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## Accepted Manuscript

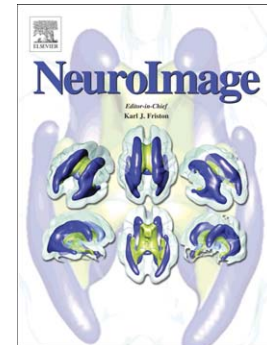
The left occipitotemporal system in reading: Disruption of focal fMRI connectivity to left inferior frontal and inferior parietal language areas in children with dyslexia

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**Title:**

**The left occipitotemporal system in reading: disruption of focal fMRI connectivity to left inferior frontal and inferior parietal language areas in children with dyslexia**

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**Abstract**

Developmental dyslexia is a severe reading disorder, which is characterized by dysfluent reading and impaired automaticity of visual word processing. Adults with dyslexia show functional deficits in several brain regions including the so-called “Visual Word Form Area” (VWFA), which is implicated in visual word processing and located within the larger left occipitotemporal VWF-System. The present study examines functional connections of the left occipitotemporal VWF-System with other major language areas in children with dyslexia. Functional connectivity MRI was used to assess connectivity of the VWF-System in 18 children with dyslexia and 24 age-matched controls (age 9.7-12.5 years) using five neighbouring left occipitotemporal regions of interest (ROIs) during a continuous reading task requiring phonological and orthographic processing. First, the results revealed a focal origin of connectivity from the VWF-System, in that mainly the VWFA was functionally connected with typical left frontal and parietal language areas in control children. Adjacent posterior and anterior VWF-System ROIs did not show such connectivity, confirming the special role that the VWFA plays in word processing. Second, we detected a significant disruption of functional connectivity between the VWFA and left inferior frontal and left inferior parietal language areas in the children with dyslexia. The current findings add to our understanding of dyslexia by showing that functional disconnection of the left occipitotemporal system is limited to the small VWFA region crucial for automatic visual word processing, and emerges early during reading acquisition in children with dyslexia, along with deficits in orthographic and phonological processing of visual word forms.

Developmental dyslexia is a severe, specific disorder of reading acquisition with a high prevalence and a familial and genetic risk (Roeske et al., 2009; Schulte-Körne, 2001). The International Dyslexia Association (IDA) defines dyslexia as “an impairment in the accuracy and / or rate of oral reading of pseudowords (...) real word reading, and passages and of spelling” (Lyon et al., 2003). By contrast, in shallow orthographies like German, the core criterion for diagnosing dyslexia as a reading disorder is often reading speed or fluency since accuracy can frequently be compensated (Richlan et al.; Wimmer et al., 2000). Converging evidence from neuroimaging studies investigating dyslexia suggests both structural and functional deficits in brain regions involved in reading, including the left inferior frontal gyrus, the left parietotemporal cortex and the left occipitotemporal gyrus (for reviews see (Eckert, 2004; Shaywitz and Shaywitz, 2005)).

Next to the well-documented phonological core deficit in dyslexia, a large and growing body of behavioural and brain research has provided evidence that an orthographic coding deficit may also be involved. This deficit has been associated with a dysfunction of the left ventral occipitotemporal cortex in adolescents and adults (e.g., (Brunswick et al., 1999; Helenius et al., 1999; Horwitz et al., 1998; Kronbichler et al., 2006; McCrory et al., 2005; Paulesu et al., 2001; Richlan et al.; Rumsey et al., 1997a; Rumsey et al., 1997b; Salmelin et al., 1996; Shaywitz et al., 2003; Wimmer et al., 2009) as well as in children with dyslexia (e.g. (Cao et al., 2006; Hoefft et al., 2007; Maurer et al., 2007; Shaywitz et al., 2002; Shaywitz et al., 2007; van der Mark et al., 2009) for a large number of languages using a wide range of functional imaging methods. A meta-analysis also identified a robust deficit in this region particularly in adolescents and adults, while evidence for a corresponding deficit in children is more limited (Richlan et al., 2009). The left ventral occipitotemporal cortex includes the so called Visual Word Form Area (VWFA; (Cohen et al., 2000)). This

brain region responds automatically and rapidly to visually presented words (Price et al., 1996) and is crucially involved in visual word recognition (Cohen et al., 2004; Dehaene et al., 2004). Recently, the VWFA was shown to be part of a larger Visual Word Form (VWF) system that plays a vital role in processing orthographic representations of visual letter-strings (Brem et al., 2006; Mechelli et al., 2005; Van der Mark et al., 2009; Vinckier et al., 2007).

Previous studies investigating the left occipitotemporal cortex have indicated the existence of a hierarchy for visual word processing, progressing from simple letter percept in the occipital cortex to more complex features in the anterior inferior temporal regions (e.g., (Fernandez et al., 2001; Hagoort et al., 1999; Vandenberghe et al., 1996). More recently, a posterior to anterior VWF-System gradient of increasing print specificity was found in adults and adolescents (Brem et al., 2006; Vinckier et al., 2007) as well as in children (Brem et al., 2009; Van der Mark et al., 2009).

In our previous fMRI study, we specifically investigated print processing in the VWF-System in children with and without dyslexia while they indicated if visual stimuli (real words, pseudohomophones, pseudowords and false-fonts) sounded like a real word (Van der Mark et al., 2009). We found that a posterior–anterior gradient of print specificity (higher anterior activity to letter strings but higher posterior activity to false-fonts) as well as a constant sensitivity to orthographic familiarity (higher activity for unfamiliar than familiar word-forms) along the VWF-System could only be detected in controls. These findings indicate that children with dyslexia show impaired VWF-System specialization for both print and orthography.

Although these conventional fMRI studies are restricted to the localization of brain regions or regional gradients involved in dyslexia (due to the nature of the activation analyses), there is considerable interest in examining the cooperation

between those brain areas. In an early positron emission tomography (PET) study by Paulesu et al. (Paulesu et al., 1996) investigating adults with and without dyslexia, the group differences in task dependent activation patterns were interpreted to suggest that good reading required cooperation and connections among brain regions, and that dyslexia resulted from a disconnection among regions. A popular method for the in vivo examination of the cooperation between brain regions is called functional connectivity MRI (fcMRI), which examines the temporal coherence in which brain areas are engaged (Biswal et al., 1995; Cordes et al., 2000; Friston, 1994; Lowe et al., 1998). This data-driven analysis allows the identification of interregional correlations (with consistent regression coefficients across subjects) in low-frequency ( $<0.1$  Hz) spontaneous BOLD fluctuations in the brain which cannot be attributed to the experimental paradigm (Arfanakis et al., 2000; Biswal et al., 1995; Cordes et al., 2000; Fox and Raichle, 2007; Friston, 1995; Horwitz et al., 1992; Lowe et al., 1998; Xiong et al., 1999). Since this technique involves correlating signal changes in a seed region with signal changes in other parts of the brain, it can reveal functional interactions between brain areas (Friston et al., 1996). The fact that fcMRI is data-driven also means that it is task-driven rather than event-driven. Therefore, neural networks differ between rest, motor, visual and language tasks, but are not influenced by the kind, order of stimuli presented in a task (Bitan et al., 2005; Cordes et al., 2000; Pugh et al., 2000; Richards and Berninger, 2008). In addition, this procedure (task-driven fcMRI) has been shown to allow for the detection of task-driven but stimulus independent brain activity (e.g., (Richards and Berninger, 2008)). With respect to the development of connectivity, Booth et al. revealed developmental differences in effective connectivity in left hemisphere regions in subjects performing a spelling task in both the visual and auditory modality (Booth et al., 2008). Their results showed developmental increases in automatic access into brain regions



involved in phonological processing in tasks that require orthographic processing. In addition, Bitan et al. found age-related increases in fronto-temporal effective connectivity in children performing rhyming judgments on visually presented words (Bitan et al., 2009).

Compared to effective connectivity (the influence one neural system exerts over another), functional connectivity (temporal correlations between remote, spontaneous neurophysiological events) has the advantage that it is a data-driven rather than a hypothesis-driven type of analysis, thus not reducing its validity to the validity of the model (Friston, 1994). This type of spontaneous activity is thought to convey neural activity that is superimposed on an intrinsic network architecture and contributes to trial-to-trial variability that cannot be explained by general linear models applied in event-related or block design fMRI tasks (Fox et al., 2006; Vincent et al., 2007). Since fcMRI is applied when the subject is in the same mental state, i.e. during a continuous resting state or continuous performance of a task (e.g. a reading task), we used an event-related task with an unpredictable sequence of stimulus conditions in the present study, in which (in contrast to a block design) the cognitive state, and particularly preparatory and strategic aspects of processing are expected to be constant over time, even though stimulus conditions vary (Abler et al., 2006; Goebel et al., 2003). In this event-related task, subjects were continuously presented with visual stimuli rather than lying still with their eyes closed (resting state) or performing alternating tasks (block design). Finally, it is important to note that the present paper focused on region of interest (ROI)-specific connectivity, which means that we controlled for other regions by excluding these regions.

Investigating effective connectivity in healthy adult readers revealed that variations in prefrontal activity in response to regular words, exception words, and pseudo-words were associated with a selective increase in effective connectivity from

distinct occipitotemporal areas (posterior, middle, anterior fusiform), depending on word-type (Mechelli et al., 2005). These results provide evidence for the important role that left hemispheric ventral visual stream connectivity plays in reading.

However, the present study for the first time investigated regionally selective connectivity along the occipitotemporal VWF-System to clarify its function in young children, and a possible dysfunction in children with developmental dyslexia.

Few previous studies have investigated functional connectivity in children with dyslexia. A recent fMRI connectivity study investigating children with dyslexia during phoneme mapping found no deviant connectivity for an occipital seed region, and focused instead on a finding of increased left inferior frontal gyrus connectivity to other frontal regions (Richards and Berninger, 2008). So far, it has not been systematically investigated how distinct areas within the extended VWF-System characterized in our previous paper (van der Mark et al., 2009) are functionally connected with the language network in children with and without dyslexia.

The aim of the present study was to examine, for the first time, functional connectivity in control children and children with dyslexia (mean age 11 years) during a continuous reading task focussing on systematic variations of connectivity in the VWF-System, given that our fMRI results had indicated altered VWF-System print tuning gradients with dyslexia in this data set (Van der Mark et al., 2009). We hypothesized that the VWFA is functionally connected with left parietal and frontal language areas during word form processing in control children and that these functional connections are reduced in children with dyslexia. In addition, we hypothesized that these functional connections correlate with behavioural measures of reading ability within the control group.

## Materials and Methods

Full detail about the participants, task and stimuli, and fMRI preprocessing is provided in Van der Mark (2009); additional results on sentence reading in an overlapping sample (Schulz et al., 2008, 2009) and longitudinal electrophysiological aspects for a subsample have been reported (Maurer et al., 2007; Maurer et al., 2003a).

### *Participants*

The 42 children (mean age 11.3 years,  $\pm 0.6$  years) who participated in this study were grouped according to their reading scores (see Table 1): 18 children with dyslexia and 24 control children. Six additional children were excluded from analysis due to head movement exceeding the a-priori maximum movement criterion ( $> \pm 2$  mm translation or  $> \pm 2^\circ$  rotation), or poor task performance (accuracy  $< 60\%$  in one or more conditions). Twenty-six children were part of an extensive longitudinal study investigating developmental dyslexia in children (Maurer et al., 2007; Maurer et al., 2003b; Schulz et al., 2008) and 16 children participated only in either 4th or 5th grade.

Subjects took a typical German test battery for dyslexia (Mayringer and Wimmer, 2000; Wimmer, 1996, 2006; Wimmer et al., 2000). The children were grouped based on their normed reading fluency scores (“correct words per minute”) of the Salzburg Reading and Spelling Test (“Salzburger Lese- und Rechtschreibtest” (SLRT); (Moll and Landerl, in press)), which is the core criterion for diagnosing dyslexia in readers of the regular German orthography (Wimmer et al., 2000). All children from the present fMRI study were categorized as dyslexic if their “correct words per minute”-score was below the 10th percentile of the corresponding norms

(<61.6) and as control children if their score was equal to or above the 20th percentile of the norms (>75.0). Although other definitions are obviously possible, these criteria were used because they are often used in clinical practice, reflect the consensus in a large European project consortium (<http://www.neurodys.com>), and allow us to relate to our previous research (Maurer et al., 2007; Schulz et al., 2008, 2009; van der Mark et al., 2009). As can be seen in Table 1, the children with dyslexia performed worse not only on word reading (the criterion for grouping), but also on pseudoword reading and on spelling. The groups were matched for gender, age, and handedness and estimated verbal and non-verbal IQ. As a measure of phonological access to lexical store, all children performed rapid automatic naming (RAN) tasks. Finally, spelling was scored as the mean % correctly written words of pooled SLRT scores of the 4th graders and DRT-5 scores (Diagnostischer Rechtschreibtest (Grund et al., 1995)) of the 5th graders.

Children with a history of neurological diseases, psychiatric disorders, uncorrected-vision problems and children from families with a foreign language background were excluded from the study. The children and their parents/caretakers gave their informed written consent to participate in the study. The study was approved by the local ethics committee.

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### *Stimuli and Task*

During fMRI acquisition, participants performed a phonological lexical decision task in which they had to decide whether a visually presented stimulus sounded like a real word or not (Kronbichler et al., 2007; Van der Mark et al., 2009; Wimmer et al.,

2009). This task not only challenges orthographic processing in order to decode the orthographically unfamiliar pseudohomophones, but also requires phonological decoding and phonological synthesis prior to the phonological judgment. This continuous reading task included 176 stimuli that consisted of 44 orthographically familiar forms of German nouns (W), 44 pseudohomophones (PH; phonologically correct but orthographically unfamiliar forms of the same words), 44 pseudowords (PW; phonologically and orthographically unfamiliar forms) and 44 false-fonts (FF). Additionally, 65 null events (fixation cross only) were presented. In the event-related design, the stimuli were presented for 700 ms with an interstimulus interval (ISI) of 2550 ms during which a fixation cross was shown. Participants were instructed to press 'Yes' for W (e.g. Taxi) and PH (e.g. Taksi) and to press 'No' for PW (e.g. Tatti) and FF (e.g. ꞑꞑꞑꞑ). For responding, they used the index finger and middle finger of their dominant hand. To become familiar with the task, the subjects were given a short practice version (with different stimuli) of the task outside the scanner.

#### *fMRI Acquisition*

MRI data was acquired on a 3.0 T (GE Healthcare) whole-body scanner. For functional imaging, 535 functional images sensitive to BOLD contrast with 25 axial slices covering the whole brain were acquired with a T2\*-sensitive multi-slice echo planar imaging (EPI) sequence (TR = 1.5s; TE = 31ms; FOV = 24cm; image matrix = 64 x 64; voxel size = 3.75 x 3.75 x 5 mm; flip angle = 50°). The first 4 scans were discarded to allow for equilibration effects. Participants were fitted with earplugs and viewed the stimuli via TFT video goggles (Resonance Technology Inc., California, USA). Particular care was taken to stabilize the children by using vacuum cushions and custom made padding.

### *Behavioural data analysis*

Response accuracy and reaction times (correct trials only) were analyzed separately in a repeated measures analysis of variance (ANOVA) with the within-subject factor 'condition' (W, PH, PW, FF) and between subject factor 'group' (controls and children with dyslexia) (Table 2). Statistical analyses were performed using SPSS software (SPSS Inc., Chicago, USA).

### *Image preprocessing*

Functional MRI data preprocessing and statistical analysis were done using SPM5 (Wellcome Department of Imaging Neuroscience, London, <http://www.fil.ion.ucl.ac.uk/spm>). The data were first motion corrected and the images were then normalized using a standard EPI template based on the Montreal Neurological Institute (MNI) reference brain using 4th-degree B-spline interpolation. Finally, functional volumes were resampled to isotropic 3 mm<sup>3</sup> voxels and spatially smoothed with a 9 mm full width at half maximum isotropic Gaussian kernel.

### *Functional connectivity analyses*

The initial step of the *seed-voxel correlation mapping* analysis (Biswal et al., 1995) was to define five non-overlapping seed regions of interest (ROIs; spheres with a 6mm radius) (Figure 1a), centered on the VWFA of the fusiform gyrus (Cohen et al., 2000) and covering neighbouring areas along a posterior-anterior axes in the left hemisphere. The four additional seed regions (two anterior and two posterior to the VWFA) were selected, in order to answer the question of specificity of possible functional connections between the VWFA and other language-related areas. The coordinates were chosen in such a way that the ROIs would follow the slight anterior decline of the temporal lobe (Brem et al., 2006; Van der Mark et al., 2009): ROI1 (-

42, -80, -14), ROI2 (-42, -68, -16), ROI3 (the VWFA; -42, -54, -17), ROI4 (-42, -42, -18), and ROI5 (MNI coordinates (x/y/z): -42, -30, -20).

In the next step, a mean time series for each ROI was computed for each subject individually using the MARSBAR toolbox (<http://marsbar.sourceforge.net/>) (Brett et al., 2002). In each subject individually, the mean signal change in all 5 ROIs simultaneously was then cross-correlated with the time series of all other voxels in the brain. A total of nine orthogonal regressors (covariates of no interest) were used to reduce variance unlikely to reflect functional connectivity-related neuronal activity (Fair et al., 2007; Fox et al., 2005; Villalobos et al., 2005): six regressors corresponding to the six parameters obtained by the rigid body head motion correction; three regressors corresponding to the whole brain, white matter and ventricular (CSF) signal, which included the averaged signals over voxels within the respective SPM template masks. Furthermore, four regressors related to the stimuli were included in order to minimize the stimulus-related variance (Brown et al., 2005; Fair et al., 2006; Miezin et al., 2000; Schlaggar et al., 2002). To this end, the BOLD response time course for each stimulus condition (W, PH, PW and FF) was constructed by convolving the stimulus onsets of each stimulus type with the hemodynamic response function (HRF). Because we used a rapid randomized event-related paradigm rather than a block design, stimulus conditions could not be disentangled in the present study.

In the second-level analysis, a repeated measures ANOVA with within-subject factor 'ROI' (all five ROIs), and between subject factor 'group' (dyslexics and controls) was computed. The analysis allowed us to examine ROI-specific connectivity, since the inclusion of all five ROIs in the ANOVA controlled for connections that were non-specific for each ROI (connections common to all ROIs

were statistically removed)<sup>1</sup>. The figures illustrate how this ROI-selective connectivity pattern (Figure 1) differs from the less selective connectivity computed for each ROI separately (supplementary Figure 1 online). For each of the five ROIs, one-sample *t*-tests were computed on regression coefficients to yield functional connectivity maps for each group separately (controls and children with dyslexia). Next, two-sample *t*-tests were computed to determine whether there were reliable group differences (control vs. children with dyslexia) in functional connectivity. The group comparisons, representing the main focus of the present article, concentrated on the main areas showing connection with the VWF-System. To this end, the functional connectivity maps of group comparisons were masked with a mask that was computed by adding all significant clusters that were present in the statistical maps of each individual ROI for both controls and children with dyslexia. We were interested in studying functional connectivity with the whole brain instead of restricting the search volume to pre-defined regions of interest. Therefore, a Monte-Carlo simulation of the brain volume was employed to establish an appropriate voxel contiguity threshold (Slotnick et al., 2003). This correction has the advantage of higher sensitivity to smaller effect sizes, while still correcting for multiple comparisons across the whole brain volume. Assuming an individual voxel type I error of  $P < 0.001$ , a cluster threshold of 21 contiguous resampled voxels (equivalent to eight original voxels) was indicated as necessary to correct for multiple voxel comparisons at  $P < 0.05$ .

Finally, in an additional analysis, subjects' performance (i.e. mean reaction times in this reading task) was inserted as a covariate of no interest into a two-sample *t*-test. This was done to evaluate if the same pattern of functional brain

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<sup>1</sup> Repeated measures ANOVA computed for each ROI separately did not show any additional connections to those already revealed by the ROI-specific analysis that included all five ROIs. See Supplementary Figure 1 online.



connectivity would be observed if individual differences in reading speed were statistically controlled.

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Please insert Figure 1 approximately here  
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## Results

### *Behavioural Results*

Reaction time, accuracy and  $p$ -values of group comparisons for the phonological lexical decision task are reported in Table 2. In the phonological lexical decision task performed inside the scanner, accuracy scores differed significantly between conditions (W, PH, PW and FF;  $F(3,38) = 74.60, P < 0.001$ ) and groups (controls and children with dyslexia;  $F(1,40) = 13.68, P = 0.001$ ). In addition, an interaction of condition with group was found ( $F(3,38) = 9.83, P < 0.001$ ). Post-hoc  $t$ -tests revealed that children with dyslexia made significantly more mistakes than control children for PH (more erroneous “no” responses) and for PW (more erroneous “yes” responses), whereas the groups performed equally well for W and FF.

Analysis of the reaction times yielded significant main effects of condition ( $F(3,38) = 170.22, P < 0.001$ ) and group ( $F(1,40) = 17.05, P < 0.001$ ) in addition to an interaction of condition with group ( $F(3,38) = 21.09, P < 0.001$ ). Post-hoc  $t$ -tests revealed that the children with dyslexia responded more slowly than the control children to all three letter string conditions. Note that there was no significant group difference for FF.

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Please insert Table 2 approximately here

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### *Functional Connectivity MRI*

Maps showing functional connectivity of each separate ROI for both control children and children with dyslexia are shown in Figure 1b, and a detailed listing of the clusters showing significant interregional connectivity is provided in Table 3. The global activation maxima of the ROI-based connectivity maps are skipped in the activation tables and will not be further discussed. As expected, these maxima simply show that each ROI was highly autocorrelated (with Z-values being infinite).

### *Control Children*

Figure 1b illustrates that, in control children, only the VWFA seed region (ROI3) is functionally connected with the remote brain areas of the traditional left-hemispheric language network (the left inferior frontal gyrus and the inferior parietal lobule) as well as the right hemispheric inferior frontal gyrus and superior parietal lobule. By contrast, the four ROIs located anteriorly and posteriorly to the VWFA, revealed functional connectivity with different brain regions. For ROI1, being the most posterior ROI in the VWF-System, significant connectivity clusters were observed mainly in the left middle occipital gyrus. For ROI2, a large cluster of connectivity was found in the left superior parietal lobule, similar to ROI3. Next, ROI4 showed significant functional connections with the left insula and the right superior temporal and the fusiform gyrus. For ROI5, being the most anterior ROI in the VWF-System, significant connectivity clusters were observed in the left fusiform gyrus and the middle temporal gyrus. In a post-hoc analysis, the direct comparison of the functional connections for ROI3 in the control group with those for all other ROIs revealed significant clusters in

the left inferior frontal gyrus and the inferior parietal lobule. These clusters were similar to those revealed by the group comparison for ROI3. This finding indicates that the functional connectivity with the language network was specific for the VWFA.

#### *Children with Dyslexia*

In the dyslexic group, ROI3 (VWFA) was found to be functionally connected with the middle occipital, the middle temporal gyrus, and the thalamus in the left hemisphere. The most posterior ROI in the VWF-System (ROI1) were connected only with the left inferior occipital gyrus. For ROI2, significant connectivity clusters were found in the left superior parietal lobule and the middle occipital gyrus. For ROI4, significant connectivity clusters included the left inferior occipital, the superior temporal gyrus, and the middle and inferior frontal gyrus. For the most anterior ROI in the VWF-System (ROI5), clusters were seen in the left middle temporal gyrus, the bilateral frontal gyrus, and the right fusiform gyrus.

#### *Group Comparison*

The results of the group comparisons are shown in Figure 1c and Table 4. Functional connectivity in children with dyslexia was significantly reduced only between the VWFA proper (ROI3) and classical left hemispheric language related regions, including the inferior parietal lobule and the inferior frontal gyrus. In contrast to this central VWFA ROI, neither the two more posterior ROIs in early, low-level visual word processing areas of the VWF-System (ROI1 and ROI2) nor for the two most anterior ROIs (ROI4 and ROI5) displayed greater connectivity for controls than dyslexics.

Inverse effects, that is, significantly greater connectivity for the dyslexic than the control group, were observed between ROI3 and the left middle temporal and

middle occipital gyrus. Greater connectivity for dyslexics than controls for ROI4 was found mainly in the left superior temporal gyrus and the left insula. By contrast, such significant group differences could not be detected for the posterior ROIs 1 and 2 or in the most anterior ROI5.

In order to investigate whether these group differences in connectivity are attributable to differences in reading skills, or whether they simply reflect other group characteristics, we performed an additional analysis in which subjects' performance served as a covariate of no interest. The results revealed that the group difference (controls vs. dyslexics) for ROI3 did no longer show stronger functional connectivity with the left inferior frontal gyrus and the inferior parietal lobule in controls than in children with dyslexia. By contrast, the increased connectivity to the left MTG and STG for children with dyslexia vs. controls remained unchanged. This means that the reduced connectivity of the VWFA proper to the classical frontal and parietal language regions can be attributed to those reading performance differences between groups, which are characteristic for dyslexia. This interpretation is supported by the finding that the RT group differences were completely absent for the false-font control condition and were limited to the letter strings where they were present regardless of difficulty (W, PW, PH), as can be seen in the behavioural results section.

#### *Correlations between Connectivity and Behaviour*

The findings of 1) reduced connectivity of the VWFA with the left inferior frontal gyrus and the inferior parietal lobule in children with dyslexia compared to controls and 2) greater connectivity for the dyslexic versus controls between ROI3 and the left middle temporal gyrus and between ROI4 and the left superior temporal gyrus raise important questions. Do these findings represent a kind of functional disconnection

syndrome, which is limited to children with dyslexia, or do they reflect a more general continuum of reading ability? And does the increased connectivity in children with dyslexia reflect at least partly successful compensation in this group? Thus, in a post-hoc analysis, we correlated – within each group separately – (a) the connectivity between ROI3 and the two voxels (the left inferior frontal gyrus and the inferior parietal lobule) that had yielded the maximal group contrast for controls vs. dyslexics, and (b) the connectivity between ROI3 and the left middle temporal gyrus and between ROI4 and the left superior temporal gyrus found by contrasting dyslexics vs. controls with behavioural measures related to phonological processing. These behavioural measures included accuracy and reaction time scores for the four stimulus categories of the task performed during scanning, as well as behavioural measures acquired outside the scanner, i.e. pseudoword reading and picture naming. This analysis within each group separately is important, because the additional analysis using reading performance as a covariate of no interest has little chance of revealing other group differences such as fundamentally different relations between performance and connectivity, which may also characterize dyslexia.

Firstly, results showed that the strength of the functional connections between the VWFA and the left inferior frontal gyrus in the controls correlated significantly with reaction time for words ( $r = -0.42$ ;  $P = 0.041$ ) during the phonological lexical decision task performed inside the scanner, and with reaction time for picture naming ( $r = -0.48$ ,  $P = 0.019$  for short object names;  $r = -0.46$ ,  $P = 0.022$  for long object names) and accuracy scores for pseudoword reading ( $r = 0.42$ ;  $P = 0.040$ ) outside the scanner. Functional connectivity of the VWFA with the left inferior parietal lobule correlated significantly with reaction time for picture naming ( $r = -0.44$ ,  $P = 0.033$  for short object names;  $r = -0.37$ ,  $P = 0.073$  trend for long object names) in the control group. These correlations suggest that more connectivity corresponds to more

efficient (faster RTs or higher accuracy) performance. The children with dyslexia did not show significant correlations with any of these behavioural measures. Secondly, the strength of the functional connections between the VWFA (ROI3) and the left middle temporal gyrus and between ROI4 and the left superior temporal gyrus as found by contrasting dyslexics vs. controls did not correlate significantly with these behavioural measures in neither the control group nor the children with dyslexia. Thus, correlating these increases in connectivity in children with dyslexia with reading measures suggested that that this increased connectivity does not reflect better performance, but instead compensation efforts, which are not necessarily successful.

Taken together, these results suggest that there is some fundamental difference between groups in terms of linking these regions together for visual word processing, that is, dyslexics may not use the network in the same way as controls.

## **Discussion**

The present study examined functional connectivity in children with dyslexia during continuous orthographic processing, focussing for the first time on systematic variations of ROI-specific connectivity in the visual word-form area (VWFA; (Cohen et al., 2000)) and neighbouring regions within the left occipitotemporal VWF-System. As detailed in our previous study, analysis of the behavioural data revealed that children with dyslexia exhibited typically poor, dysfluent reading performance but were not impaired with false-font processing (Van der Mark et al., 2009). These results indicate that these children had problems with phonological decoding of visual letter strings varying in orthographic familiarity during the phonological lexical decision task.

The functional connectivity MRI data support our main hypothesis that reduced functional connectivity exists during reading acquisition in children with dyslexia and is linked to a specific left occipitotemporal region crucial for visual word processing (the VWFA). First, we found that only the VWFA was functionally connected with the typical, remote left frontal and parietal language areas in control children, whereas the adjacent posterior and anterior occipitotemporal ROIs in the VWF-System did not show such connectivity. This finding suggests that these long-range functional connections outside the occipital lobe were specific for the VWFA and did not generalize to the left occipitotemporal regions neighbouring the VWFA, confirming the special role that this core region plays in print processing (Cohen et al., 2004; Dehaene et al., 2004). Second, the group comparison revealed a disruption of functional connectivity in the VWF-System, which was again confined to the connections between the VWFA and left inferior frontal and inferior parietal reading-related brain regions in children with dyslexia. We were able to show that this functional disruption may be linked to dyslexics' deficits in phonological processing since connectivity was correlated with phonological performance inside and outside the scanner in the control group but not in the children with dyslexia. We propose that a focal disruption in functional connections between left hemispheric regions of the reading network involved in processing visual word forms is at the core of the dyslexics' reading problems. Although the group difference in correlations was not significant, the pattern is consistent with deficits in phonological processing.

#### *ROI-specific functional connectivity in Control Children*

The five ROIs in the left occipitotemporal VWF-System showed systematically different ROI-specific connections outside the VWF-System between controls and dyslexics during orthographic processing of visual word-forms. The results for the

control children revealed a separation of functional connectivity networks, depending on the posterior-anterior axis of the left inferior occipitotemporal gyrus. Specifically, the central ROI in the left occipitotemporal gyrus (ROI3), at the coordinates of the VWFA (Cohen et al., 2000), showed bilateral functional connections with other major components of the traditional language network (i.e. the inferior parietal lobule and the inferior frontal gyrus). The brain regions to which VWFA seed region is connected replicate those in which children with and without dyslexia differed depending on task, as demonstrated by the meta-analysis of (Richlan et al., 2009). By contrast, the two ROIs in early visual areas showed little connectivity with higher-order processing areas but were mainly connected with adjacent visual areas (ROI1), and the left superior parietal lobule (ROI2), the latter suggesting involvement of visuospatial analysis and attention (Kanwisher and Wojciulik, 2000). Furthermore, the two most anterior ROIs (ROI4 and ROI5) did not show interlobar connections but instead were connected with the left insula (for ROI4) and the left middle temporal gyrus (for ROI5), suggesting a link to auditory phonological or modality independent lexical-semantic processing (Lau et al., 2008; Vigneau et al., 2006). These results indicate that – within the ventral VWF-System – the VWFA may be the only brain region that is consistently functionally connected to higher-order regions of the language network, which is in agreement with the belief that the left fusiform gyrus functions as a major relay of visual stimuli into the network, considering that it encodes a wide variety of complex visual percepts, including both verbal and nonverbal stimuli (Cohen et al., 2000; Haxby et al., 2001; Kanwisher et al., 1997).

The connectivity patterns in the controls provide new direct evidence that already in young readers, the VWFA serves as an interface between invariant visual and higher order representations (Devlin et al., 2006), and suggests that this function



is confined to the VWFA proper despite print tuning in adjacent VWF-System areas (Van der Mark et al., 2009).

### *Disruption of ROI-specific Functional Connectivity in Children with Dyslexia*

The group comparisons revealed that children with dyslexia showed a focal reduction of ROI-specific functional connectivity between the VWFA and two major components of the language network: (i) the left inferior parietal lobule and (ii) the left inferior frontal gyrus. By revealing that a disconnection between these reading-related brain regions is already present in children with dyslexia, our findings significantly extend those of previous fMRI studies in adults with dyslexia that showed that functional connectivity of the left occipitotemporal gyrus with the left angular gyrus was weaker (Horwitz et al., 1998; Pugh et al., 2000) and connections between a left occipitotemporal seed region and the left inferior frontal gyrus were absent during reading (Shaywitz et al., 2003; Stanberry et al., 2006). In addition, our findings extend those of a recent fMRI connectivity study examining children with dyslexia during phoneme mapping, which did not find deviant connectivity for an occipital seed region, and focused instead on a finding of increased left inferior frontal gyrus connectivity to other frontal regions (Richards and Berninger, 2008). Furthermore, our results are in congruency with an effective connectivity study demonstrating a weaker influence of the left fusiform gyrus upon the left inferior parietal lobule and the left inferior frontal gyrus in children with dyslexia compared to controls during a visual word rhyming task (Cao et al., 2008). However, in contrast to the present study, Cao et al. investigated connectivity from a single location within the left fusiform gyrus rather than ROI-specific connectivity throughout the VWF-System, and due to the nature of the effective connectivity method, their analysis was more dependent on the model than that of the present study.

In addition, group comparison revealed a small number of areas showing greater ROI-specific functional connectivity for dyslexics than controls. For the VWFA, dyslexics demonstrated significantly greater connectivity than controls to the left middle occipital and middle temporal gyri. The ROI located directly anterior to the VWFA (ROI4) also demonstrated significantly increased connectivity for children with dyslexia: to the left superior temporal gyrus and the left insula. These findings of greater connectivity for dyslexics than controls suggest increased auditory-phonological and lexical-semantic processing in children with dyslexia, possibly reflecting alternative strategies. In contrast to these central ROIs, no group differences were found for the two most posterior ROIs (ROI1 and ROI2) or the most anterior ROI (ROI5) in the VWF-System. This suggests that children with dyslexia have normal functional connections in the lower-level visual areas of the VWF-System, in line with findings of fMRI studies in adults with dyslexia (Booth et al., 2003a,b, 2004, 2007) and of event-related potential (ERP) studies in children with dyslexia at age 11 or 12 years (Brandeis et al., 1994; Simos et al., 2000).

These group differences in connectivity were performance-driven, as revealed by two additional analyses. Firstly, our analysis in which subjects' performance served as a covariate of no interest showed that, unlike the reduced functional connectivity between ROI3 and left frontal and parietal language regions found in children with dyslexia, their increased connectivity to midtemporal and STG regions was not eliminated through controlling for reading performance. This suggests that their increased connectivity may reflect successful compensation associated with relatively better relative performance. Secondly, correlating connectivity and behaviour within each group separately revealed that the strength of the functional connectivity of the VWFA with especially the left inferior frontal gyrus but also the left inferior parietal lobule was related with performance measures of phonological

processing in the control children. By contrast, no such correlation between performance and spontaneous task-driven neural network activity was found in the children with dyslexia. Furthermore, no significant correlations with performance were found in either of the two groups for the peak voxels showing greater connectivity in dyslexics vs. controls. This indicates that a disconnection disturbs the relationship between performance and connectivity in children with dyslexia. This finding extends that of a previous fMRI study demonstrating correlations between reading ability and functional connectivity between the left angular gyrus and Broca's area (Hampson et al., 2006). Furthermore, it is interesting that ROI-specific connectivity correlated significantly with performance outside the scanner, particularly because our functional connectivity measure reflects spontaneous wide-range covariations while controlling for differences due to stimulus categories.

Furthermore, the correlation between connectivity and behavioural measures of phonological processing is consistent with the dyslexics' phonological deficits (Ramus et al., 2003). Thus, we propose that children with dyslexia may not demonstrate functional connectivity of the VWFA with the left inferior parietal lobule because they are unable to effectively engage this region during the integration of orthography and phonology (e.g., (Damasio and Damasio, 1983; Friedman et al., 1993; Geschwind, 1965). Similarly, we propose that the lack of connectivity between the VWFA and the left inferior frontal gyrus may be linked to their inability to successfully engage this region during phonological processing of written words (e.g. (Poldrack et al., 1999; Price, 2000; Pugh et al., 1996). This link between connectivity and reading performance is consistent with the finding that connectivity may increase after effective treatment, as shown by Richards et al. (2008). Furthermore, recent studies have shown that the nature and duration of the instruction children have received at school is important for predicting whether reading functions have

normalized ((Aylward et al., 2003; Richards and Berninger, 2008; Simos et al., 2002; Simos et al., 2007); for a review see (Shaywitz et al., 2008)). However, we consider this issue of minor importance for the present group of children because they have learned to read in a regular orthography and because they have already had several years of reading experience. It would be of interest to test if maturation or controlled training intervention would change the pattern of functional connectivity found in the present study.

Next to studies reporting abnormalities within the left occipitotemporal cortex in dyslexia, other studies identified altered activation in the temporo-parietal junction (for a review see (Shaywitz and Shaywitz, 2005)). Therefore, one could argue that abnormal connectivity with the inferior parietal lobule and the occipitotemporal cortex found in the present study may be a consequence of temporo-parietal abnormalities rather than the left occipitotemporal cortex, which may simply serve as the input route in this task. In our previously published fMRI study (van der Mark et al., 2009), we investigated functional abnormalities using the same sample of children with dyslexia and the same task as in the present study. In this study, the whole brain analysis did not reveal left temporo-parietal abnormalities in the children with dyslexia. However, we did find functional differences in the left inferior frontal gyrus, the left superior parietal lobule and the left occipitotemporal cortex.

The findings of the present study raise an important question: what does reduced functional connectivity mean and how is it different from reduced activity in two brain areas? While functional connectivity analyses describe the level of temporal coherence in which brain areas are engaged, conventional activation analyses are restricted to localizing brain areas that are involved in dyslexia. This means that brain areas may show reduced activity but similar functional connectivity, and vice versa. In the present study, children with dyslexia showed *increased* ROI-

specific functional connectivity between the left occipitotemporal cortex and the left middle occipital, the left middle and the superior temporal gyrus, and the left insula in comparison to control children (Figure 1c). By contrast, as demonstrated in our previous study (van der Mark et al., 2009), these brain regions showed *similar* activity in controls and dyslexics while reading words and false-font and *decreased* activity in dyslexics compared to controls while reading pseudohomophones and pseudowords. This finding of increased connectivity in dyslexics versus controls may therefore reflect alternative strategies in children with dyslexia. The disruption in functional connectivity between the VWFA and the left inferior parietal and inferior frontal cortex in children with dyslexia indicates that brain regions necessary for fluent reading may not work together properly during reading. A probable explanation for this disruption in long-range functional connections outside occipital lobe could be a disruption of anatomical connectivity. This hypothesis is supported by a study of a patient who developed pure alexia following a small surgical lesion close to his VWFA. The lesion, while leaving the VWFA anatomically uninjured, caused a disruption of the inferior longitudinal fasciculus - essential for normal reading, being the anatomical link between the VWFA and the occipital cortex (Epelbaum et al., 2008). However, it is still unknown how changes in anatomical connections of the VWFA are related to developmental dyslexia, since Epelbaum et al. (2008) investigated pure alexia. Furthermore, most studies using diffusion tensor imaging (Beaulieu et al., 2005; Deutsch et al., 2005; Klingberg et al., 2000; Niogi and McCandliss, 2006) and voxel-based morphometry (VBM) (Eckert et al., 2005; Silani et al., 2005) have associated dyslexia with changes in anatomical connections of temporo-parietal regions. To date, only one VBM study found reduced gray matter density in the left inferior occipitotemporal cortex in adults and adolescents with dyslexia (Kronbichler et al., 2008). Accordingly, specifically designed studies combining techniques for examining

functional and anatomical connections are necessary to fully understand the neurobiological basis of such focally reduced functional connectivity in dyslexia.

Since different task demands are known to elicit different and partly age dependent connectivity networks, we must leave open whether this altered VWF-System connectivity generalizes to different task conditions and age groups. Our reading task was designed to challenge orthographic and phonological processing during lexicality judgments on four word-like categories, in order to elicit activation in the VWF-System which distinguishes children with and without dyslexia (van der Mark et al., 2009). It would therefore be of interest for future studies to examine functional connectivity between the VWF-System and the language network using variations of reading, language or other task conditions. Similarly, correlations between performance and imaging data are not a substitute for testing alternative hypotheses based on contrasting tasks. In addition, our post-hoc tests should be taken with caution due to the large number of tests that were included. None of these tests would survive stringent corrections for multiple comparisons. Therefore, future studies with partly different tasks and designs will be needed to test the robustness and generality of our findings on altered spontaneous BOLD fMRI in children with dyslexia. Similarly, future study with different groups are needed to clarify whether the present findings generalize to other definitions of dyslexia, and also hold for children suffering primarily from deficits in reading accuracy or spelling.

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**Figure 1. Functional Connectivity Maps.**

**a)** Illustration of the 5 ROIs in the VWF-System: ROI1 (white) was located most posterior, ROI5 (black) most anterior in the left occipitotemporal cortex. ROI3 corresponds to the centre of the VWFA described in previous studies. **b)** Functional connectivity maps for control children, children with dyslexia, and **c)** the group comparison (red: controls > dyslexics, blue: dyslexics > controls) for ROI 3 and 4 separately. Significant clusters indicate the regions functionally connected with the corresponding left occipitotemporal ROI and were overlaid on a surface-rendered single subject brain normalized to MNI template. Statistical threshold was  $P < 0.001$  corrected for multiple comparisons,  $k = 21$ . Maps of group comparison were masked with a group mask (see methods section for details).

**Table 1. Demographic Characteristics of Controls and Children with Dyslexia and Group Differences (t-test or chi-square).**

	Children with Dyslexia	Control Children	<i>P</i> -value
n	18	24	–
Age (years)	11.4 ± 0.7	11.3 ± 0.4	n.s.
Sex (male:female)	10:8	10:14	n.s.
Handedness (right:left)	15:3	17:7	n.s.
Estimated Verbal IQ	109 ± 11	114 ± 14	n.s.
Estimated Non-verbal IQ	111 ± 12	112 ± 11	n.s.
Correctly read W/min	49 ± 8	93 ± 16	<i>P</i> < 0.001
Correctly read PW/min	32 ± 5	54 ± 14	<i>P</i> < 0.001
Spelling	30 ± 23	86 ± 21	<i>P</i> < 0.001
RAN letter z	0.60 ± 0.9	-0.45 ± 0.8	<i>P</i> = 0.001
RAN picture (short) z	0.43 ± 1.1	-0.32 ± 0.8	<i>P</i> = 0.021
RAN picture (long) z	0.53 ± .089	-0.40 ± 0.9	<i>P</i> = 0.002
RAN digit z	0.21 ± 0.9	-0.16 ± 1.0	n.s.

Means and standard deviations (SD) are displayed. RAN: rapid automatic naming task, i.e. time needed for pronouncing randomly presented letters, pictures with short or long object names, and digits in rows. Fisher-Z transformations were used to convert raw values scores into standardized Z-scores. Significant *p*-values indicate group differences (controls versus children with dyslexia). Abbreviations: z: z-scores mean = 0, SD = 1; n.s.: non-significant.

**Table 2. Performance During Phonological Lexical Decision Task.**

Measures	Words	Pseudohomophones	Pseudowords	False-Fonts
<b>Task Performance</b>				
<i>Phonological lexical decision task (fMRI)</i>				
Accuracy (%)				
Control children	94 (±7)	87 (±9)	91 (±8)	99 (±1)
Children with dyslexia	92 (±8)	80 (±9)	78 (±7)	98 (±3)
<i>p</i> -value	n.s.	<i>P</i> = 0.017	<i>P</i> < 0.001	n.s.
Reaction time (ms)				
Control children	1033 (±299)	1196 (±340)	1338 (±361)	837 (±227)
Children with dyslexia	1401 (±297)	1608 (±252)	1904 (±288)	895 (±198)
<i>p</i> -value	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> < 0.001	n.s.

Means and standard deviations (SD) are displayed for the controls and the children with dyslexia and all four item types. Significant *p*-values indicate group differences (controls versus children with dyslexia); n.s.: non-significant.

**Table 3.** Clusters of Functional Connectivity for Control Children and Children with Dyslexia.

Region	MNI Coordinates			Z	Voxels	BA
	x	y	z			
<i>ROI1</i>						
Control Children						
L Cuneus	-42	-87	21	4.64	823	18
L Middle Occipital g.	-30	-87	3	4.54		18
R Middle Occipital g.	27	-84	9	3.75	26	19
Children with Dyslexia						
L Inferior Occipital g.	-12	-90	-15	3.52	392	17
<i>ROI2</i>						
Control Children						
L Postcentral g.	-36	-48	60	4.97	317	5
L Superior Parietal l.	-21	-66	57	4.66		7
L Precuneus	-24	-75	30	3.94		19
R Postcentral g.	33	-36	48	4.02	113	3
R Postcentral g.	36	-45	60	3.69		5
R Thalamus	15	-33	0	3.58	25	-
Children with Dyslexia						
L Superior Parietal l.	-21	-72	57	3.80	23	7
L Middle Occipital g.	-27	-84	21	3.68	27	19
<i>ROI3</i>						



## Control Children

L Inferior Frontal g.	-45	6	33	7.05	569	9
L Middle Frontal g.	-48	27	21	5.08		46
L Precentral g.	-42	-9	57	4.00		6
L Superior Parietal l.	-21	-69	42	6.82	471	7
L Precuneus	-24	-81	27	4.61		31
R Inferior Frontal g.	45	9	33	6.75	124	9
R Superior Parietal l.	27	-63	42	5.87	190	7
R Middle Frontal g.	48	33	18	4.68	49	46
R Inferior Frontal g.	33	27	-3	4.44	33	47
R Fusiform g.	27	-42	-30	3.72	28	20

## Children with Dyslexia

L Middle Occipital g.	-42	-75	3	5.14	1126	19
L Middle Temporal g.	-36	-63	12	4.09		19
R Lingual g.	12	-78	-12	4.05	27	18
L Inferior Parietal l.	-45	-33	27	3.82	21	40
L Thalamus	-21	-21	12	3.76	38	-

*ROI4*

## Control Children

L Postcentral g.	-63	-15	21	5.29	2202	43
L Insula	-30	-12	24	4.77	148	13
L Cuneus	-18	-81	18	4.31	24	18
R Superior Temporal g.	36	6	-33	4.28	41	38
R Fusiform g.	36	-33	-21	4.04	156	20

R Parahippocampal g.	33	-42	-12	4.00		37
R Lingual g.	12	-57	3	3.83	34	18
L Inferior Occipital g.	-42	-72	-12	3.76	22	19
L Cingulate g.	-24	-27	45	3.72	29	31
Children with Dyslexia						
L Inferior Occipital g.	-36	-81	-12	3.77	935	19
L Posterior Cingulate	-18	-54	12	6.19	151	30
L Superior Temporal g.	-51	-51	9	6.10	149	22
L Postcentral g.	-51	-15	21	5.41	798	43
L Middle Temporal g.	-60	-12	-12	4.26	89	21
L Middle Frontal g.	-51	33	15	4.22	33	46
L Inferior Frontal g.	-54	27	0	3.25		47
R Posterior Cingulate	12	-51	12	4.03	21	29
<i>ROI5</i>						
Control Children						
L Fusiform g.	-45	-9	-30	5.60	1193	20
L Middle Temporal g.	-51	-12	-24	4.82		21
R Inferior Temporal g.	54	-6	-24	3.58	24	20
Children with Dyslexia						
L Middle temporal g.	-51	-12	-24	6.83	1273	21
R Fusiform g.	36	-15	-30	5.38	100	20
R Parahippocampal g.	18	-18	-30	4.03		28
L Cingulate g.	-21	9	36	5.30	143	32
R Middle Frontal g.	42	30	45	5.14	47	8

R Caudate	12	-6	30	4.33	126	-
L Precentral g.	-33	-15	33	4.13	48	6
R Fusiform g.	42	-69	-18	3.62	35	19

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MNI coordinates (*x/y/z*) are listed for local maxima of significant clusters ( $p < 0.001$ , uncorrected for multiple comparisons). *Z*-values are listed for voxels at the local maxima. BA is the Brodmann area nearest to the coordinate and should be considered approximate (L is left hemisphere, R is right hemisphere, g. is gyrus, l. is lobule).

**Table 4.** Clusters of Functional Connectivity for Group Differences between Control Children and Children with Dyslexia.

Region	MNI Coordinates			Z	Voxels	BA
	x	y	z			
<i>Controls vs. Dyslexics</i>						
ROI3						
L Inferior Parietal l.	-36	-48	45	4.70	178	40
L Precuneus	-21	-72	39	3.51		7
L Inferior Frontal g.	-48	18	30	4.04	46	9
<i>Dyslexics vs. Controls</i>						
ROI3						
L Middle Temporal g.	-36	-63	15	3.72	43	19
L Middle Occipital g.	-42	-75	6	3.71		19
ROI4						
L Superior Temporal g.	-51	9	-6	3.69	32	22
L Insula	-42	-15	0	3.55		13

MNI coordinates (x/y/z) are listed for local maxima of significant clusters ( $p < 0.001$ , uncorrected for multiple comparisons). Z-values are listed for voxels at the local maxima. BA is the Brodmann area nearest to the coordinate and should be considered approximate (L is left hemisphere, R is right hemisphere, g. is gyrus, l. is lobule).

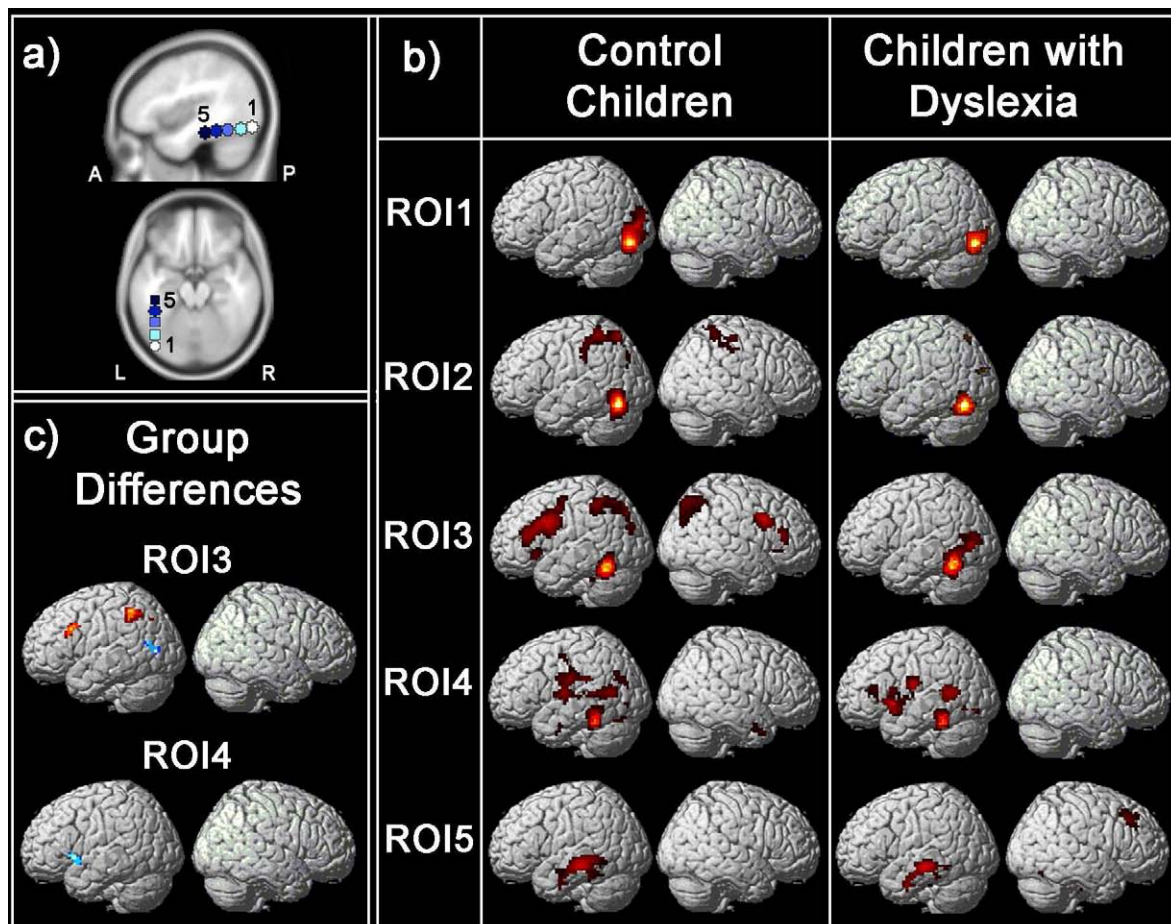


Fig. 1

**Research highlights:**

- Mainly the VWFA was functionally connected with typical left frontal and parietal language areas in control children, pointing to a focal origin of connectivity from the VWF-System.
- Children with dyslexia showed a significant disruption of functional connectivity between the VWFA and left inferior frontal and left inferior parietal language areas.
- A functional disconnection of the left occipitotemporal system in children with dyslexia is limited to the small VWFA region crucial for automatic visual word processing
- This functional disconnection may be linked to dyslexics' deficits in phonological processing since connectivity was correlated with phonological performance in the control group but not in the children with dyslexia.
- This functional disconnection emerges early during reading acquisition in children with dyslexia, along with deficits in orthographic and phonological processing of visual word forms.

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