Impaired tuning of a fast occipito-temporal response for print in dyslexic children learning to read

Urs Maurer,[1,2] Silvia Brem,[1] Kerstin Bucher,[1] Felicitas Kranz,[1] Rosmarie Benz,[1] Hans-Christoph Steinhausen[1] and Daniel Brandeis[1,3]

[1]Department of Child and Adolescent Psychiatry, University of Zurich, Switzerland, [2]Sackler Institute for Developmental Psychobiology, Weill Medical College of Cornell University, New York, USA and [3]Center for Integrative Human Physiology, University of Zurich, Switzerland

Correspondence to: Daniel Brandeis, Department of Child and Adolescent Psychiatry, Brainmapping Research, Neumünsterallee 9, CH-8032 Zurich, Switzerland
E-mail: brandeis@kjpd.unizh.ch

Developmental dyslexia is defined as a disorder of learning to read. It is thus critical to examine the neural processes that impair learning to read during the early phase of reading acquisition, before compensatory mechanisms are adapted by older readers with dyslexia. Using electroencephalography-based event-related imaging, we investigated how tuning of visual activity for print advances in the same children before and after initial reading training in school. The focus was on a fast, coarse form of visual tuning for print, measured as an increase of the occipito-temporal N1 response at 150–270 ms in the event-related potential (ERP) to words compared to symbol strings. The results demonstrate that the initial development of reading skills and visual tuning for print progressed more slowly in those children who became dyslexic than in their control peers. Print-specific tuning in 2nd grade strongly distinguished dyslexic children from controls. It was maximal in the inferior occipito-temporal cortex, left-lateralized in controls, and reduced in dyslexic children. The results suggest that delayed initial visual tuning for print critically contributes to the development of dyslexia.

Introduction

Learning to read represents a developmental milestone in literate societies and is mastered by most children within a few years. In about 5–10% of children, however, learning to read is severely impaired and results in developmental dyslexia, a specific reading disability. Studies of the neural correlates of dyslexia have advanced our understanding of the brain basis of the disorder, and may eventually yield useful measures for early prediction of dyslexia and evaluation of intervention methods (Posner and Rothbart, 2005).

Phonological brain functions, which are predictors of reading acquisition and implicated as the core deficit in dyslexia (Bradley and Bryant, 1983; Ramus *et al.*, 2003) have been well studied in younger children, including those at risk for dyslexia (Maurer *et al.*, 2003; Guttorm *et al.*, 2005).

However, brain imaging studies of reading have so far focussed mainly on the outcome rather than on the process of reading acquisition (Rumsey *et al.*, 1997; Shaywitz *et al.*,

1998; Brunswick *et al.*, 1999; Temple *et al.*, 2001; Shaywitz *et al.*, 2002; Brambati *et al.*, 2006; Kronbichler *et al.*, 2006), even though dyslexia is defined as a disorder of *learning* to read (Dilling *et al.*, 1991).

These studies have consistently detected reduced activation in posterior parts of the reading network in the brain of adults and older children with dyslexia (for reviews: McCandliss and Noble, 2003; Shaywitz and Shaywitz, 2005). Whereas reduced activation in superior temporal regions has been linked to phonological processing and thus to the phonological core deficit in dyslexia, reduced activation in inferior occipito-temporal regions suggests deficits in specialized visual word processing. It is unclear, whether this deviant tuning of visual regions for print emerges during initial reading acquisition or at a later stage (McCandliss and Noble, 2003).

Several studies have also shown increased frontal activation in dyslexics during reading, indicating

compensation (Shaywitz *et al.*, 1998; Georgiewa *et al.*, 2002). Such compensatory brain activity does not need to be restricted to frontal areas (Shaywitz *et al.*, 2002) and may also occur in posterior brain areas. Thus, neural correlates of dyslexia in older children and adults presumably reflect both deficient and compensatory brain processes at the same time. One way to reduce confounding effects of compensatory brain processes is to investigate dyslexic readers during early reading acquisition, i.e. during the time window which is also critical for the definition of dyslexia.

Here, we characterize deviant tuning of visual brain processes in dyslexia during learning to read itself, and present data from a longitudinal electroencephalography (EEG) study comparing the same dyslexic children before and after the start of reading training at school.

Studies combining fMRI and EEG techniques with healthy adults suggest that word-specific activation in inferior occipito-temporal regions occur during the first 200 ms (Cohen *et al.*, 2000; Brem *et al.*, 2006). In the event-related potential (ERP) of the EEG, the earliest consistent word-specific processing corresponds to the N1 or N170 component. Words consistently elicited larger N1 amplitudes than low-level visual control stimuli like symbol strings, especially over the left hemisphere (Bentin *et al.*, 1999; Brem *et al.*, 2005; Maurer *et al.*, 2005, 2006).

Such fast specialization for print appears to be attenuated in adults with dyslexia. Whereas typical readers showed event-related MEG (magnetoencephalogram) sources in the left occipito-temporal cortex that were sensitive for differences in word and symbol processing and that were activated between 100 and 200 ms (Tarkiainen *et al.*, 1999), such sources were greatly reduced in adults with severe dyslexia (Helenius *et al.*, 1999). In children, on the other hand, the word N1 did not significantly differ between children with and without dyslexia at age 11 or 12 years (Brandeis *et al.*, 1994; Simos *et al.*, 2000). As no low-level visual control condition was used in the studies with dyslexic children, measuring the *coarse* N1 *tuning* (the word–symbol difference) may be more sensitive for deficits in dyslexia, as the N1 response presumably includes additional processing that is not specific for words. Thus it remains unclear, whether fast visual word processing is already impaired in children with dyslexia early during reading acquisition or whether a visual word processing deficit only develops after years of unsuccessful reading.

Recent studies investigated early reading acquisition in normal reading children by using a low-level visual control condition, and reported that visual processes get tuned for print rapidly after the start of reading training (Maurer *et al.*, 2006; Parviainen *et al.*, 2006). Whereas a reliable coarse N1 tuning for print was not present before the start of reading acquisition in non-reading kindergartners despite their considerable letter knowledge (Maurer *et al.*, 2005), a follow-up recording of the same children in the middle of 2nd grade showed that a reliable coarse N1 specialization had developed after the children
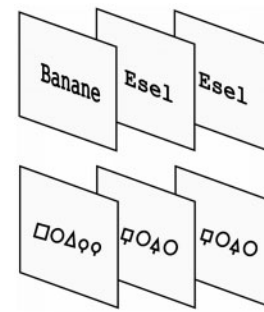

Fig. 1 Experimental design and stimuli. During EEG recording children were detecting immediate repetitions (17%) of blocked word, pseudoword, symbol-string (Brem *et al.*, 2005; Maurer *et al.*, 2005), similar to (Helenius *et al.*, 1999; Tarkiainen *et al.*, 1999) and picture presentations. Words, pseudowords, and symbol-strings were matched for character size (including ascenders and descenders), font size and string length, and ranged from 1.6 to 3.6° of visual angle. Stimuli were presented every 2050 ms for 700 ms in black on a white screen 120 cm away from the subject. We focussed on the word–symbol comparison which had revealed the largest effects due to learning to read (Maurer *et al.*, 2006).

had mastered initial reading skills (Maurer *et al.*, 2006). Presenting similar word and symbol string stimuli to first graders, another study found word-specific MEG sources in the inferior occipito-temporal cortex (Parviainen *et al.*, 2006). Whereas in the 2nd graders the word–symbol difference had increased in every single child (Maurer *et al.*, 2006), in the first graders word-specific sources were found in only slightly more than half of the children (Parviainen *et al.*, 2006). Comparing word activation to low-level visual activation seems to be critical in order to detect tuning for print with learning to read, as in another study the activation increase from kindergarten to 1st grade in occipito-temporal regions was only marginally significant, and the 1st grade children already showed reading-related activation typical for older children (Simos *et al.*, 2005). Taken together these studies suggest that coarse tuning for print develops within the first 2 years of reading training and that there is individual variability how fast this specialization develops.

In the present study, we report for the first time how tuning for print develops in dyslexic children, and compare this to our previous normative longitudinal findings for typical reading acquisition (Maurer *et al.*, 2006). Children from families with and without familial risk for dyslexia (Maurer *et al.*, 2003) performed a repetition detection task with words, symbol strings (Fig. 1), pseudowords and pictures in kindergarten and in 2nd grade, while their ERPs were recorded. This implicit reading task could also be solved by the children when they were still in kindergarten and not yet able to read (Maurer *et al.*, 2005, 2006). This design allowed us to compare how those children who develop a reading disability—according to a reading test in 2nd grade—differ from control children in the way their visual specialization for print emerges with initial reading training in school. We focussed on the word–symbol

Table I Group description of dyslexic children compared to children without dyslexia

		Control group *n* = 22	Dyslexic *n* = I5
	Sex (male : female)	II : II	6 : 9
	Handedness (right : left)	I9 : 3	I4 : I
	Familial risk for dyslexia (with : without)[***]	0 : 22	I3 : 2
Kindergarten	Age (years)	6.47 (±0.36)	6.53 (±0.3I)
	IQ[*]	I09.4 (±I3.7)	I02.I (±9.0)
	Phonological risk[*]	1.45 (±1.I0)	2.53 (±1.64)
	Letter knowledge[*]	I3.3 (±6.5)	7.7 (±8.4)
	Early readers (>I word)	3	3
Second grade	Age (years)	8.25 (±0.38)	8.29 (±0.29)
	Reading test (time, s) : frequent words[***]	29.4 (±I0.0)	68.2 (±I2.0)
	Reading test (time, s) : short text[***]	24.6 (±I0.4)	54.I (±9.2)
	Reading test (time, s) : pseudowords I[***]	59.9 (±2I.6)	84.5 (±I5.7)
	Reading test (time, s) : pseudowords II[***]	52.5 (±I9.6)	74.5 (±I5.4)
	Spelling test (errors)[**]	7.5 (±4.3)	I2.3 (±4.0)

Group difference (*t*-test or chi-square): [***]$P < 0.00I$, [**]$P < 0.0I$, [*]$P < 0.05$.

comparison, as in our earlier work this was the critical contrast to measure tuning for print during learning to read (Maurer *et al.*, 2005, 2006).

We expected that visual tuning for print would be delayed in children with dyslexia, leading to a smaller increase of the N1 tuning in dyslexic compared to control children.

Methods and materials
Participants
Twenty-eight children with a familial history of dyslexia and 29 children without such familial risk (Maurer *et al.*, 2003) were recorded at the end of kindergarten before they had received official reading training.

Children from families with a risk for dyslexia were included, because about 35–55% of children with a familial risk were expected to experience reading difficulties themselves (Gallagher *et al.*, 2000; Pennington and Lefly, 2001). About $1\frac{3}{4}$ years later in the middle of 2nd grade, 48 of them (at risk: *n* = 24, no risk: *n* = 24) participated again after they had received reading training in school. At both occasions visual and auditory acuity was assessed, and parents filled out questionnaires regarding deviant behaviour and neurological disorders. In kindergarten intelligence (Weiss and Osterland, 1997), phonological abilities (Jansen *et al.*, 1999) and word and letter knowledge were tested (for details see Maurer *et al.*, 2003, 2005). In 2nd grade the children were tested for reading and spelling (SLT, Landerl *et al.*, 1997), and their parents filled out questionnaires about the child's handedness (Oldfield, 1971).

Children were grouped based on their SLT correct word-per-minute reading score. They were defined as dyslexic if their score was below, or as non-dyslexic if their score fell above the 10th percentile of the population used for the SLT norms (Landerl, personal communication).

Dyslexic children were compared to non-dyslexic control children who did not have a familial history of dyslexia (Table 1). Early readers in kindergarten were not excluded, but matched between the two groups.

Procedure
Participants were seated in a video-controlled, electrically shielded, soundproof and air-conditioned recording room 1.2 m away from the computer screen. The visual word and form processing experiment was one of several short experiments, which were pseudo randomized in order of presentation. As compensation, each child received a present after the study. The entire session lasted about 3.5 h in kindergarten and about 3 h in 2nd grade.

The stimuli of the word, pseudoword, symbol and picture conditions were shown in black on a white background (Maurer *et al.*, 2005) in the centre of the screen. The 72 stimuli per condition were presented in two blocks of 36 stimuli and contained 17% immediate repetitions serving as targets. The block sequence was counterbalanced (2 × 4 blocks). The participants were asked to press a mouse button with their preferred hand after an immediate stimulus repetition. The stimulus duration was 700 ms followed by a 1350 ms interstimulus interval (ISI).

Words, pseudowords and symbol strings were matched for character size (including ascenders and descenders), font size and string length, and extended 3.3 to 7.5 cm (1.6–3.6°). Words and pseudowords were in lowercase letters starting with an uppercase. Pictures were drawn from the Snodgrass pictures (Snodgrass and Vanderwart, 1980). For the analysis we focussed on the word and symbol conditions, as they had shown the biggest effects due to learning to read (Maurer *et al.*, 2006).

ERP recording and analysis
The 43-channel ERPs were recorded at 500 Hz/channel with filter settings 0.1–70 Hz and with calibrated technical zero baselines. Caps (FMS, Munich) were used for the montage which included all 10–20 system electrodes plus additional electrodes: Fpz (recording reference), Oz, FT9/10, FC5/6, TP9/10, CP5/6, PO9/10, AF1/2, FC1/2, C1/2, CP1/2, PO1/2 and two EOG electrodes below the outer canthus of each eye. O1'/2' and Fp1'/2' were placed 2 cm laterally from the standard positions for more even coverage. In the 2nd grade four additional occipital channels (POz, Iz, Ol1/2) were used, but excluded from statistical analysis and source localization, and only used for map illustrations. Impedance was kept below 20 kΩ. The continuous

EEG was corrected for horizontal and vertical eye movements and in some cases for slow wave artefacts. An advanced method which minimizes topographic EEG distortions was used (multiple source eye correction method, Berg and Scherg, 1994). During this procedure the ERPs were transformed to average reference (Lehmann and Skrandies, 1980), which was also used for all subsequent analyses. Corrected files were digitally lowpass filtered (30 Hz, 48 dB/oct), downsampled to 256 Hz and segmented (from 125 ms prior to until 1125 ms following the stimulus). Trials with artefacts exceeding ±100 μV in any channel (threshold adjusted for children with higher-amplitude EEG) were automatically rejected before averaging. Individual ERPs were computed by averaging separately for each age and condition including only non-target stimuli. Individual ERP differences between conditions were computed for each age. Grand averages of the condition ERPs and of the between-condition ERP-differences were computed separately for each age and subject group.

Adaptive segmentation according to Global Field Power (GFP) minima (Brandeis *et al.*, 1994; Brandeis and Lehmann, 1998; Maurer *et al.*, 2005) was done for the averaged word and symbol grand means from kindergarten and 2nd grade (time range 0–850 ms). The resulting ERP segments are similar to the classical ERP components derived from single channels. For each segment mean, GFP, a measure for the electric field strength, was computed at the individual level for each age and condition separately (Lehmann and Skrandies, 1980).

Statistical analysis

To test for differences between dyslexic children and controls in fast print processing, we focussed on the crucial word–symbol difference (Maurer *et al.*, 2005) and analysed GFP for the P1 and the N1 segments in two Multivariate Analyses of Variance (MANOVA, procedure GLM) for repeated measures with within subject factors 'age' (kindergarten versus 2nd grade), and 'word-like' (words versus symbols) and the between-subject factor 'dyslexia' (dyslexic children versus control children).

To test for lateralization differences we computed similar MANOVAs at the left and right occipito-temporal channels (O1' and O2') using the same factors as in the GFP analysis with the additional within-subject factor 'hemisphere' (O1' versus O2'). Significance level in the MANOVA analyses was set to 0.05.

In addition, *t*-maps of word–symbol differences for dyslexic and control children were used for interpreting GFP differences and for better comparison with more conventional analysis methods.

In order to localize the sources of the visual specialization for print, we statistically compared distributed source solutions for words with those for symbols computed with LORETA [Low Resolution Electromagnetic Tomography, (Pascual-Marqui *et al.*, 1994, 1999)] for each individual in kindergarten and 2nd grade, separately for the two groups. In order to localize the increase of visual specialization for print due to learning to read, we compared in the same way the LORETA sources of the word–symbol difference in 2nd grade with those in kindergarten. LORETA computes the smoothest possible 3D distributed current source density solution constrained to grey matter. This approach does not need an *a priori* number of hypothesized generators, and produces a correct but blurred solution of focal sources due to the smoothness constraint. Results are illustrated in Talairach space. For statistical comparison between the individual source solutions a non-parametric randomization test was applied

(Holmes *et al.*, 1996), and the significance level ($P < 0.01$) of the resulting *t*-values was corrected for multiple comparisons.

Behavioural data (accuracy and reaction time) were analysed computing two MANOVAs for repeated measures with within-subject factors 'age' (kindergarten, 2nd grade) and 'wordlike' (words and symbols). Two children missed all targets in one condition at kindergarten, and were excluded from reaction time analyses including this condition.

For correlations with N1 tuning we used two reading measures from the reading test in 2nd grade (SLT, Landerl *et al.*, 1997): correct word-per-minute score (two subtests; also used for building the two groups) and correct pseudoword-per-minute score (two subtests). In addition we used IQ, letter knowledge and rhyming measures from kindergarten (Maurer *et al.*, 2003, 2005). Correlations were computed across the whole group of children, but also for the dyslexia and the control groups separately.

Results
Dyslexic and control children

The 15 children who were below the 10th percentile of the norms of the Salzburger reading test (Landerl *et al.*, 1997); correct word-per-minute norms: Karin Landerl, personal communication), were regarded as dyslexic and compared to 22 children who did not show reading problems and who also did not have a familial history of dyslexia. According to this criterion 54.2% of the children at risk were dyslexic versus only 8.3% of the children without familial risk. This was in the expected range for both groups considering the 10th percentile cut-off used (Shaywitz and Shaywitz, 2005), and confirms the importance of familial factors for dyslexia (Gallagher *et al.*, 2000; Pennington and Lefly, 2001).

As can be seen in Table 1 the dyslexic children did not differ from the control children regarding age, sex, handedness and inclusion of early readers, but they differed strongly in reading and spelling scores in 2nd grade, and also differed in their phonological abilities (phonological risk for dyslexia) and intelligence (IQ) in kindergarten. To account for possible confounding effects of IQ, we additionally tested dyslexia effects with IQ as covariate and report cases in which a dyslexia effect changed the significance level.

Visual specialization for print (word–symbol contrast)

Behavioural data

After the initial reading training the children were more accurate at detecting targets than they had been 1.75 years earlier in kindergarten [age, $F(1,35) = 46.6$, $P < 0.001$, compare Table 2]. This improvement was more pronounced for words than for symbols [age × wordlike, $F(1,35) = 12.6$, $P < 0.01$], especially in control children, but less so in dyslexic children [age × wordlike × dyslexia, $F(1,35) = 8.2$, $P < 0.01$] reflecting the reading impairment of the latter. Planned comparisons separately for age
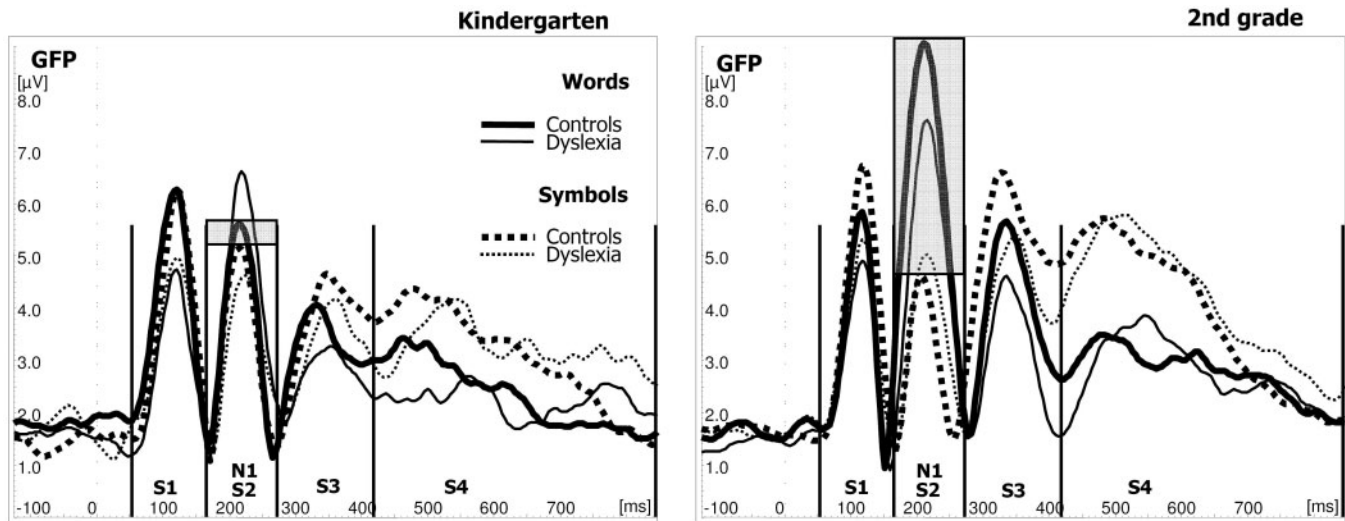
Fig. 2 Segmentation and GFP effects due to learning to read. ERP segmentation according to Global Field Power (GFP) minima resulted in four segments. Grey boxes mark the control children's large increase in GFP difference between words and symbols during the N1 segment from kindergarten (left) to 2nd grade (right). The corresponding increase with learning to read was much smaller for children with dyslexia, both due to a smaller difference in 2nd grade and a larger difference in kindergarten.

Table 2 Behavioural results

	Kindergarten		Second grade	
	Controls	Dyslexia	Controls	Dyslexia
Accuracy (% ±SD)				
Words	47.7 (±23.5)	52.7 (±21.3)	93.2 (±8.1)	72.7 (±17.7)
Symbols	54.3 (±23.1)	52.7 (±28.1)	70.5 (±16.2)	69.4 (±19.3)
Reaction time (ms ±SD)				
Words	1055 (±238)	1033 (±124)	879 (±165)	1060 (±168)
Symbols	917 (±191)	994 (±162)	826 (±182)	829 (±102)

revealed no dyslexia effects in kindergarten (*dyslexia* and *dyslexia × wordlike*: both $F < 1$), but in 2nd grade: Children with dyslexia were less accurate [*dyslexia*, $F(1,35) = 7.6$, $P < 0.01$, $P < 0.05$ with IQ-covariate], especially after word stimuli [*dyslexia × wordlike*, $F(1,35) = 8.5$, $P < 0.01$].

In general, children responded faster in 2nd grade than in kindergarten [*age*, $F(1,32) = 11.7$, $P < 0.01$]. In addition, reaction time was faster for symbols than for words [*wordlike*, $F(1,32) = 22.2$, $P < 0.001$]. Both these main effects were modulated in a three-way interaction by the 'dyslexia group' factor [*age × wordlike × dyslexia*, $F(1,32) = 12.0$, $P < 0.01$]. Planned comparisons for each age separately revealed no significant dyslexia effect in kindergarten (*dyslexia* and *dyslexia × wordlike*: both $F < 2$), but in 2nd grade, when the longer RT for words compared to symbols was more pronounced in dyslexic children than in controls (*wordlike × dyslexia*, $F(1,35) = 10.9$, $P < 0.01$).

ERP data

Segmentation. Segmentation of the ERPs according to GFP minima of the grand average means (Maurer *et al.*, 2005,

2006) across both ages and word and symbol conditions resulted in four segments (Fig. 2: segment 1: 55–163 ms, 'P1'; segment 2: 164–272 ms, 'N1'; segment 3: 273–417 ms; segment 4: 418–843 ms). As we were mainly interested in visual specialization effects that occur early during processing, we focussed the analysis on the first two segments, the P1 and the N1. Mean values of the two segments were analysed in two analyses regarding global map strength (GFP) and lateralization at occipito-temporal electrodes (O1' versus O2') focussing on word–symbol differences between children with dyslexia and control children (without familial risk and without dyslexia). Responses to words and symbols in all segments and *t*-maps of the within and between-subject contrasts are illustrated in the Supplementary Material (Supplementary Material Fig. 1).

P1 segment. The early P1 response in the ERPs was smaller for words than for symbols according to both ERP measures (*wordlike*; GFP: $P < 0.05$; occipito-temporal channels: $P < 0.05$; Table 3). This word–symbol difference, however, occurred mainly after learning to read (*age × wordlike*: GFP: $P < 0.05$; occipito-temporal channels: $P < 0.05$). This interaction also modulated the main effect of age in the GFP analysis ($P < 0.01$). In addition, children with dyslexia showed smaller P1 amplitudes than controls across both stimulus conditions and age levels, but this effect was focussed on the occipito-temporal electrodes ($P < 0.05$, Fig. 3) and did not quite reach significance over the whole map (GFP: $P < 0.13$).

N1 segment. The subsequent N1 response was stronger for words than symbols (*wordlike*, GFP and occipito-temporal: $P < 0.001$), but mainly in 2nd grade after the children had learned to read (*age × wordlike*, GFP and occipito-temporal channels: $P < 0.001$). Critically, this

increase was reduced in children with dyslexia (*dyslexia* × *age* × *wordlike*, GFP: $P < 0.01$, occipito-temporal channels: $P < 0.001$, Fig. 4). This three-way interaction also modulated the additional main effect of age (only GFP: $P < 0.01$) and the 'wordlike' by 'dyslexia' interaction (GFP and occipito-temporal channels: $P < 0.05$). In addition, whereas the word–symbol difference was slightly right-lateralized in kindergarten, it became more left-lateralized in 2nd grade (*hemisphere* × *age* × *wordlike*: occipito-temporal: $P < 0.001$).

Planned comparisons on the GFP measure for the groups separately, revealed that, while in both groups there was a difference between words and symbols (*wordlike*, controls: $P < 0.001$; dyslexics: $P < 0.01$), this main effect was significantly modulated by learning to read in the control children only (*wordlike* × *age*, controls: $P < 0.001$, dyslexics: $P > 0.11$).

Table 3 N1 effects in map strength and lateralization

	Map strength (GFP)	Lateralization (O1' *vs.* O2')
S1 (P1)	W, $F_{1,35} = 5.9^*$	W, $F_{1,35} = 7.5^*$
	A, $F_{1,35} = 10.7^{**}$	A × W, $F_{1,35} = 5.3^*$
	A × W, $F_{1,35} = 7.4^*$	D, $F_{1,35} = 6.5^*$
S2 (N1)	A, $F_{1,35} = 12.5^{**}$	W, $F_{1,35} = 65.6^{***}$
	W, $F_{1,35} = 48.3^{***}$	A × W, $F_{1,35} = 45.1^{***}$
	A × W, $F_{1,35} = 26.2^{***}$	W × D, $F_{1,35} = 4.1^*$
	W × D, $F_{1,35} = 4.7^*$	A × W × D, $F_{1,35} = 25.0^{***}$
	A × W × D, $F_{1,35} = 10.3^{**}$	H × A × W, $F_{1,35} = 11.7^{***}$

W = *wordlike*; A = *age*; D = dyslexia, H = hemisphere.
$^{***}P < 0.001$, $^{**}P < 0.01$, $^*P < 0.05$.

Separate group comparisons at each age level revealed that in 2nd grade the N1 GFP was stronger for words than for symbols (*wordlike*, $P < 0.001$), but that this difference was reduced in the dyslexic children (dyslexia × wordlike, $P < 0.001$). In kindergarten, despite a considerable word–symbol difference in the dyslexic children's grandmeans (Fig. 2) and significant *t*-map differences at several right posterior sites (Fig. 4) no N1 GFP effects reached significance.

In additional *t*-tests, in both groups the word–symbol difference was significant in 2nd grade, although at a lower significance threshold in dyslexia (controls: $P < 0.001$, children with dyslexia: $P < 0.01$; compare Fig. 4), but not significant in kindergarten (control: $t < 1$; children with dyslexia: $t < 1.6$). Moreover, the increase of the word N1 from kindergarten to 2nd grade was only significant in the control children ($P < 0.001$), but not in the children with dyslexia ($t < -1.7$).

In 2nd grade the groups thus differed with regard to their N1 marker of print-specific processing ('tuning'). However, they did not significantly differ with regard to N1 measures of word processing or symbol processing alone (see *t*-maps in Supplementary Material, Supplementary Material Fig. 1).

N1 correlations with reading ability. The group difference between dyslexic and control children resulted in a significant correlation between reading speed (correct word-per-minute) and the negative word–symbol N1 effects at occipito-temporal electrodes in 2nd grade (left: $r = -0.59$, right: $r = -0.58$) for the full group (Fig. 5). Similar full
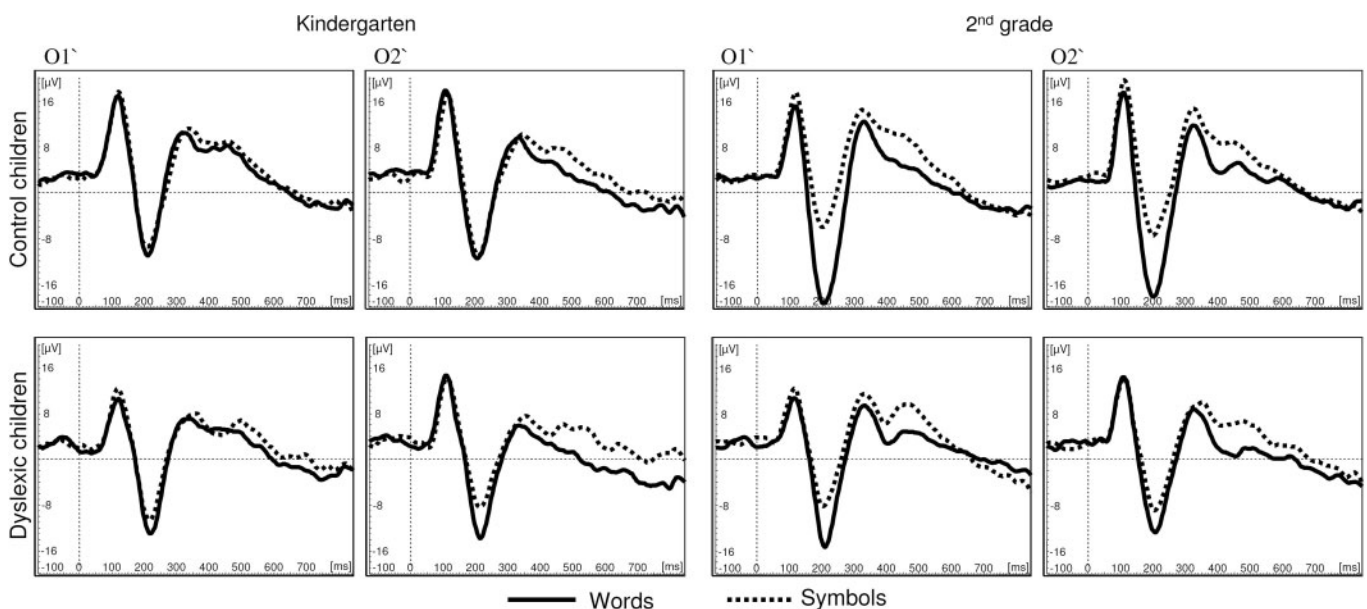

Fig. 3 Occipito-temporal waveforms. Waveforms at the left (O1') and right (O2') occipito-temporal channels for words (solid line) and symbols (broken line) illustrate the time course of the strongest N1 effects. The control children (1st row) showed no difference between words and symbols in the N1 (at about 200 ms) in kindergarten, but a large difference in 2nd grade after they had learned to read.
In contrast, the N1 of the dyslexic children (2nd row) showed a reduced word–symbol difference in 2nd grade, and a precursor difference in kindergarten at the right occpito-temporal channel.

group correlations were obtained between this N1 tuning in 2nd grade and pseudoword reading speed, i.e. for a measure which had not been used for grouping (left: $r = -0.60$, right: $r = -0.52$). The same correlations did not reach significance tested for each subgroup separately, although they suggested a similar relation as across the whole group (Table 4).

The correlations between reading speed in 2nd grade and N1 tuning in kindergarten were low and had even the opposite direction ($r = 0.02$ for word and $r = 0.08$ for pseudoword reading at O1'; $r = 0.18$ for word and $r = 0.24$ for pseudoword reading at O2', all $p = $ns). In addition, higher IQ correlated with faster word reading ($r = -0.37$), but not with the word–symbol difference in 2nd grade (at O1': $r = -0.02$). Letter knowledge in kindergarten was not associated with the N1 tuning in 2nd grade, but children with better rhyming abilities in Kindergarten showed a larger N1 tuning in 2nd grade (at O1': $r = -0.41$) for the full group. This correlation was reduced in the control group ($r = -0.15$) but similar in the dyslexic group ($r = -0.42$), although it did not reach significance ($p = 0.12$) because of the smaller group size. Finally, the increase of the N1 tuning over the left hemisphere from kindergarten to 2nd grade correlated significantly with reading speed (word reading: $r = -0.47$; pseudoword reading: $r = -0.51$), but not with rhyming ability in kindergarten ($r = -0.32$) across the whole group, but in none of the subgroups.

Source localization of specialization for print. As illustrated in Fig. 6, the control children's specialization for print in 2nd grade was localized to the inferior and lateral occipito-temporal cortex for the N1 segment using the LORETA algorithm (Pascual-Marqui *et al.*, 1994, 1999). While more significant voxels were found in the right hemisphere, the voxel with the maximal significance was located in the left hemisphere within the region of the putative Visual Word Form Area (Cohen *et al.*, 2000). Moreover, the increase of the specialization for print with learning to read was more dominant in the left hemisphere. No significant voxels for the word–symbol contrast in 2nd grade, nor for the increase from kindergarten to 2nd grade were found for the dyslexic children.

Discussion

The present study investigates for the first time the neurophysiology of impaired learning to read, which is the hallmark of developmental dyslexia. Previous research has demonstrated that children who learn to read normally develop a coarse form of visual tuning for print within the first 2 years of reading training, which is reflected by an increase in their fast occipito-temporal brain activity for words compared to symbol strings (mainly during the

Table 4 Correlations between N1 tuning in second grade (at O1') and behavioral measures

	All	Controls	Dyslexia
Word reading	−0.59***	−0.26	−0.07
Pseudoword reading	−0.60***	−0.35	−0.32
IQ in KG	−0.02	0.24	0.11
Letter knowledge in KG	−0.04	0.31	0.25
Rhyming in KG	−0.41*	−0.15	−0.42

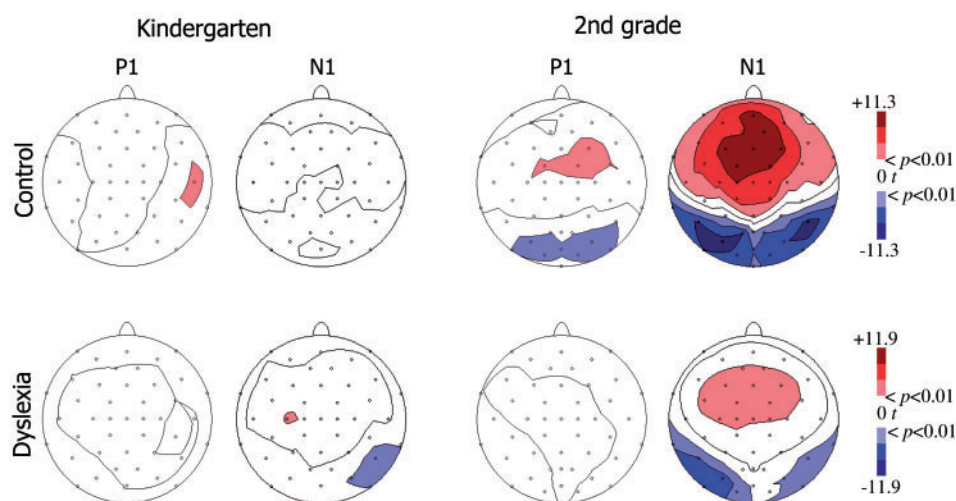KG = Kindergarten. ***$P < 0.001$, *$P < 0.05$.

Fig. 4 Specialization for print in P1 and N1 segments (*t*-maps). The *t*-maps for the N1 segment in control children (dF = 21) showed no significant word–symbol differences in kindergarten, but highly significant differences in 2nd grade ($P < 0.01$ to correct for multiple comparisons). The dyslexic children (dF = 14) in contrast showed weaker effects of learning to read in the N1 segment with a reduced word–symbol difference in 2nd grade and an increased precursor difference in kindergarten at a few occipito-temporal channels over the right hemisphere. Word–symbol differences also occurred during the P1 segment, but mainly in control children after learning to read with a similar topography as in the subsequent N1 segment.
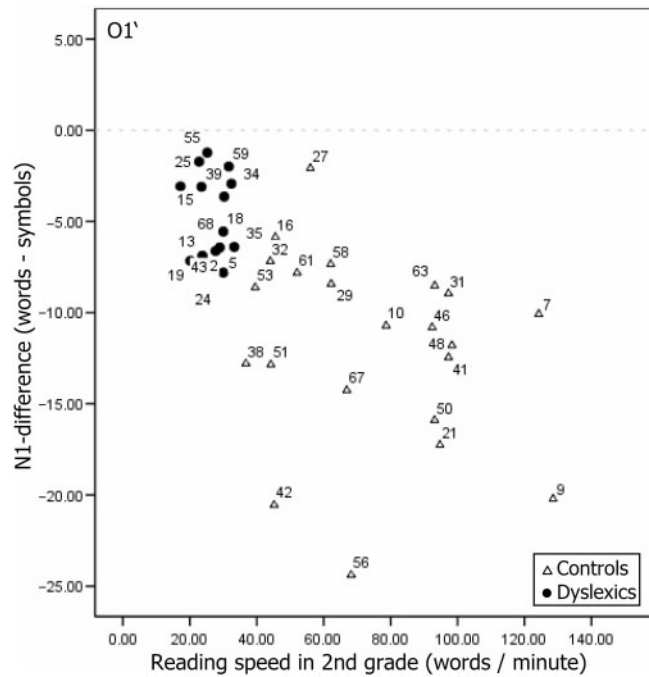
Fig. 5 Individual data of reading speed and N1 tuning in 2nd grade. While in 2nd grade all children showed a larger N1 in response to words than to symbol strings, this N1 tuning was smaller in dyslexic children than in controls. Note that each child with dyslexia (<10th percentile: less than 35.2 words/min) had a smaller N1 tuning than each of the control children above the 40th percentile (more than 65.5 words/min).

N1 at 164–272 ms, but starting already during the P1 at 55–163 ms; Maurer *et al.*, 2006; Parviainen *et al.*, 2006). Here, we examined whether deviant development of this fast print-specific tuning during initial reading acquisition characterizes dyslexia.

One main result confirms that children who developed dyslexia showed an atypical development of how their fast visual brain processes became specialized for print. Over the course from kindergarten to 2nd grade the increase in N1 specialization with reading training was not significant for the dyslexic children. This strongly contrasted with the highly significant increase in those children who learned to read normally. The initial N1 tuning in the control children is even more prominent than in adults (Maurer *et al.*, 2006), since tuning for print apparently plays a particularly important role in the early phase of reading acquisition.

The dyslexic children's striking absence of additional tuning for print with the beginning of reading training implies that deviant print-specific plasticity in the visual brain plays an important role for the initial *development* of dyslexia. As we will discuss later, this tuning failure was mainly due to a reduced specialization in 2nd grade, but to some degree also due to a larger precursor specialization in kindergarten.

The outcome in 2nd grade was a smaller N1 specialization in dyslexic children compared to normally reading control children. This result clarifies that in dyslexia,
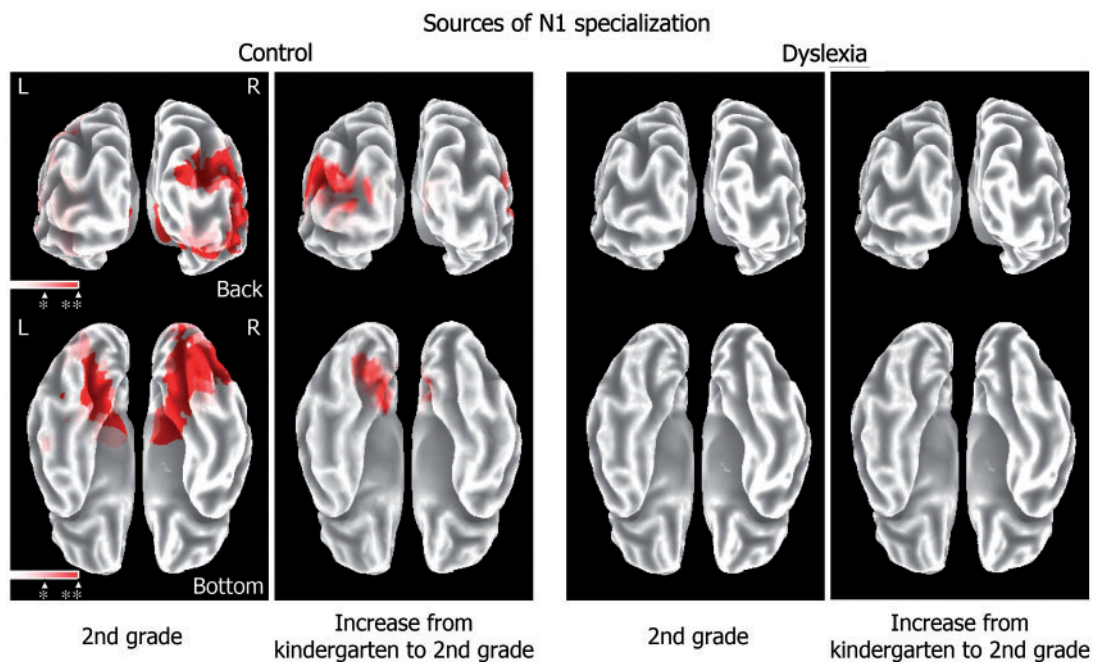

Fig. 6 Source localization. LORETA localized specialized print processing during the N1 segment in 2nd grade (1st panel) and its increase with learning to read from kindergarten to 2nd grade (2nd panel) to inferior and lateral occipito-temporal regions in control children. The most significant activation difference between words and symbols in 2nd grade was found within the region of the Visual Word Form Area in the left hemisphere (Tal: −31, −53, −6), close to the increases with learning to read in the left hemisphere (Tal: −45, −60, 22; Tal: −17, −59, −6). No voxels were found for the dyslexic children (3rd and 4th panels) that showed any significant activation differences between word and symbol processing below the corrected $P < 0.05$ threshold (red).

coarse visual tuning for print is reduced during the initial phase of learning to read. This suggests that the coarse visual tuning plays an important functional role for early reading, and that the N1 specialization represents a neural marker of emerging dyslexia. Success or failure of learning to read may be related to the degree of plasticity underlying coarse visual tuning for print during the early phase of reading acquisition.

Although reading speed was correlated with N1 tuning in 2nd grade across the whole group, the separate correlations within each group did not reach significance. This indicates that N1 tuning best differentiates between children with and without reading problems, thus supporting the results of the group analysis.

Although the coarse tuning deficit clearly occurred in the visual processing stream, it may directly relate to the phonological core deficit of dyslexia, as grapheme–phoneme mapping during reading acquisition could map phonological processing difficulties to reading-related visual processing (McCandliss and Noble, 2003). This interpretation is consistent with the significant correlation between rhyming ability in kindergarten and the N1 tuning in 2nd grade. Alternatively, the visual tuning deficit may constitute an independent visual processing deficit adding up to the phonological deficit, or a more basic neural anomaly affecting regions for both phonological processing and visual tuning (Ramus, 2004).

In contrast to the previous results from adults and older children with dyslexia, the present findings are less likely to be confounded with compensatory brain activation which dyslexic readers develop over time (Shaywitz *et al.*, 1998; Georgiewa *et al.*, 2002), and represent a more authentic neural correlate of an initial visual word processing deficit in dyslexia.

A similar reduction of word-specific MEG activity was reported in an earlier MEG study for adults with particularly severe dyslexia (Helenius *et al.*, 1999). Although the technique and the analysis method differed from the present study, that result may suggest that the reduced specialization for print continues until adulthood, at least in the case of severe dyslexia. While studies without a visual control condition did not find any reduction in the word N1 in older children with dyslexia (Brandeis *et al.*, 1994; Simos *et al.*, 2000), such control strings may be critical to detect deviant print specialization, as the N1 presumably also reflects other aspects of visual processing that are not related to reading.

Alternatively, the size of the coarse N1 specialization for print may only reflect the initial reading skills while learning to read, as further reading practice seems to increase automatization reflected by smaller amplitudes and shorter latencies (Maurer *et al.*, 2006). Accordingly, the size of the N1 specialization may best discriminate dyslexic children from controls at the beginning of learning to read, while differences later on are restricted to cases with particularly severe dyslexia (Helenius *et al.*, 1999).

Studies on N1 specialization with older dyslexic children may help to clarify the developmental time course of this deficit.

The control children's specialization for print in 2nd grade was localized maximally in the left inferior occipito-temporal region, overlapping with the proposed VWFA area in the left mid-fusiform gyrus (Cohen *et al.*, 2000). While some sources were also localized to regions of the right hemisphere in 2nd grade, the increase with learning to read from kindergarten to 2nd grade was limited to the left hemisphere reflecting the increase in left-lateralization on the scalp surface. This increase in left-lateralization may be induced by the influence of left-lateralized language processes (such as phonological processing) during reading acquisition, as hypothesized previously (Maurer and McCandliss, 2007). At the same statistical threshold, no source activation was found for the dyslexic children's specialization in 2nd grade, nor for the increase of their specialization with learning to read. This is in agreement with reduced activation in dyslexics compared to controls in response to visual words that has been reported in inferior occipito-temporal regions in fMRI studies (Paulesu *et al.*, 2001; Shaywitz *et al.*, 2002; Brambati *et al.*, 2006). Although fMRI activation in these regions may also reflect re-entrant later activation (Dale *et al.*, 2000), correlations between activation in these regions with N1 activation suggests that at least part of this activation occurs already within the first 200 ms (Brem *et al.*, 2006).

The slower development of N1 tuning in the dyslexic children was accentuated by their slightly larger specialization in kindergarten, although their precursor difference only reached significance ($P < 0.01$) in *t*-maps for a few right-hemisphere electrodes. This right-lateralized precursor specialization may be due to visual familiarity with print as reported in our earlier work (Maurer *et al.*, 2005).

In addition to their reduced specialization for print in the N1 segment, dyslexic children also differed from control children during the preceding segment where their P1 response was reduced. This reduction was already found in kindergarten, and was not specific for word stimuli, but also present for the non-orthographic symbol strings. A similar reduction in the P1 was reported in older children with dyslexia in a sentence reading paradigm (Brandeis *et al.*, 1994). This suggests the presence of a more basic, non-specific visual deficit, which precedes reading acquisition and also occurs during processing of non-language control stimuli. Visual deficits and reduced neural activation have also been reported with other paradigms for dyslexic subjects, e.g. during visual motion detection (e.g. Solan *et al.*, 1990; Slaghuis *et al.*, 1996; Eden *et al.*, 2000). In the present study, however, the more basic visual deficit played a less important role for the development of dyslexia than the print-specific tuning deficit, as it showed smaller group effects and weaker correlations with reading speed.

In conclusion, the absence of a neural tuning gain for print despite intense reading training in dyslexic children indicates a print-specific impairment of visual plasticity in dyslexia at the beginning of reading acquisition, consistent with the behavioural definition of *developmental* dyslexia.

Supplementary material
Supplementary material is available at *Brain* online.

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References
Bentin S, Mouchetant-Rostaing Y, Giard MH, Echallier JF, Pernier J. ERP manifestations of processing printed words at different psycholinguistic levels: time course and scalp distribution. J Cogn Neurosci 1999; 11: 235–60.

Berg P, Scherg M. A multiple source approach to the correction of eye artifacts. Electroencephalogr Clin Neurophysiol 1994; 90: 229–41.

Bradley L, Bryant PE. Categorizing sounds and learning to read - a causal connection. Nature 1983; 301: 419–21.

Brambati SM, Termine C, Ruffino M, Danna M, Lanzi G, Stella G, et al. Neuropsychological deficits and neural dysfunction in familial dyslexia. Brain Res 2006; 1113: 174–85.

Brandeis D, Lehmann D. Functional brain mapping with cognitive evoked potentials. Schweizer Archiv für Neurologie und Psychiatrie 1998; 149: 273–9.

Brandeis D, Vitacco D, Steinhausen HC. Mapping brain electric micro-states in dyslexic children during reading. Acta Paedopsychiatr 1994; 56: 239–47.

Brem S, Bucher K, Halder P, Summers P, Dietrich T, Martin E, et al. Evidence for developmental changes in the visual word processing network beyond adolescence. Neuroimage 2006; 29: 822–37.

Brem S, Lang-Dullenkopf A, Maurer U, Halder P, Bucher K, Brandeis D. Neurophysiological signs of rapidly emerging visual expertise for symbol strings. Neuroreport 2005; 16: 45–8.

Brunswick N, McCrory E, Price CJ, Frith CD, Frith U. Explicit and implicit processing of words and pseudowords by adult developmental dyslexics: a search for Wernicke's Wortschatz? Brain 1999; 122 (Pt 10): 1901–17.

Cohen L, Dehaene S, Naccache L, Lehericy S, Dehaene-Lambertz G, Henaff MA, et al. The visual word form area: spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. Brain 2000; 123: 291–307.

Dale AM, Liu AK, Fischl BR, Buckner RL, Belliveau JW, Lewine JD, et al. Dynamic statistical parametric mapping: combining fMRI and MEG for high-resolution imaging of cortical activity. Neuron 2000; 26: 55–67.

Dilling H, Mombour W, Schmidt MH. International classification of mental diseases, ICD-10 (German edition). Bern: Huber.

Eden G, VanMeter JW, Rumsey JM, Maisog JM, Woods RP, Zeffiro TA. Phonological and visual motion processing in reading impaired children. Neuroimage 2000; 11: 183.

Gallagher A, Frith U, Snowling MJ. Precursors of literacy delay among children at genetic risk of dyslexia. J Child Psychol Psychiatry 2000; 41: 203–13.

Georgiewa P, Rzanny R, Gaser C, Gerhard UJ, Vieweg U, Freesmeyer D, et al. Phonological processing in dyslexic children: a study combining functional imaging and event related potentials. Neurosci Lett 2002; 318: 5–8.

Guttorm TK, Leppanen PH, Poikkeus AM, Eklund KM, Lyytinen P, Lyytinen H. Brain event-related potentials (ERPs) measured at birth predict later language development in children with and without familial risk for dyslexia. Cortex 2005; 41: 291–303.

Helenius P, Tarkiainen A, Cornelissen P, Hansen PC, Salmelin R. Dissociation of normal feature analysis and deficient processing of letter-strings in dyslexic adults. Cereb Cortex 1999; 9: 476–83.

Holmes AP, Blair RC, Watson JD, Ford I. Nonparametric analysis of statistic images from functional mapping experiments. J Cereb Blood Flow Metab 1996; 16: 7–22.

Jansen H, Mannhaupt G, Marx H, Skowronek H. BISC Bielefelder Screening zur Frueherkennung von Lese-Rechtschreibschwierigkeiten (Bielefeld Screening Battery for Early Diagnosis of Problems in Reading and Writing). Göttingen: Hogrefe; 1999.

Kronbichler M, Hutzler F, Staffen W, Mair A, Ladurner G, Wimmer H. Evidence for a dysfunction of left posterior reading areas in German dyslexic readers. Neuropsychologia 2006; 44: 1822–32.

Landerl K, Wimmer H, Moser E. SLRT Salzburger Lese- und Rechtschreibtest (Salzburg Reading and Orthography Test). Bern: Huber; 1997.

Lehmann D, Skrandies W. Reference-free identification of components of checkerboard-evoked multichannel potential fields. Electroencephalogr Clin Neurophysiol 1980; 48: 609–21.

Maurer U, Brem S, Bucher K, Brandeis D. Emerging neurophysiological specialization for letter strings. J Cogn Neurosci 2005; 17: 1532–52.

Maurer U, Brem S, Kranz F, Bucher K, Benz R, Halder P, et al. Coarse neural tuning for print peaks when children learn to read. Neuroimage 2006; 33: 749–58.

Maurer U, Bucher K, Brem S, Brandeis D. Altered responses to tone and phoneme mismatch in kindergartners at familial dyslexia risk. Neuroreport 2003; 14: 2245–50.

Maurer U, McCandliss BD. The development of visual expertise for words: the contribution of electrophysiology. In: Grigorenko EL & Naples AJ, editor. Single-word reading: biological and behavioral perspectives, Mahwah, NJ: Lawrence Erlbaum Associates, 2007.

McCandliss BD, Noble KG. The development of reading impairment: a cognitive neuroscience model. Ment Retard Dev Disabil Res Rev 2003; 9: 196–204.

Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 1971; 9: 97–113.

Parviainen T, Helenius P, Poskiparta E, Niemi P, Salmelin R. Cortical sequence of word perception in beginning readers. J Neurosci 2006; 26: 6052–61.

Pascual-Marqui RD, Lehmann D, Koenig T, Kochi K, Merlo MC, Hell D, et al. Low resolution brain electromagnetic tomography (LORETA) functional imaging in acute, neuroleptic-naive, first-episode, productive schizophrenia. Psychiatry Res 1999; 90: 169–79.

Pascual-Marqui RD, Michel CM, Lehmann D. Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. Int J Psychophysiol 1994; 18: 49–65.

Paulesu E, Demonet JF, Fazio F, McCrory E, Chanoine V, Brunswick N, et al. Dyslexia: cultural diversity and biological unity. Science 2001; 291: 2165–7.

Pennington BF, Lefly DL. Early reading development in children at family risk for dyslexia. Child Dev 2001; 72: 816–33.

Posner MI, Rothbart MK. Influencing brain networks: implications for education. Trends Cogn Sci 2005; 9: 99–103.

Ramus F. Neurobiology of dyslexia: a reinterpretation of the data. Trends Neurosci 2004; 27: 720–6.

Ramus F, Rosen S, Dakin SC, Day BL, Castellote JM, White S, et al. Theories of developmental dyslexia: insights from a multiple case study of dyslexic adults. Brain 2003; 126: 841–65.

Rumsey JM, Nace K, Donohue B, Wise D, Maisog JM, Andreason P. A positron emission tomographic study of impaired word recognition

and phonological processing in dyslexic men. Arch Neurol 1997; 54: 562–73.

Shaywitz BA, Shaywitz SE, Pugh KR, Mencl WE, Fulbright RK, Skudlarski P, et al. Disruption of posterior brain systems for reading in children with developmental dyslexia. Biol Psychiatry 2002; 52: 101–10.

Shaywitz SE, Shaywitz BA. Dyslexia (specific reading disability). Biol Psychiatry 2005; 57: 1301–9.

Shaywitz SE, Shaywitz BA, Pugh KR, Fulbright RK, Constable RT, Mencl WE, et al. Functional disruption in the organization of the brain for reading in dyslexia. Proc Natl Acad Sci USA 1998; 95: 2636–41.

Simos PG, Breier JI, Fletcher JM, Bergman E, Papanicolaou AC. Cerebral mechanisms involved in word reading in dyslexic children: a magnetic source imaging approach. Cereb Cortex 2000; 10: 809–16.

Simos PG, Fletcher JM, Sarkari S, Billingsley RL, Francis DJ, Castillo EM, et al. Early development of neurophysiological processes involved in normal reading and reading disability: a magnetic source imaging study. Neuropsychology 2005; 19: 787–98.

Slaghuis WL, Twell AJ, Kingston KR. Visual and language processing disorders are concurrent in dyslexia and continue into adulthood. Cortex 1996; 32: 413–38.

Snodgrass JG, Vanderwart M. A standardized set of 260 pictures: norms for name agreement, image agreement, familiarity, and visual complexity. J Exp Psychol [Hum Learn] 1980; 6: 174–215.

Solan HA, Sutija VG, Ficarra AP, Wurst SA. Binocular advantage and visual processing in dyslexic and control children as measured by visual evoked potentials. Optom Vis Sci 1990; 67: 105–10.

Tarkiainen A, Helenius P, Hansen PC, Cornelissen PL, Salmelin R. Dynamics of letter string perception in the human occipitotemporal cortex. Brain 1999; 122: 2119–32.

Temple E, Poldrack RA, Salidis J, Deutsch GK, Tallal P, Merzenich MM, et al. Disrupted neural responses to phonological and orthographic processing in dyslexic children: an fMRI study. Neuroreport 2001; 12: 299–307.

Weiss R, Osterland J. German version. CFT 1, Grundintelligenztest Skala 1 - Culture Fair Intelligence Test, Scale 1. (Cattell, R.B., 1996), German version. Göttingen: Hogrefe; 1997.