Early identification and intervention in children at risk for reading difficulties

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Bestaat dat: niets weten?

schreef de eekhoorn op een dag aan de mier.
   De mier dacht heel lang na, maakte een kleine sprong in de
   lucht, krabde achter zijn oor en schreef terug:

   Ja. Alles bestaat.

Uit: Toon Tellegen (2002), 'Misschien wisten zij alles' (p. 485)
Chapter 2

Efficiency of visual information processing in children at-risk for dyslexia: Habituation of single-trial ERPs

To investigate underlying learning mechanisms in relation to the development of dyslexia, event-related potentials to visual standards were recorded in five-year-old pre-reading children at risk for familial dyslexia ($N = 24$) and their controls ($N = 14$). At the end of second grade the children aged 8 years were regrouped into three groups according to literacy level and risk factor. Single-trial analyses revealed N1 habituation in the normal-reading controls, but not in the normal-reading at-risks, and a N1 amplitude increase in the group of poor reading at-risks and controls. No P3 habituation was found in either group. The normal-reading at-risk group exhibited the longest N1 and P3 latencies, possibly compensating for their reduced neuronal activity during initial information extraction. In contrast, the poor-reading group only showed prolonged P3, and their increase in (initial small) N1 amplitude together with normal N1 latencies, suggests inefficient processing in an early time window, which might explain automatization difficulties in dyslexic readers.

2.1 Introduction

It is internationally recognized that dyslexia is neurobiological in origin and characterized by slow and inaccurate reading as well as poor spelling. These difficulties are often unexpected in relation to other cognitive abilities and the provision of effective classroom instruction (Goswami, 2003; Lyon, Shaywitz, & Shaywitz, 2003). Up to 10% of the population shows mild to severe symptoms of dyslexia. In the case of a family related history of dyslexia prevalence is estimated between 33% and 50% (Pennington & Lefly, 2001). Having at least one dyslexic parent forms a considerable risk for a young child to develop dyslexia himself (Gilger, Hanebuth, Smith, & Pennington, 1996). Over the years a strong consensus has arisen among investigators that reading is primarily a linguistic skill and that the central difficulty in dyslexia reflects a deficit within the language system, in particular a phonological deficit (e.g., Lyon et al., 2003; Pennington, 1990; Ramus et al., 2003; Vellutino, Fletcher, Snowling, & Scanlon, 2004). Neurobiological evidence supporting this hypothesis comes from a large amount of literature on reading disability in adults and children, describing dysfunction in particular left hemisphere posterior brain systems (e.g., Helenius, Tarkkainen, Cornelissen, Hansen, & Salmelin, 1999; Paulesu et al., 2001; Rumsey, Andreasen, Zanetkin, & Aquino, 1992; Rumsey et al., 1997; Shaywitz et al., 2002; Silani et al., 2005; Simos, Breier, Fletcher, Bergman, & Papanicolaou, 2000), considered to be critical in the development of skilled, automatized reading (Lyon et al., 2003).

In comparison to the abilities of normal-reading children, it is evident that the reading and spelling of dyslexic children lack automaticity, in particular indicated by relatively slow response rates on measurements of (repeated) reading. For example, it has become clear that although familiar words may be processed accurately, the processing rate stays relatively slow (Seymour, 1986; van der Leij & van Daal, 1999). Furthermore, the process of learning how to read and spell lacks the normal characteristics of skill automatization (see for a review Adams, 1990). Skills that become automatized are performed more quickly, with less effort, autonomously or unintentionally, and with less conscious awareness (Logan, 1997). Although it is commonly assumed that dyslexic children have a specific learning disorder concerning the domain of reading and spelling, the problem in mastering automaticity might imply a learning problem of a more general
nature than difficulties in the learning of correspondences between letters and constituent sounds per se.

Evidence for this line of hypothesizing comes from two studies by Nicolson and Fawcett (2000) concerning long term training in dyslexic children on a keyboard spatial task and a choice reaction task. They showed that the dyslexic subjects acquired a normal ‘strength’ of automatization as measured by resistance to unlearning, and long-term retention. In terms of speed and accuracy however, their automatized performance was of a lower quality. The learning curves of the dyslexic subjects in the above tasks displayed slower and more error-prone initial performance leading to lower final skill levels as compared to subjects without dyslexia. These ‘dyslexic’ rates of learning resemble the rates derived from repeated practice in the domain of reading (Thaler, Ebner, Wimmer, & Landerl, 2004; van der Leij & van Daal, 1990). Assuming that automaticity develops with learning (Logan, 1997) and that automaticity in children with dyslexia is of a lower quality in terms of speed but not in strength (Nicolson, Fawcett, & Dean, 2001), how are we to explain this lower quality? The relevance of this question is not restricted to children already facing severe reading and spelling problems, but may also hold for children genetically at-risk for developmental dyslexia, who are still in the pre-reading age and have not developed any reading skill.

An approach that may be crucial in explaining the automatization difficulties in dyslexic children is examining its possible relation with underlying mechanisms of information processing. As all learning consists of linking new to old information and new to old abilities, the degree in which the outcome of that process can be called automatized is determined by the ability to process new and changing information and to differentiate between relevant and irrelevant information. Of particular interest in this light are the orienting response (OR) and habituation of the OR. As the OR is a mechanism controlling involuntary changes in information-processing ability, leading to an increase in alertness and attention, the functional significance of the OR is to help investigate the eliciting stimuli in greater detail (Spinks & Siddle, 1983). However, after repeated presentation of stimuli, decline or habituation of the OR is thought to take place because the updating of the neuronal model of the stimulus becomes automated (Ravden & Polich, 1998). All information contained within the stimulus is ‘learned’ and the brain no longer responds to it. At a functional level habituation can be seen as an elementary form of learning (Sambeth, Maes,
Quian Quiroga, Van Rijn, & Coenen, 2004; Stephenson & Siddle, 1983). Assuming that rate of habituation reflects the level of efficiency of the brain to process information in a progressively automated manner, habituation may reflect a rate of learning. As a result of the automatized processing, there is a reduced need for attentional resources, and the limited processing capacity of short-term store becomes available for evaluation of novel or significant stimuli.

Both orienting and habituation can be defined by behavioural (overt) and physiological (covert) responses. Gaining insight into the latter responses calls for neurophysiological investigations, for example of the brain mechanisms involved, by registration of Event-Related Potentials (ERP). ERPs are relatively small changes in the electroencephalogram (EEG) in time locked to a given event or stimulus. ERP components of relevance to the dynamics of the OR can provide evidence for the existence, order and timing of independent processes in information processing (see Kenemans, 1990; Polich & Kok, 1995; Sokolov, Spinks, Näätänen, & Lytinen, 2002, for extensive reviews). Given that habituation usually takes place within 10 to 20 trials (Kenemans, 1990; Verbaten, Roelofs, Sjouw, & Slangen, 1986) and traditional ERPs require many artifact free trials, a technique is needed that allows deriving single-trial ERPs. There are only few habituation studies using single-trial techniques that compute single ERP within a habituation series of subsequent trials, such as orthogonal polynomial trend analysis (OPTA, see Woestenburg, Verbaten, Van Hees, & Slangen, 1983) or a dynamic factor model (Molenaar, 1994). In a sample of young adults, Kenemans, Verbaten, Roelofs, and Slangen (1989) observed an amplitude decrease of single-trial ERP components to a sequence of identical neutral as well as task-relevant visual stimuli for a non-specific N1 and for a posteriorly distributed P3. The N1, thought to represent the initial extraction of information from the sensory analysis of the stimulus, is in particular affected by stimulus novelty, and shows its sensitivity to subsequent repetition of a stimulus with rapid decrement (e.g., Kenemans, 1990; Näätänen & Picton, 1987). Although the P3 is associated with higher level processing, upon for instance, stimulus relevance, with short term repetition the P3 appears to decrease as rapidly as well (e.g., Kenemans, 1990; Polich & Kok, 1995). Habituation research including various single-trial procedures shows that occurrence and rate of habituation are heavily dependent on stimulus type, complexity and relevance, task and ISI conditions, and subjects (e.g., Cohen & Polich, 1997; Geisler & Polich,
1994; Lew & Polich, 1993; Ravden & Polich, 1998; Riggins & Polich, 2002; Verbaten et al., 1986). Although the evidence about atypical brain- and skill-related development of young children with a family history of dyslexia is still growing (e.g., Elbro & Petersen, 2004; Koster et al., 2005; Lyttinen et al., 2005; Maurer, Bucher, Brem, & Brandeis, 2003; Snowling, Gallagher, & Frith, 2003; van Leeuwen et al., 2006), to our knowledge ERP habituation has not been studied in pre-reading at-risk children. The scarce evidence regarding differences between groups of older children appears to be inconsistent. For example, no differences in habituation to simple visual and auditory stimuli were found between normally learning and learning disabled groups (Hirano, Russell, Ornitz, & Liu, 1996; John et al., 1989). Conversely, absence of habituation of the N1 to auditory stimuli was reported in a small group of children with fragile X syndrome in contrast to habituation shown by the control children (Castrén, Pääkkönen, Tarkka, Ryynänen, & Partanen, 2003).

Rate of learning depends heavily on the speed at which new and changing information is processed. Assuming that the latencies of ERP components reflect the processing time required for information extraction, stimulus evaluation and categorization, the lower quality of automatized performance in dyslexic children may be reflected in prolonged latencies of N1 and P3. Of interest to the present study are any delays in non-linguistic information processing, and ERP literature of relevance provides some evidence for speed differences between dyslexic and normal-reading subjects. Prolonged lower-level (visual) processing in dyslexic readers is, however, mostly reported to targets or low-probability stimuli (Breznitz & Meyler, 2003; Fawcett et al., 1993; Silva Pereyra et al., 2003; Taylor & Keenan, 1990). Conversely, studies using non-targets in passive tasks report no (Bernal et al., 2000; Stelmack, Rourke, & van der Vlugt, 1995) or inconsistent evidence for prolonged processing (see for a review, Dool, Stelmack, & Rourke, 1993). Thus, it appears that dyslexics are in particular delayed in the triggering of involuntary attention following stimulus change, possible the result of weakened attention capture (Hari & Renvall, 2001), or in the alternation between different cognitive processes related to stimulus relevance (Breznitz & Meyler, 2003). Note, however, that above findings were obtained in adults or children older than the subjects in the present study, and by averaging ERPs over series, rather than based upon single trial techniques.
The present paper is an attempt to investigate the role of underlying learning mechanisms in relation to the development of dyslexia by assessing the neural efficacy of the brain in genetically at risk children who are still in the pre-reading phase. In this group of children the presence of deficient underlying learning mechanisms at the age of five years may signify the onset of difficulties in the acquisition of reading and spelling. Given that a substantial number of genetically at-risk children will not develop reading problems (Elbro & Petersen, 2004; Hindson et al., 2005; Snowling et al., 2003), it is of great interest, theoretically and practically, to establish whether the at-risk children, who are facing reading difficulties, can be distinguished from the at-risk children who manage to learn to read and spell fluently. Therefore, we will study the efficiency of the processing of novel information in five year-old children at-risk and not-at-risk, before they have started formal reading-instruction. On the basis of their literacy skills two years later, children are either assigned to a group of poor-reading children or to one of the two groups of normal-reading children. This way, both the at-risk factor and the reading and spelling ability can be taken into account in explaining possible differences between the three groups of children. A similar approach, that is, the recording of ERPs in young children before the emergence of reading disabilities has been used previously in normal and at-risk populations. For instance, Molfese (2000) reported that auditory ERPs recorded at birth discriminated with 81.3% accuracy among groups of eight-year old normal, poor and dyslexic readers. Lyytinen et al. (2005) reported predictive correlations between ERPs to sounds at six months in at-risk children and their later literacy skills just before school entry.

While employing a passive non-attending set-up, in the present study short-term habituation and speed of processing to visual stimuli over a series of subsequent trials will serve as the qualitative and temporal measures of learning as indexed by ERP components N1 and P3. The combination with a single-trial technique assures recording of trial-to-trial variation in each subject (Molenaar, 1994). Without disputing the importance of auditory-phonological processing ability in reading acquisition, we will focus on underlying learning within the visual modality, to stress that if the learning disorder in dyslexic children implicates not only a deficit in phonological processing, but also in automatization, it is less specific than commonly assumed. In that case learning deficiencies need not necessarily be restricted to the auditory modality.
We presume that the ability to process new information more efficiently and intensively will result in learning at a higher rate. Thus, with respect to the effects of stimulus repetition on amplitude of the ERP components we expect a normal pattern of habituation, that is, a sharp decline of amplitude over the first trials, in particular for the N1 component, to be shown by the children identified as normal readers. In contrast, poor-reading children are expected to be less susceptible to habituation, based on the assumption that they are ‘slower’ learners of unfamiliar stimulus content. Subjects’ processing times are assessed by a series of identical abstract visual patterns that bear no task relevance. Longer latencies in the poor readers may be expected on the very first trial(s) only, due to a delayed attentional shift. Once attention is engaged, we do not expect substantial group differences over the subsequent trials in timing of early processing and stimulus evaluation.

2.2 Method

2.2.1 Subjects

Twenty-seven children from at risk families (mean age 5 years; 6 months, range 59-73 months, 14 boys, 13 girls) and 16 control children (mean age 5 years, 4 months, range 58-69 months; 9 boys, 7 girls) participated in the study. All children were recruited in the beginning of the second year of kindergarten, but some of them attended kindergarten for an extra year. In the Netherlands, the primary educational system includes kindergarten that spans two years. The majority of Dutch children enter school at age four. Formal schooling starts in Grade 1 at the age of six. The children were pupils of elementary schools in the area of Amsterdam, except for some of the at-risk children who visited an elementary school outside this area. All families participated voluntarily in response to handouts distributed by the kindergarten teachers. On enrolment, parents were requested to fill out an information form, including data on parental education level, and the medical history of the child. None of the children were showing serious emotional disturbances or attentional problems, according to their parents. All children had normal hearing, but some of the control children were wearing glasses, mainly for correcting problems with near-sightedness.

Selection of the subjects at risk or as controls was based on self-report of the parents confirmed by a questionnaire and the parent’s performance on a screening test. This test included two standardized measures of speeded
decoding of single words and pseudowords, the One-Minute-Test (OMT) (Brus & Voeten, 1999) and the Klepel (van den Bos, lute Spelberg, Scheepstra, & de Vries, 1999), as well as the Wechsler Adult Intelligence Scale (WAIS) subtest Similarities (Wechsler, 1997) measuring concept formation. For inclusion in the at-risk group the reading performance of (at least one of) the parents had to fall below or at the 10th percentile on either one of the reading tests or below or at the 20th percentile on both reading tests. Also leading to inclusion was a discrepancy score which represented a difference of at least 60 percentiles between a high score on the WAIS subtest Similarities and the score on either one of the reading tests (Koster et al., 2005; Kuijpers et al., 2003). For inclusion in the control group reading performance of both parents had to be on or above the 40th percentile on both reading tests.

Only children for whom ERP and behavioural data were available were included in the data analysis. Consequently, three at-risk children who dropped out prior to the acquisition of literacy data were excluded (attrition at risk group = 11%). Furthermore, artefact rejection resulted in an insufficient number of trials in the habituation series for two control children and they were also excluded from further data analyses (attrition control group = 13%). For 24 at-risk children (13 boys and 11 girls) and 14 not-at-risk control children (8 boys and 6 girls) habituation data measured at the beginning of the second year of kindergarten and literacy data measured two years later were available.

Preceding single trial data analysis, the remaining children in the two samples were regrouped taking into account both the risk factor and children’s reading and spelling ability at the end of Grade 2. The five standardized measures we used to determine literacy proficiency were three decoding speed tests consisting of mono- and polysyllabic words (Verhoeven, 1995), a decoding speed test consisting of mono- and polysyllabic pseudowords (van den Bos et al., 1999), and a spelling test (van den Bosch, Gillijns, Krom, & Moelands, 1993) consisting of mono- and polysyllabic words with orthographic patterns of various complexities. Reclassification of the children resulted into three groups consisting of poor reading at-risk and control children, normally reading at-risk children, and normally reading control children. The group of poor readers (N = 11, mean age 5 years; 6 months, range 59-72 months, 6 boys, 5 girls) consisted of 9 children at-risk and 2 control children with scores below the 25th percentile on at least two of the word decoding tests, and scores below the
25th percentile on either pseudoword decoding or word spelling. The normally reading at-risk children (N = 15, mean age 5 years; 5 months, range 59-71 months, 9 boys, 6 girls); and the normally reading control children (N = 12, mean age 5 years, 4 months, range 58-69 months; 6 boys, 6 girls) consisted of the remaining at-risk and control children, respectively, with scores above the 25th percentile on all reading measures.

With respect to differences in parental performance on the screening tests, parents of the normal-reading control children performed better on the reading measures, but not on verbal competence as compared to the two poor-reading and normal-reading at-risk groups. No differences were found between these latter groups on any of the selection measures. According to the selection criteria, 36% of the parents in the poor-reading group (including those that were selected as control children) and 33% of the parents in the normal-reading at-risk group scored below or equal to the 10th percentile on both reading measures; 18%, respectively 27% of the parents scored below or equal to the 20th percentile on both measures and/or below or equal to the 10th percentile on one of the measures. Twenty-seven percent of the poor-reading group and 40% of the normal-reading at-risk group were included on the basis of a discrepancy-score. Dyslexic problems in relatives of the affected parents were reported in 64% and 60% of the poor-reading group and the normal-reading at-risk group, respectively. The three groups did not significantly differ in gender or age, nor in cognitive ability, as assessed with two standardized measures, a test of receptive vocabulary (Verhoeven & Vermeer, 2001) and the Coloured progressive matrices (Raven, 1984), measuring non-verbal intelligence. Halfway through the second year of kindergarten, all subjects scored above the 10th percentile of receptive vocabulary, and one year later all subjects (except for one poor-reading child) performed within or above the normal range (between the 25th and 75th percentiles) on non-verbal intelligence. Since the child with a below average score on non-verbal intelligence scored in the average range in the receptive vocabulary measure, we refrained from excluding it from the analyses. With respect to reading and spelling performance, regardless of risk factor, normal-reading children performed better than poor-reading children on all literacy measures. On none of the measures differences were found between the normal-reading at-risk and normal-reading control group. The descriptive statistics for the literacy measures appear in Table 2.1.
Table 2.1  
Mean raw scores (M) and standard deviations (sd) for poor-reading children, normal-reading at-risk (AR) children and normal-reading control (C) children on Grade 2 measures.

<table>
<thead>
<tr>
<th>Measures</th>
<th>Poor</th>
<th>Normal AR</th>
<th>Normal C</th>
<th>F(2, 35)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 11</td>
<td>N = 15</td>
<td>N = 12</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td></td>
</tr>
<tr>
<td>sd</td>
<td>sd</td>
<td>sd</td>
<td>sd</td>
<td></td>
</tr>
<tr>
<td>Speeded decoding</td>
<td>41.0 12.9</td>
<td>76.9 10.0</td>
<td>78.9 13.9</td>
<td>35.78***</td>
</tr>
<tr>
<td>(max=150)</td>
<td>12.9</td>
<td>10.0</td>
<td>13.9</td>
<td>1&lt;2=3</td>
</tr>
<tr>
<td>Wordlist 2</td>
<td>26.7 10.3</td>
<td>71.2 12.7</td>
<td>74.2 14.1</td>
<td>52.41***</td>
</tr>
<tr>
<td>(max=150)</td>
<td>10.3</td>
<td>12.7</td>
<td>14.1</td>
<td>1&lt;2=3</td>
</tr>
<tr>
<td>Wordlist 3</td>
<td>16.1 9.0</td>
<td>54.9 13.5</td>
<td>54.7 14.9</td>
<td>35.50***</td>
</tr>
<tr>
<td>(max=120)</td>
<td>9.0</td>
<td>13.5</td>
<td>14.9</td>
<td>1&lt;2=3</td>
</tr>
<tr>
<td>Speeded decoding</td>
<td>15.5 4.6</td>
<td>41.7 10.3</td>
<td>49.3 10.3</td>
<td>44.26***</td>
</tr>
<tr>
<td>Pseudowords</td>
<td>15.5</td>
<td>4.6</td>
<td>41.7</td>
<td></td>
</tr>
<tr>
<td>(max=116)</td>
<td>4.6</td>
<td>10.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>49.3</td>
<td>10.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>44.26***</td>
<td></td>
<td></td>
<td>1&lt;2=3</td>
</tr>
<tr>
<td>Spelling words</td>
<td>21.4 7.0</td>
<td>32.3 5.3</td>
<td>34.0 6.2</td>
<td>14.68***</td>
</tr>
<tr>
<td>(max=38)</td>
<td>7.0</td>
<td>5.3</td>
<td>6.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32.3</td>
<td>5.3</td>
<td>6.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.68***</td>
<td></td>
<td></td>
<td>1&lt;2=3</td>
</tr>
</tbody>
</table>

**p < .001

2.2.2 Apparatus

A 32-channel electrocap was used employing sintered Ag/AgCl electrodes in a 10-20 system montage including locations Oz, O1/2, Pz, P3/4, P7/8, CPz, CP3/4, TP7/8, Cz, C3/4, T7/8, FCz, FC3/4, F7/8, Fz, F3/4, F7/8, and Fp1/2). Additional electrodes were used for recording the vertical electro-oculogram (VEOG; above and below the left eye) and the horizontal electro-oculogram (HEOG; at the outer canthus of each eye). Linked ear electrodes served as the inactive reference. Electrocortical activity was recorded with 500 Hz per channel and filter settings of 0.1-70 Hz (Synamps model 5083, Neuroscan Inc). Impedances were kept below 20 kΩ (Ferree et al., 2001).

2.2.3 Stimuli

Stimuli were two abstract, black and white patterns, with equal luminance (same number of black and white pixels), and an information value of 26 bits for the standard and 60 bits for the deviant, as has been determined employing a procedure developed by Attnave (1954), and similar to the ones used by Kenemans et al. (1989). They were presented in the centre of a computer screen, with a presentation time of 1000 ms. To facilitate proper central fixation, a fixation cross was presented in the inter-stimulus interval. The screen was positioned in front of the subject at a distance of 100 cm from the subject’s eyes. Stimulus presentation and sampling procedures
were controlled by a standard PC. A total of 211 stimuli were presented in a single block, in which the first 14 presentations were identical standards, followed by a deviant on the 15th trial. On the remaining 196 trials, (13) additional deviants were pseudo-randomly presented with a 6.6% probability. Following this procedure, the first 14 ‘habituation’ trials could be assessed separately from following trials, and here only data pertaining to this first series will be presented. A variable ISI was used (to accommodate additional conditions, not presented here) with increasing task requirements with a mean of 1500 ms and a range between 1000 ms and 2000 ms.

2.2.4 Procedure

The ERP recording session took about 1-1½ hours. An adult, in most cases one of the parents, accompanied the child. Upon arrival, the child was put at ease and familiarized with the procedure and the methods employed which started only when the child was ready to cooperate. To distract attention during preparation of the electrocap the child was given a picture book. Recording took place in an adjacent room with dimmed lights and the door closed. Subjects received task instructions as soon as they were seated in a chair that was positioned in front of the computer screen. They were told that pictures would be presented, but that they merely had to watch them by looking at the middle of the screen, and that they did not have to pay particular attention to them. The children were instructed to maintain fixation on a small black cross at the center of the screen appearing between presentations, to sit as still as possible and to prevent eye blinking during presentation of the stimulus as much as possible. During the experiment an assistant sat with the child to assure that the child remained fixating the screen centrally. Parents were not allowed to be present in the recording room but joined the experimenter.

2.2.5 EEG processing and scoring

ERPs. The EEG was bandpass filtered (.5-20 Hz, 48 dB/octave) and eye blinks were corrected according to a spatial filter transform based on a linear derivation approach (see User Guide: Vol. II; Neuroscan Inc). Subsequently, artefacts exceeding 100 μV in any channel were automatically rejected and epochs (starting 100 ms before stimulus onset and lasting 1024 ms) were obtained for the first fourteen standards (referred to as habituation trials). Individual habituation trials were subsequently inspected for remaining
artefacts and occasional missing trials were replaced by averaging preceding and following trials, to ensure 14 trials for each subject. Grand average ERPs (across the habituation series) yielded two distinct Global Field Power peaks (microstates; Lehmann), one for the N1 (130-260 ms) and one for P3 (450-850) with peaks at Cz and Pz, respectively. Traditionally, N1 and P3 are quantified at these electrode locations, so we decided to restrict the further analysis to these sites. Subsequently, single-trial ERPs were determined by a dynamic factor analysis technique (Molenaar, 1994). Next, for each resulting single trial ERP, N1 amplitude and latency were scored at Cz as the largest negative going peak within a latency window between 130 and 260 ms, relative to the largest positive going peak within 100 ms preceding the N1. Similarly, P3 amplitude and latency were scored at Pz as the largest positive going peak within a latency window between 450 and 850 ms, relative to the largest negative going peak preceding it.

2.2.6 Statistical analysis

The Linear Mixed Model procedure as implemented in the statistical software package SPSS was used to test whether the groups differed per trial over time for the habituation stimuli. The Linear Mixed Model (see Verbeke & Molenberghs, 2000) is essentially similar to a standard Repeated Measures ANOVA but offers more flexibility in model specification. Dummy parameters were used to represent the groups, where one dummy parameter is sufficient to represent two groups, and the two dummy parameters are sufficient to represent three groups. A different parameterization of the dummy parameters was used to test specific hypotheses on group differences, similar to the post hoc group comparisons of standard ANOVA. ERP components N1 and P3 were analyzed in two linear mixed model designs (fixed effects only) by means of maximum likelihood (ML) estimation. In the first design the dependent variables were measured at 14 occasions and 3 groups of readers (poor-reading children (Poor), normal-reading at-risk children (Normal-AR) and normal-reading control children (Normal-C). In each of the three groups intercepts and linear slopes were estimated for amplitude and latency. The intercepts were defined as the status at the first trial, and the slopes represent the linear change across trials. For testing the expectations regarding group differences in the intercepts of latency, and in the intercepts and slopes of amplitude, the first design contains the following set of dummies: Normal-C versus Poor, Normal-C versus Normal-AR. The second design resembles the first in all
major aspects with the exception of the included groups (poor-reading and normal-reading at-risk) represented by the dummy: Poor versus Normal-AR. Main effects and interactions were tested by means of the Likelihood Ratio (LR) test (i.e. a $\chi^2$-difference test), the dummy parameters are tested by means of the t-test (e.g. estimate/ standard error). We started with a full model containing all main and interaction effects, and subsequently constrained the model further. For each ERP component the estimates of the most parsimonious model will be presented. Then, effects for group are reported on intercept (for amplitude and latency), and lastly, effects for group are reported on slope (for amplitude only). Following the presentation of the first design the same procedure was used for the second.

2.3 Results

Mean single-trial ERPs at Cz (where N1 was scored) and Pz (where P3 was scored) are shown in Figures 2.1 and 2.2, for Trials 1, 2, 5, 8, 10 and 13. Mean intercepts and linear slopes of N1 and P3 latency and amplitude, and mean linear slopes of N1 and P3 amplitude are listed in Table 2.2.

Figure 2.1. Mean single-trial ERPs of N1 at Cz for poor readers (solid), normal at-risk readers (dashed) and normal control readers (dotted): trials 1, 2, 5, 8, 10 and 13
Table 2.2

N1 and P3 intercepts (for latency and amplitude) and slopes (for amplitude), per group.

<table>
<thead>
<tr>
<th></th>
<th>N1 Intercept</th>
<th>N1 Slope</th>
<th>P3 Intercept</th>
<th>P3 Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor</td>
<td>183.11</td>
<td>a</td>
<td>617.51</td>
<td>b</td>
</tr>
<tr>
<td>Normal AR</td>
<td>194.58</td>
<td></td>
<td>639.42</td>
<td></td>
</tr>
<tr>
<td>Normal C</td>
<td>186.99</td>
<td>a</td>
<td>573.98</td>
<td></td>
</tr>
</tbody>
</table>

Note: Values that share the same subscript do not differ.

2.3.1 Amplitude: intercept and slope

N1 Starting with the full model, within the first design there were both significant main and interaction effects for the intercept and the slope for N1 amplitude. The full model fitted the data significantly better than a restricted model without interaction effects for the slope ($\chi^2(2) = 15.92, p < .001$). Given the full model, the dummy parameters representing the main effect for the intercept showed a significantly less negative intercept for the Poor ($t(248.61) = 3.92, p < .001$), and the Normal-AR readers ($t(248.61) = 3.31, p < .01$) as compared to the Normal-C. With regard to linear slope, the dummy parameters showed that the Poor ($t(261.36) = -4.05, p < .001$), and the Normal-AR readers ($t(261.36) = -2.17, p < .05$) differed significantly.
from the Normal-C. As shown in Figure 2.3, in the Normal-C N1 amplitude had a more negative initial level and gradually decreased in negativity over trials, whereas in the Poor readers amplitude increased strongly over trials. In the Normal-AR N1 amplitude neither decreased nor increased in negativity. The second design showed also significant main and interaction effects for the intercept and the slope and the full model fitted the data significantly better than a restricted model without the interaction effect for slope ($\chi^2(1) = 7.20, p < .01$). The dummy parameters representing the effects for group and slope showed that the groups did not differ significantly for the intercept ($\chi^2(148.09) = -1.53, p = .128$), but that the Normal-AR showed a less negative slope for N1 amplitude than the Poor readers ($\chi^2(189.15) = 2.73, p < .01$).

![Figure 2.3. Intercepts and slopes of N1 (left panel) and P3 (right panel) amplitude for poor readers (solid), normal at-risk (dashed) and normal control (dotted) for trials 1 to 14](image)

**P3** Within the first design, no main and interaction effects for the intercept or for the slope were found for P3 amplitude. The full model and the most parsimonious model appeared not to differ significantly ($\chi^2(5) = 2.86, p = .72$), indicating that there were no differences between the normal-reading control children and the poor-reading and normal-reading at-risk children for the intercept and the slope, see Figure 2.3. Within the second design there was no significant difference between the full and the most parsimonious model either ($\chi^2(3) = 2.24, p = .52$). Poor-reading and normal-reading at-risk subjects did also not differ for the intercept and the slope of P3 amplitude.
2.3.2 Latency: intercept

N1 Starting with the full model within the first design, no main and interaction effects for slope were found for N1 latency. That is, removing these effects from the model did not lead to a significant deterioration in model fit \(\chi^2(3) = 2.68, p = .44\). Given this restricted model the main effect for group on intercept was significantly different from zero \(\chi^2(2) = 12.03, p < .01\). The dummy parameters representing this main effect showed a significantly higher N1 intercept for Normal-AR as compared to the Normal-C \((t(528.02) = 2.33, p < .05)\), as can be seen in Figure 2.4. No significant difference was found between the Normal-C and the Poor readers. Within the second design no main and interaction effects for slope were found either, and these terms could be removed from the model \(\chi^2(2) = 2.68, p = .26\). Given this restricted model group had a significant effect on the intercept \(\chi^2(1) = 12.21, p < .001\). The dummy parameter representing this main effect showed a significantly higher intercept for the Normal-AR as compared to the Poor readers \((t(355.58) = 3.64, p < .001)\).

Figure 2.4. Intercepts of N1 (left) and P3 (right) latency for poor readers (solid), normal at-risk (dashed) and normal control (dotted) for trials 1 to 14.

P3 For P3 latency within the first design no main and interaction effects for slope were found \(\chi^2(3) = 1.41, p = .70\). Given this model group had a significant effect on the intercept \(\chi^2(2) = 32.80, p < .001\). The dummy parameters representing this main effect showed a significantly higher intercept for the Poor readers \((t(572.11) = 3.57, p < .001)\), and the Normal-AR \((t(572.11) = 5.79, p < .001)\) as compared to the Normal-C. See Figure 2.4. Within the second design no main and interaction effects for the slope
and the intercept were found ($\chi^2(3) = 3.87, p = .28$). Given this most parsimonious model there was no effect for group on the intercept. The Poor and the Normal-AR did not differ significantly for the intercept of P3 latency.

2.4 Discussion

2.4.1 Effects of stimulus repetition

The normal-reading control children showed a N1 amplitude decrease over trials, whereas such habituation was not present in the normal-reading at-risk children and the poor-reading children. In contrast, the P3 component appeared not to be sensitive to any form of habituation, nor in the normal-reading control children and neither in the other groups. Interestingly, for N1 amplitude the effects of stimulus repetition appeared to turn out quite different for the three groups. The assumption that the normal-reading at-risk children would show habituation to the same degree as the normal-reading control group was not supported by our data. However, the poor-reading children differed in an even more striking manner from the group of normal-reading control children, because they displayed an increase of N1 amplitude over trials. Given that N1 amplitude may also reflect endogenous processing (Taylor, Chevalier, & Lobaugh, 2003) and is susceptible to attention level (Näätänen & Picton, 1987; Vogel & Luck, 2000), the abnormal strong covert orienting in the poor-reading children towards non-task relevant stimuli could reflect a subjective interpretation of task relevance, despite the use of the standard instruction to merely watch the stimuli. Task uncertainty may have let poor-reading children gradually develop some kind of expectancy about the stimuli to come (see also discussion below regarding P3 amplitude). It is unclear, however, why this effect was absent in the two other groups.

Another remarkable group difference concerned the size of the intercept, an indication of the amplitude on the very first trial. In contrast to the normal-reading controls, the poor-reading children as well as the normal-reading at-risk children showed a much higher, that is, less negative initial amplitude. Following the instruction to direct the attention to the screen, the poor-reading and normal-reading at-risk subjects may have been slower in shifting their attentional focus (Dykman, Ackerman, Holcomb, & Boudreau, 1983; Hari & Renvall, 2001) to the first uncued stimulus in the
series. Only recently, poor control of spatial attention shifting was also reported in a group of dyslexic students (Wijers, Been, & Romkes, 2005). This slower directing of attention towards the stimulus location may be related to their lower levels of orienting. In combination with the ensuing perception of a fast sequence of stimuli, this may have caused a subjective experience of increased stimulus intensity. This concept was raised before by Castrén et al. (2003) to explain an enhanced N1 to auditory standards in an oddball paradigm and the absence of habituation to a train of stimuli in a small group of children with fragile X syndrome. These authors suggested that both findings could be caused by excessive responses in neurons leading to changes in alertness as well as in general attentiveness and heightened state of arousal. This conjecture may be further corroborated by evidence that increasing stimulus intensity has the effect of augmenting P1N1 amplitude slopes at midline sites, and that this pattern of sensory modulation can be seen in the majority of children (Carrillo de la Pena, Holguin, Corral, & Cadaveira, 1999). Thus, the possibility that an inclination to respond with increased excitability to repeated stimuli played a part in early processing differences between the groups of poor- and normal-reading children cannot be ruled out. In the last section we will discuss however the increment of N1 amplitude over trials in poor-reading children in relation to their inability to acquire reading and spelling fluency.

The present absence of a P3 amplitude effect suggests either that we cannot always assume rapid decrement upon stimulus repetition for this component in young children, or that we did not control adequately for additional situational or cognitive interference. The trial-to-trial variation in neural responding might reflect a varying expectancy about the stimuli to come (Sambeth, 2004). Quite a few of the present subjects in fact inquired if or when other ‘pictures’ would be presented. Then, with every new presentation a kind of mismatch may have occurred between anticipation and external event, which in turn may have given subjective relevance to the standard stimulus. Also, it may be assumed that ERPs to stimuli presented at variable ISIs, as in the present study (mandatory for the task relevant blocks, not presented here), do less readily habituate due to increased uncertainty about temporal probability (Graham, 1997; Kenemans, 1990; Mallardi, 1979; Papanicolaou, Loring, & Eisenberg, 1985). Moreover, amplitude decrement to visual as opposed to auditory stimuli has been reported to be slower, unless many successive trial blocks are presented, because visual processing requires a greater utilization of attentional
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resources (Geisler & Polich, 1994; Ravden & Polich, 1998). Nevertheless, the application of a single-trial technique enabled us to identify N1 habituation in the normal-reading controls, thus revealing groups differences in trial-dependent effects of stimulus repetition, which otherwise would have gone unnoticed in traditional grand averages, as nicely demonstrated by the fact that overall group means to all (197) standards presented were comparable.

2.4.2 Effects of speed of processing

The latency of the P3 peak amplitude (as an index of the children’s stimulus evaluation time (Polich, Ladish, & Burns, 1990)) appeared to be longer in the poor-reading children in comparison to the normal-reading controls. In particular the normal-reading at-risk children, however, displayed longer latencies for the N1 and the P3. For both components, latencies are age related with values decreasing with age (Fuchigami et al., 1993; Polich et al., 1990; Taylor et al., 2003), but the developmental changes that are observed for P3 latencies are also related to changes in memory capacity (Polich et al., 1990). Although it seems not very likely that age related maturational processes were involved in the longer latencies of the poor-reading and normal-reading at-risk children, being in the same age range does not necessarily mean that their neuronal maturation was similar. Regarding differences in memory function, recently a relation between risk of dyslexia and poorer, albeit verbal, memory skills at five years of age was reported in an (follow-up) ERP study with newborns at genetic risk of dyslexia (Guttorm et al., 2005).

Task difficulty and/or subjectively perceived complexity are known to influence processing times (Breznitz & Meyler, 2003). So, the prolonged processing of non-targets under passive conditions, might either imply that stimulus processing per se proved to be more taxing for the poor-reading and the normal-reading at-risk subjects, due to a lagging neuronal maturation or a reduced memory capacity, or that the new situation instigated a more prolonged extracting of stimulus information to promote processing and analyzing. The normal-reading at-risk children’s delays in both the earlier and later stage of processing show that their passively processing of incoming stimuli as well as their more controlled stimulus processing were affected. The involuntary tendency towards a lower speed of processing in this group might be seen as an adaptation, that is, as a kind of trade-off for their relatively (i.e., compared to normal-reading controls)
reduced neuronal activity to ensure a better encoding of stimulus occurrence and content. Given that the poor-reading children were only delayed in the later stage of processing, speed of processing among poor-reading children seems in particular be slowed down in evaluating information, but not in the modelling (of occurrence) of novel information. Thus, unlike the normal-reading at-risk children, poor-reading children did not adapt their early timing to their (initial) reduced brain activity. So, speed of processing might signal a deficient underlying factor affecting learning in children at-risk for dyslexia.

2.4.3 Early visual processing in the pre-reading phase and reading proficiency

The apparent increase in brain activity over 14 trials shown by the poor-reading children in response to a repeatedly presented stimulus may indicate a less efficient way of processing new information. The poor-reading children needed much more exposures to reach the (initial) level of neuronal responding of the normal-reading control children. By contrast, in combination with their slower processing times the normal-reading at-risk children seemed to have mobilized a sufficient amount of early brain activity to deal with the stimulus presentation. Dissimilar to the poor-reading children their initial small negative responses were not followed by an increase over trials, although no decrement occurred either. To clarify why adjustment of initial reduced brain activity in response to newly presented, unfamiliar but neutral information may account for the problematic development of automatized reading in dyslexic children, we first need to address some theoretical considerations about automaticity acquisition.

In general, processing may occur without subjective awareness of the stimulus that produced it. However, often pre-attentive processing is not sufficient for the perceptual organization of (visual) input. Attentive processing is needed to integrate the various features belonging to one object, otherwise object representation would be incoherent (Spekreijse, 2000). According to Logan, Taylor, & Etherton (1999) attentive processing is a necessary condition for automaticity, that is, ‘what is learned during automatization depends on what is attended to and how attention is deployed’ (p. 179). It has been suggested that the early N1 component signals a pre-attentive comparison stage of the OR, providing the informational basis for attentional selection (Näätänen, 1990). Thus, the entrance of visual stimuli into subjective awareness might not only be the
intentionally result of (self)-controlling, for example acting upon instructions to attend, but also the result of an involuntary process, for example an evoked OR. Although pre-attentive processing is not to be considered a necessary condition for automaticity (Logan, 1992), through attracting attention to novel or salient features it may benefit the acquisition of automaticity. In his instance theory of automatization, Logan (1997) points out that in gaining automaticity the number of presentations is less important than the number of times a stimulus is interpreted in a particular way. This notion relates to one of the theories’ main assumptions, namely that automaticity is processing based on memory retrieval. Retrieval might be considered a race between different but equivalent memory traces or instance representations encoded and stored separately in memory. The first trace to finish, providing either a correct or an incorrect response, directs performance. The more traces there are in memory the quicker a trace will be retrieved. This argument implies that the more traces signify a correct response, the greater the chance a subject will perform well. Thus, initial small amplitudes and relative normal processing times at an early stage of processing together with an increase in negativity upon stimulus repetition, might signal that upon the initial observation of (novel) information insufficient neuronal resources are being allocated, thereby failing an effective attraction of attention to and encoding of distinguishing features. As a consequence, multiple observations of the same aspects of information are necessary.

Assuming that inefficient dealing with novel information may result in storage of relative less, more diffuse or incorrect memory traces of form and detail, it follows that memory retrieval and as a consequence, automatization is hampered. If such initial inadequate processing of abstract visual information in poor-reading children is extended to the processing of novel orthographic information, it might explain why children with severe dyslexia are able to obtain an adequate level of accuracy and even to gain in speed on highly practised words, whereas no transfer takes place to non-practised words that bear orthographic resemblance (van der Leij & van Daal, 1990). With enough practice, these children are able to rely on sufficient correct word-specific orthographic memory traces. However, accuracy and speed problems are to be expected with non-practised words, since in those cases decoding will be based on retrieval and combining of several traces of sublexical orthographic information, presumably of lower quality. Under
more complex reading conditions like oral reading, decoding of unfamiliar words will deteriorate even more.

Since the automatic processing of words is strongly influenced by problems with phonemic awareness shown by a majority dyslexics, if not by all (Ramus et al., 2003), a deviant processing of novel (absolutely or relatively) information may not be restricted to the visual modality, operating in isolation, but may also hold for the auditory/ phonological system. In this light it is very interesting that deviances in early phonological processing also have been found in infants with later reading difficulties (Espy, Molfese, Molfese, & Modglin, 2004), as well as in infants at familial risk for dyslexia (see for a review, Lyytinen et al., 2005). Espy et al. (2004) reported variations in the development of the N1 component as the most evident relation between ERP responses to speech and non-speech stimuli between the ages of one and four years and subsequent pseudoword reading proficiency at 8 years, with N1 amplitudes consistently more negative in less proficient readers. Leppänen et al. (2002) found more positive responses (at about 190 ms) to sound onsets discriminated between infants with and without familial risk and preliminary analyses showed that these could be linked to better later phonological skills in both groups (Lyytinen et al., 2005). It is unclear, however, whether these positive responses reflect the same information-processing mechanisms as manifest in N1. Evidence for deviances in early phonological processing shown by adult dyslexics comes from two studies using magnetoencephalography (MEG). Helenius, Salmelin, Richardson, Leinonen, and Lyytinen (2002) reported an abnormally strong N1m response to the beginning of a speech sound under actively listening and ignored speech conditions as the most robust difference between dyslexic and normal-reading individuals. Strong enhancement of a pre-semantic N1m was also found in dyslexic adults to spoken words within a sentence (Helenius, Salmelin, Service et al., 2002). However, it should be stressed that none of these studies directly addressed the issue of habituation. Nevertheless, together with our findings the presented evidence suggests that the pre-attentive level of information processing, either visual or auditory, could be an important indicator or predictor of (later) reading problems.

In summary, by studying covert processing of abstract visual information we attempted to find evidence for differences in underlying learning mechanisms in children genetically at-risk for dyslexia, as possible early indications of reading disability. We were able to show that in a mixed
group of at-risk children particularly the ones with a lower reading proficiency showed differences in allocation of brain resources. In combination with a discrepancy between relative fast early and slow later processing times this mode of early processing of novel information is suggestive of deficient learning at a basic level. That the initial processing of repeatedly presented stimuli was similarly affected in the two poor-reading children who were not at risk, seems to support the association between efficiency of early processing and reading abilities. Although we realize that the implication of our findings is limited due to small sample sizes, we would like to emphasize that especially the association between passive responding to new information at an early stage of processing and later literacy skills seems strong enough to pursue as a line of investigation. An obvious suggestion for future research is a replication of our habituation paradigm involving meaningless auditory as well as complex phonological stimulus processing to investigate whether the reported deficient early processing in poor-reading children are modality non-specific and/or related to problems with phonological coding. Equally interesting we consider the question whether deficient early processing is to be found in young children only, as a possible precursor of difficulties in learning to read and spell, or that older subjects are similarly affected. If that is the case, inefficient information processing resulting in less automatized learning might be an underlying characteristic of dyslexia.

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