for the frequently repeated standard stimuli, 99.50 (19.97) for the shorter version (400 ms) of the rarely presented stimuli, and 98.50 (20.26) for the longer version (460 ms) of the rarely presented stimuli. Within the at-risk group, the numbers were 358.62 (85.50) for the frequently repeated stimuli, 99.00 (24.22) for the shorter version (400 ms) of the rarely presented stimuli, and 97.88 (23.74) for the longer version (460 ms) of the rarely presented stimuli. The mean number of accepted epochs did not differ between the groups.

Statistical analyses

For correlation analyses, amplitude averages were calculated across time points around the main deflections identified by visual inspection in grand average waveforms (see Fig. 1; described in Leppänen et al., 2002). Means of the frontal and central electrodes were calculated separately for the left (F3, C3) and right (F4, C4) hemispheres. The time windows for averages were 40–80 ms, 135–215 ms, 260–340 ms, and 370–470 ms for the response to the frequently repeated stimuli, 470–550 ms for the response to the 400 ms rarely presented stimuli, and 420–500 ms and 540–620 ms for the response to the 460 ms rarely presented stimuli. Pearson's correlation coefficients were calculated between the amplitude averages, preschool neurocognitive measures, reading speed and reading accuracy within the at-risk and control groups by using IBM SPSS Statistics 22 and applying a false discovery rate

(FDR) correction of $q = .05$ (Benjamini & Hochberg, 1995). Significance of the difference between the correlation coefficients of the groups was tested in Excel (on correlation testing, see McNemar, 1969). Linear regression analyses were executed based on the significant correlations with reading speed as a dependent variable, and infant ERPs to the standard stimuli and preschool-age neurocognitive measures as independent variables. Mediation analysis was conducted using the SPSS macro which applies the Sobel test testing the significance of the indirect effect to resolve whether preschool-age RAN and/or phonology act as mediators between infant ERP and reading speed at the age of 14 years (for the macro see Preacher & Hayes, 2004; Preacher & Hayes, 2008).

Results

Based on visual inspection, the grand average waveforms corresponded with those previously reported and described in Leppänen et al., 2002 despite the slight difference between participant groups included (because of the dropouts from the study in pre-school age, see Fig. 1; Leppänen et al., 2002). For statistics of group differences see Leppänen et al., 2002.

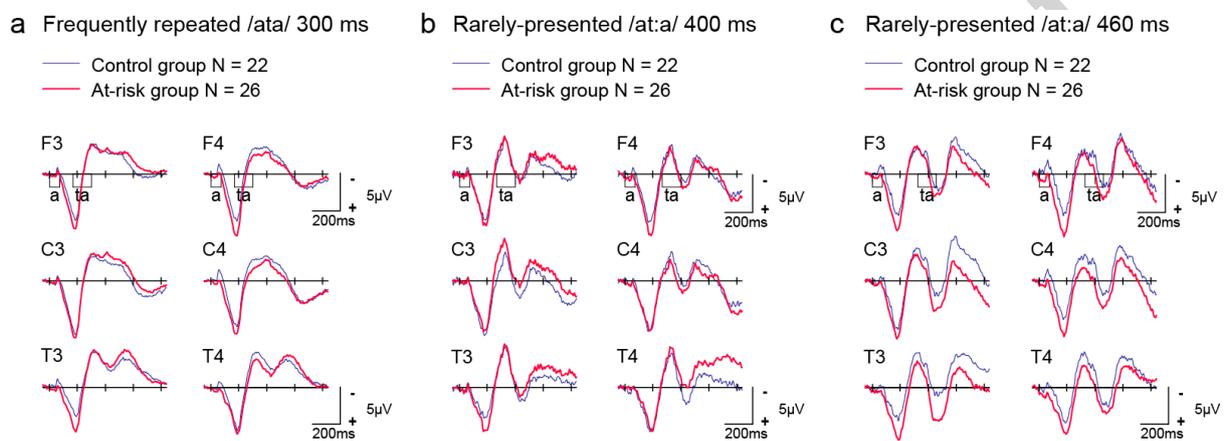


Figure 1. Brain activation at 6 months. Grand average ERP waveforms of 6-month-old infants with familial risk for dyslexia (red line) and control group (blue line). (a) Responses for the frequently repeated standard stimulus short /ata/ (300 ms). (b) Responses for the shorter (400 ms) variation of rarely presented deviant stimuli /at:a/. (c) Responses for the longer (460 ms) variations of rarely presented deviant stimuli /at:a/. Horizontal tick marks represent 200 ms and vertical scale 5 μ V (negativity up). The stimuli are marked with boxes below the baseline.

Correlation analysis

Correlations were examined on the basis of calculated average amplitudes around the peaks seen in Figure 1. Within the at-risk group, larger negative ERP amplitudes at left fronto-central channels (F3 and C3) between 370–470 ms to the standard stimuli were associated with faster reading speed assessed at 8th grade at 14 years ($r(25) = -.66, p = .0003$, better scores in phonology ($r(26) = -.66, p = .0002$), and faster rapid naming speed ($r(26) = .64, p = .0004$) assessed at 5.5 years (see Fig. 2; Correlation to reading speed differed significantly from corresponding correlation within control group ($p = .003$). There were also significant correlation between rapid naming at 5.5 years and reading speed at 14 years ($r(25) = -.71, p = .00006$), between phonology and letter naming at 5.5 years ($r(26) = .65, p = .0003$), and between phonology (5.5 yrs.) and non-verbal intelligence quotient (IQ) at 8 years ($r(26) = .71, p = .00005$) within the at-risk group. In the control group, no correlations with brain measures survived the false discovery rate (FDR) correction, but significant correlations between letter naming (5.5 yrs.) and non-verbal IQ (8 yrs; $r(21) = .64, p = .002$), as well as between rapid naming (5.5 yrs.) and reading accuracy at 14 years ($r(21) = -.66, p = .001$), were found. In addition, several significant correlations between reading speed and reading accuracy measures were observed in both groups at 8, 10, and at 14 years. The whole correlation matrices are provided online as Tables S1 and S2.

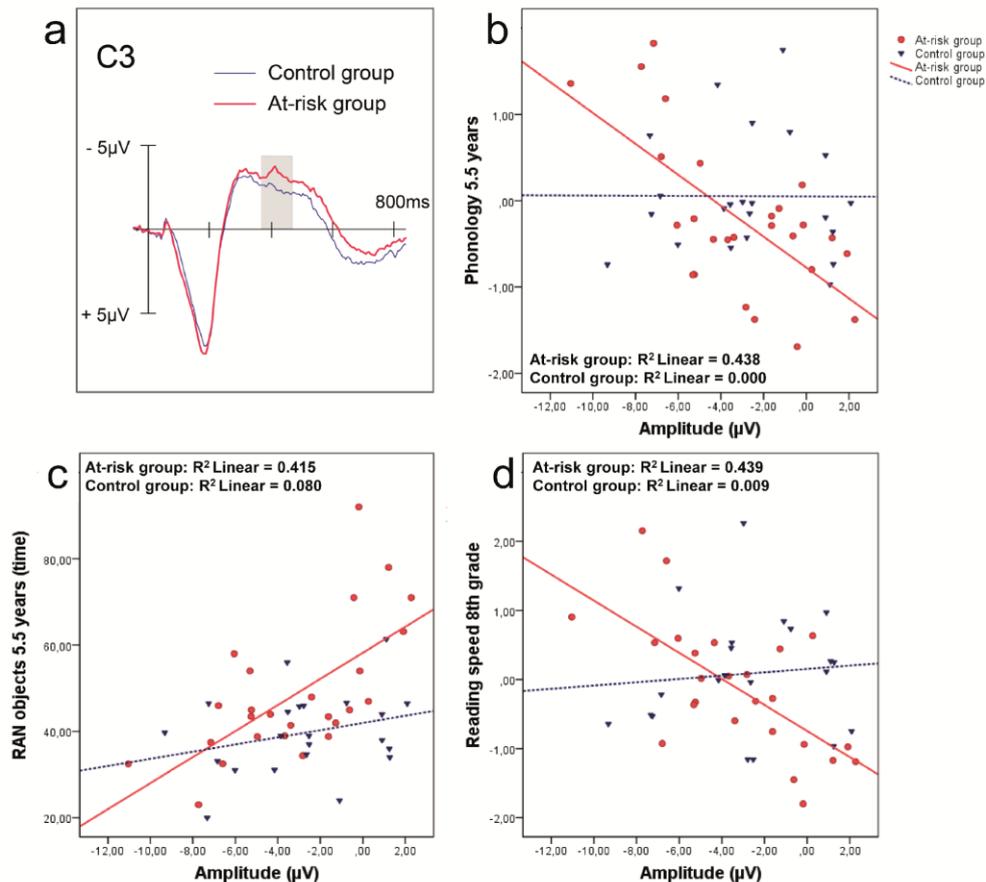


Figure 2. Associations of brain activation and cognition. **(a)** Grand average ERP waveform of 6-month-old infants with (red line) and without (blue line) familial risk for dyslexia for the frequently repeated stimulus at C3 channel. The gray box indicates the time scale of 370–470 ms used for correlations. Scatter plots of the linear association between the infant ERP amplitude to the frequently repeated stimulus at left hemisphere (mean across electrodes F3 and C3, and time points between 370–470 ms) and preschool measures of **(b)** phonology and **(c)** RAN (time in seconds), and **(d)** reading speed at 14 years.

Regression and mediation analyses

Regression analyses were carried out on the basis of the significant correlations. We found that infant brain responses to the frequently repeated pseudo-word /ata/ explained 44% of the reading speed score at 14 years (Table 2, model A). Brain activation also significantly improved the prediction by 18 – 31% if inserted into the model after preschool measures of phonology, letter naming, and verbal short-term memory (models C, D, E). Rapid naming time explained around 51% of the reading speed in the at-risk group, and when ERP amplitude was forced (entered) into the model after rapid naming time, the improvement to the prediction of the reading speed at adolescence was not significant (model B). The same brain index explained reading speed in the at-risk group also at 8 and 10 years. None of the measures predicted reading speed in the control group or reading accuracy in either of the groups between ages 8 to 14 years.

Table 2. Predictors of reading speed at 14 years in the at-risk group. Linear regression analyses (stepwise method) showing brain ERP amplitude of 6-month-old infants with familial risk for dyslexia at left fronto-central electrodes between 370–470 ms and preschool measures predicting reading speed at 14 years in 8th grade. None of the predictors were significant in the control group.

Dependent variable					
Reading speed at 14 years					
	<i>B</i>	<i>C .95 for B</i>	<i>SE B</i>	<i>β</i>	<i>ΔR²</i>
Model A** (AdjR ² = 0.42)					
Step 1: Constant	-0.75	[-1.17; -0.32]	0.21		
ERP left 370-470 ms	-0.19	[-0.28; -0.10]	0.04	-.66***	.44
Model B*** (AdjR ² = 0.55)					
Step 1: Constant	1.01	[-0.36; 2.38]	0.66		
RAN 5.5 years	-0.03	[-0.05; -0.01]	0.01	-.49*	.51
Step 2: ERP left 370-470 ms ^a	-0.10	[-0.21; -0.00]	0.05	-.35	.08
Model C** (AdjR ² = 0.40)					
Step 1: Constant	-0.63	[-1.17; -0.08]	0.26		
Phonology 5.5 years	0.17	[-0.30; 0.65]	0.23	.16	.27
Step 2: ERP left 370-470 ms	-0.16	[-0.28; -0.04]	0.06	-.56*	.18
Model D** (AdjR ² = 0.45)					
Step 1: Constant	-0.59	[-1.06; -0.13]	0.23		
Verbal STM 5 years	0.28	[-0.10; 0.66]	0.18	.25	.19
Step 2: ERP left 370-470 ms	-0.17	[-0.26; -0.07]	0.05	-.58**	.31
Model E** (AdjR ² = 0.43)					
Step 1: Constant	-1.03	[-1.67; -0.39]	0.31		
Letter naming 5.5 years	0.03	[-0.02; 0.07]	0.02	.21	.22
Step 2: ERP left 370-470 ms	-0.16	[-0.26; -0.06]	0.05	-.57**	.25

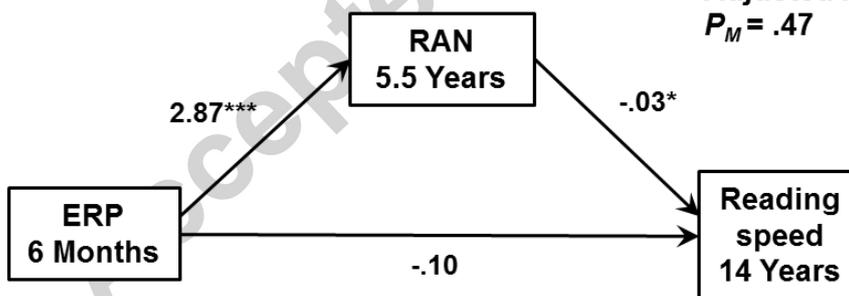
Note. * $p < .05$, ** $p < .01$, *** $p < .001$. ^a Variable entered.

The mediation analysis confirmed the hypothesis (that arose from the above regression analyses) that there was a significant indirect effect of the infant ERP amplitude on reading speed at 14 years mediated through rapid naming at the age of 5.5 years. The coefficient for indirect effect of ERP at 6 months on reading speed in 14 years through mediator RAN in 5.5 years $ab = -0.09$, bias corrected and accelerated confidence interval (.95) [-0.17; -0.02]. The mediator accounted for nearly half of the total effect, Percent mediation $P_M = .47$. The results of the mediation analysis are shown in Figure 3.

a Direct effect



b Indirect effect via mediator



Model: $F(2, 22) = 15.41^{***}$
Adjusted $R^2 = .55$
 $P_M = .47$

Figure 3. Mediator analysis. The significance of (a) the direct effect of infant ERP amplitude on reading speed at 14 years and (b) indirect effect through rapid naming at 5.5 years in the at-risk group. P_M = Percent mediation, * $p < .05$, *** $p < .001$ (2-tailed).

Discussion

Based on previous research, it is known that children at risk for dyslexia manifest abnormalities in brain function related to reading at different ages, and these abnormalities are likely to be associated with anatomical differences in the primary auditory cortex, occipitotemporal, posterior-temporal, and occipital regions (Leppänen et al., 2002; Guttorm et al., 2005; Raschle, Chang, & Gaab, 2011; Raschle, Zuk, & Gaab, 2012; Leppänen et al., 2012; van Zuijlen et al., 2013; van der Leij et al., 2013; Clark et al., 2014). Also, previous longitudinal studies have consistently found that various infant brain measures predict preschool language and elementary school reading problems (Molfese, 2000; Guttorm et al., 2005; Guttorm, Leppänen, Hämäläinen, Eklund, & Lyytinen, 2010; Leppänen et al., 2010; van der Leij et al., 2013). Because we here found the first evidence of infant electrical brain responses predicting reading skills until adolescence, the search for the explanations for the associations between speech perception deficit in infancy and reading failure at later age became necessary. The finding that rapid naming acts as a mediator between infant brain responses to speech and reading speed at adolescence could be linked to an explanation related to access or connectivity problems to phonological representations (Boets et al., 2013).

The preschool-age cognitive skills, rapid naming and phonology, were found to be strongly associated with at-risk infants' brain activation at the left hemisphere; larger negative ERP responses denoting better performance in rapid naming and phonology. In the at-risk group, left-hemisphere activation was found to predict 44% of reading speed at the age of 14 years, whereas in the control group the ERP measure did not predict reading skills. The ERP

measure significantly improved the prediction by 15–28% even after taking into account phonology, verbal short-term memory, and letter naming scores (Table 2). This provides evidence for a dissimilar development of speech sound processing in the brain. The dissimilar brain processes could lead to differential correlations between the control and at-risk groups likely linked to the variation of the underlying genetic risk factors for dyslexia.

Infant brain responses to frequently repeated stimuli were found to share common variance with rapid naming time and phonology before formal reading instruction. This suggests that early brain responses share cognitive processes with preschool-age cognitions that are important for future reading. However, the association between infant ERPs and adolescent reading speed is mostly mediated by preschool-age rapid naming ability. Fast performance in rapid naming is thought to reflect automatized lexical access of visual stimuli; by adolescence, also reading should already be a well-automatized process (Blomert, 2011; Norton & Wolf, 2012). Therefore, it seems that similar cognitive processes of automatized access to representations of objects and written symbols (i.e., lexicon) are needed in rapid naming and fluent reading, but this automatized access is not needed to the same extent in letter knowledge and verbal short-term memory (Norton & Wolf, 2012). If this is indeed the case, based on our data, infant brain activation to speech seems to play a part in processing that is crucial for the development of automatized lexical access. How speech processing at infancy is linked to lexical access remains unclear, although several possibilities exist: through the formation of speech sound representations for the repeated stimuli (Leppänen et al., 2002) or through the access to these representations (Boets et al., 2013).

It is somewhat surprising that infant ERPs to frequently repeated standard stimuli, but not to rarely presented deviant stimuli, explain reading speed in adolescence. The functional significance of the response to the standard stimulus around 400 ms could be related to encoding of the rapidly occurring second syllable or the formation of the memory trace.

The different association pattern between groups and stimuli could imply differences either in the role of fast extraction of acoustic information and/or the subsequent formation of representations of the standard stimuli, which is required by the rapid onset of the second syllable in the repeated stimuli. The first explanation would be supported by the time window in which the correlation was found, at around 400 ms after stimulus onset (around 250 ms after onset of the second syllable) corresponding to the processing of the rapidly occurring second syllable. Problems in this fast extraction would hinder the formation of the representations for the second syllable. In the deviant stimuli the silent gap between the syllables is longer allowing more time for the processing of the stimulus features. This could result in the non-significant correlations between the ERP and cognitive measures.

The results could also stem from the formation of the memory trace for stimuli containing a fast onset of the second syllable. The larger the response to the standard stimuli at around 400 ms at infancy, the better the build-up of a memory trace for the repeated stimulus (see Karhu, Herrgård, Luoma, Airaksinen, & Partanen, 1997 for results in older children) leading to better encoding of the stimulus and therefore better pre-reading and reading abilities in later life in at-risk children. This would be particularly pronounced in the case of increased time pressure for processing speech sounds, as was the case for the

frequently repeated stimulus in the present study.

One could also argue that the correlation only involving the standard response could stem from the better signal-to-noise ratio of that response. There were approximately 3.5 times more stimuli in the standard stimulus responses compared to the deviant stimulus responses. This could result in a more stable ERP response and therefore more systematic association to cognitive skill measures. However, the correlations only arose from the specific time window at around 400 ms, and not for example from the positivity at 135–215 ms. This would suggest that mere difference in the signal-to-noise ratio cannot explain this result.

Two issues were limiting the interpretation of the results: rather small sample size and relatively large amount of correlations examined. Especially in EEG measurements of awake, active infants the number of participants to be excluded is relative high, because of noisy data. Furthermore, in prospective study designs drop out ratio between infancy and adolescence decreases the sample size as well. Despite this the total sample size of 48 was still large enough for the current analyses.

We used the false discovery rate (FDR) correction (Benjamini & Hochberg, 1995) for p -values of the correlations, and only correlations which p -values survived the correction (ps under the critical value 0.0025) were taken into consideration to be non-false positive, and were interpreted. Also, the correlations were systematic in the sample. Therefore we consider the results to be plausible and reliable, and despite of limitations important to publish as a unique attempt to longitudinally understand factors behind the familial risk for dyslexia.

To conclude, in the present study we show that at-risk infants exhibit atypical brain responses to speech sounds and that brain responses measured in infancy can predict reading speed even until adolescence in children at risk for dyslexia. The association between infant brain responses to speech and reading speed in adolescence is mediated by rapid naming ability at preschool age. Based on our results and previous literature reviewed in the present study we allude that the common denominator behind these three processes is related to problems in automatization of the retrieval process from a mental lexicon via phonological representations. Atypical brain activation to speech sounds in infancy seems to implicate a deficient development of phonological representations or connectivity to those representations in at-risk infants that later hinders access to mental lexicon, and therefore also reading. Our findings tie therefore together the hypothesis on deficits in lexical access and deficits in speech sound representations as causes for dyslexia.

Acknowledgments

This work was supported by the Centre of Excellence Program of the Academy of Finland (grant numbers 44858, 213486). We thank the participants and their families and students who took part in data collection.

Author contributions

H. Lyytinen and P. H. T. Leppänen developed and tested the EEG procedure, and supervised data collection. K. Lohvansuu performed the data analysis, and all authors contributed to the interpretation of the results. K. Lohvansuu drafted the manuscript, and J. A. Hämäläinen, L. Ervast and P. H. T. Leppänen provided critical revisions. All authors approved the final version of the manuscript for submission.

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Highlights

- Associations of infant ERPs to speech and reading speed in 14 years were studied.
- ERPs of infants at-risk for dyslexia predicted 44% of reading speed at 14 years.
- The prediction was mediated via preschool-age rapid naming (RAN).
- This suggests that poor automatization of lexical access hinders reading and RAN.
- Atypical infant ERPs index a deficient development of representations on background.