

Deviant processing of letters and speech sounds as proximate cause of reading failure: a functional magnetic resonance imaging study of dyslexic children

Vera Blau,^{1,2} Joel Reithler,^{1,2} Nienke van Atteveldt,^{1,2} Jochen Seitz,^{1,2} Patty Gerretsen,³ Rainer Goebel^{1,2} and Leo Blomert^{1,2}

1 Maastricht University, Faculty of Psychology & Neuroscience, Department of Cognitive Neuroscience, P.O. Box 616, 6200 MD, Maastricht, The Netherlands

2 Maastricht Brain Imaging Center (M-BIC), P.O. Box 616, 6200 MD, Maastricht, The Netherlands

3 Regionaal Instituut voor Dyslexie, Universiteitssingel 40, 6229 ER, Maastricht, The Netherlands

Correspondence to: Vera Blau,
Vanderbilt University,
465 21st Ave South,
Nashville, TN, USA
E-mail: vera.c.blau@vanderbilt.edu

Learning to associate auditory information of speech sounds with visual information of letters is a first and critical step for becoming a skilled reader in alphabetic languages. Nevertheless, it remains largely unknown which brain areas subserve the learning and automation of such associations. Here, we employ functional magnetic resonance imaging to study letter–speech sound integration in children with and without developmental dyslexia. The results demonstrate that dyslexic children show reduced neural integration of letters and speech sounds in the planum temporale/Heschl sulcus and the superior temporal sulcus. While cortical responses to speech sounds in fluent readers were modulated by letter–speech sound congruency with strong suppression effects for incongruent letters, no such modulation was observed in the dyslexic readers. Whole-brain analyses of unisensory visual and auditory group differences additionally revealed reduced unisensory responses to letters in the fusiform gyrus in dyslexic children, as well as reduced activity for processing speech sounds in the anterior superior temporal gyrus, planum temporale/Heschl sulcus and superior temporal sulcus. Importantly, the neural integration of letters and speech sounds in the planum temporale/Heschl sulcus and the neural response to letters in the fusiform gyrus explained almost 40% of the variance in individual reading performance. These findings indicate that an interrelated network of visual, auditory and heteromodal brain areas contributes to the skilled use of letter–speech sound associations necessary for learning to read. By extending similar findings in adults, the data furthermore argue against the notion that reduced neural integration of letters and speech sounds in dyslexia reflect the consequence of a lifetime of reading struggle. Instead, they support the view that letter–speech sound integration is an emergent property of learning to read that develops inadequately in dyslexic readers, presumably as a result of a deviant interactive specialization of neural systems for processing auditory and visual linguistic inputs.

Keywords: development; reading; dyslexia; audiovisual; fMRI

Abbreviations: fMRI = functional magnetic resonance imaging; GLM = general linear model

Introduction

Learning to read is an important milestone in individual cognitive development characterized by the complex interplay of various kinds of skills and knowledge (Adams, 1994). However, the first critical step in reading development and the focus of most early reading instruction is to learn the correspondences between visual letters and auditory units of speech (speech sounds) (Ehri, 2005). Successful acquisition of letter–speech sound associations, in turn, has been theorized to be critical for the development of fluent reading skills by impacting the early phases of literacy acquisition (Bradley and Bryant, 1983; Ehri, 2005). Once letter–speech sound associations have been successfully formed they may consequently refine a child's awareness for the existence of isolated speech sounds. Thus, the relationship between reading acquisition and awareness for speech sounds is likely to be reciprocal (Perfetti *et al.*, 1987; Wagner and Torgesen, 1987; Torgesen *et al.*, 1994; Ehri, 2005; Ziegler and Goswami, 2005).

In largely transparent languages, such as Dutch, most school-aged children fully master letter–speech sound associations within one year of reading instruction (Blomert and Vaessen, 2009). Nonetheless, a substantial number of individuals fail to meet the standard criteria for fluent reading even after several years of schooling. Specific reading disorder (or developmental dyslexia), which affects ~4–10% of the population (Esser *et al.*, 1990; Shaywitz *et al.*, 1990; Blomert, 2005), is characterized by persistent difficulties in reading and/or spelling that are unexpected in relation to age, motivation or other cognitive abilities (Lyon *et al.*, 2003). Advances in understanding the origin of dyslexia support a core deficit in phonological processing characterized by difficulties in recognizing and manipulating the sound structure of language (Share, 1995; Snowling, 2001; Vellutino *et al.*, 2004; Shaywitz and Shaywitz, 2005). Although various other factors may play a role as well (Livingstone *et al.*, 1991; Tallal *et al.*, 1993; Stein and Walsh, 1997; Nicolson *et al.*, 2001), impaired phonological awareness constitutes the most common behavioural explanation for reading failure (Ramus, 2003). Given this primacy of phonological deficits and the reciprocity between reading and phonological awareness in dyslexia, it is surprising that the learning of letter–speech sound associations and the neural mechanisms supporting it have hardly been investigated as a function of reading ability.

In literate adults, functional MRI (fMRI) has been employed to reveal the involvement of superior temporal cortex (superior temporal gyrus/superior temporal sulcus) and auditory cortex (Heschl sulcus/planum temporale) in the integration of letters and speech sounds (Raij *et al.*, 2000; van Atteveldt *et al.*, 2004, 2007). More importantly, we recently tested the hypothesis that dyslexic adult readers differ from controls in letter–sound integration (Blau *et al.*, 2009). The results showed that, relative to fluent readers, dyslexic readers underactivate the superior temporal gyrus for the integration of passively presented letter–speech sound stimuli. This reduced integration was directly associated with reduced auditory processing of speech sounds, which in turn

predicted performance on phonological tasks. This finding suggested that the ability to integrate letters efficiently with speech sounds might indeed be one of the direct neurofunctional correlates of reading failure. Intervention studies furthermore provide good evidence for the relevance of letter–speech sound associations in learning to read as many training protocols include a condition focused on teaching such associations (Simos *et al.*, 2002; Aylward *et al.*, 2003; Shaywitz *et al.*, 2004; Eden *et al.*, 2004). A consistent result seen in these studies has been behavioural improvements in reading ability as well as changes in brain activation in the left temporoparietal cortex. An important question that arises in response to such findings is whether the observed neural deficit in integrating letters and speech sounds resulted from a lifetime of reading difficulties or constituted a more fundamental problem instrumental in producing later reading failure.

To date, paediatric fMRI studies have not directly investigated the associations of letters and speech sounds. Instead, often complex phonological tasks have been employed to study reading impairments in children, such as pseudoword reading or visual rhyming (Temple *et al.*, 2001; Shaywitz *et al.*, 2002; Cao *et al.*, 2006; Hoeft *et al.*, 2007). These studies converge on the finding of underactivation in perisylvian cortex and occipito-temporal gyri in dyslexia. Moreover, deviant patterns of activation in frontal cortex are reported in some but not all child fMRI studies (Maisog *et al.*, 2008; Gabrieli, 2009). What is not clear from these studies is to what degree the rather complex phonological tasks tap into the neural mechanisms related to the processing of the most basic orthographic and phonological stimuli (letters, speech sounds) and their combinations.

Given the relevance of letter–speech sound associations for learning to read and reading failure, the main goal of the present fMRI study was to investigate directly the neural correlates subserving the processing and integration of letters and speech sounds in early reading development. In contrast to previous developmental fMRI studies, we used a basic perceptual task in an attempt to study stimulus-induced rather than task-induced group differences in neural activity. Moreover, the two reading groups in the present study were well-matched in age and educational standard, in order to control for maturational and experiential changes that otherwise might interfere with reading-related group effects. Importantly, the selected age range coincides with the earliest time in development at which reading disabilities are typically diagnosed and hence one of the earliest possible time-points to investigate the neurocognitive basis of letter–speech sound integration in dyslexia. An additional goal of the present study was to investigate whether potential letter–speech sound integration deficits in dyslexic children are related to the processing of those same stimuli presented in unisensory conditions. Given the proposed reciprocal connection between speech and print (Ziegler and Goswami, 2005), insights into the neurofunctional mechanisms supporting the visual, auditory and audiovisual aspects of letter–speech sound processing seem critical

for understanding the emergence of reading difficulties in dyslexia. Finally, we examined whether the neural processing of letters, speech sounds and their combination correlated with behavioural performance on reading and reading-related tasks to further probe the hypothesis that a neural deficit in letter–speech sound integration is indeed predictive of reading failure.

Methods

Participants

Eighteen children with a diagnosis of dyslexia [mean age: 9.39, standard deviation (SD): 0.43, one female] and 16 children without reading impairment (mean age: 9.43, SD: 0.44, four females) participated in the study. All subjects were healthy, right-handed, native Dutch speakers with normal or corrected-to-normal vision and normal audition. Dyslexic subjects were recruited via the Dutch Regional Institute for Dyslexia and diagnosed using an extensive, standardized cognitive-behavioural test procedure. Non-impaired readers were recruited via local schools. The groups were matched for educational level, age, handedness and IQ, (≥ 85 , Wechsler Intelligence Scale estimated IQ within 1 SD of norm) and were tested on various measures for reading status using a standard test battery (Blomert and Vaessen, 2009). These included a computerized reading test consisting of three levels of difficulty comprising high-frequency, low-frequency and pseudowords. Two measures were derived from this test: overall reading score, reflecting a combination of speed and accuracy (number of correct words read in 1.5 min), and a separate accuracy score (number of words read correctly/ total number of words read). Next to the reading test, the battery further included a phoneme-deletion task in order to assess subjects' phonological abilities, a decoding (i.e. spelling) task and a letter-to-sound matching task. Criteria for dyslexia were based on a discrepancy score between performance on the reading test and IQ, according to which children with a standard reading score within the lower 10th percentile, but average IQ score were classified as dyslexic (Table 1). Informed consent was obtained from children and parents, in accordance with the local ethical guidelines.

Stimuli and task design

Stimuli were visual letters and auditory speech sounds corresponding to Dutch single letters (consonants: b, d, g, h, k, l, n, p, r, s, t, z; vowels: a, e, i, y, o, u) adapted from van Atteveldt *et al.* (2004). Stimuli were presented using the software Presentation (Neurobehavioral Systems Inc., Albany, USA) in blocks corresponding to four experimental conditions: unisensory letters, unisensory speech

sounds, multisensory congruent letter–speech sound pairs, multisensory incongruent letter–speech sound pairs. During multisensory stimulation, stimuli were presented simultaneously. The experiment included four experimental runs, eight blocks and nine fixation periods each. One block (20.8 s) consisted of four miniblocks (see 'image acquisition'). Each block contained 16 stimuli (four per miniblock) and was repeated twice per run, resulting in 128 stimuli per condition. The order of blocks was pseudo-randomized within runs and the order of runs was counterbalanced across subjects. Children were instructed to listen carefully to the speech sounds and/or view the letters. To ensure that children attended to the stimuli, a line drawing ('nemo'-fish), a voice (saying 'nemo'), or a combination of the two was presented (8/128 trials or every 45 s on average) pseudo-randomized. Children were instructed to detect the stimuli by pressing a button.

Image acquisition

All children were acquainted to the scanning environment and trained to hold still using a simulation scanner. In the actual fMRI session, blood-oxygen-level-dependent signals were measured using a 3 T Siemens head scanner (Allegra; Erlangen, Germany). Functional MRI data were acquired using a T_2^* -sensitive gradient echo planar imaging sequence covering the whole-brain (24 slices, slice-thickness 4.5 mm, 3×3 in-plane resolution, repetition time = 5.2 s, slice/echo time = 63/32 ms, field of view: 192 mm², matrix size: $64 \times 64 \times 24$). Volume acquisition time was 1.5 s followed by a silent delay of 3.7 s in which stimuli were presented, resulting in a total repetition time of 5.2 s. The long inter-scan delay was used to minimize the effects of scanning noise on experimental activation (van Atteveldt *et al.*, 2004). A high resolution T_1 -weighted anatomical image (voxel size: $1 \times 1 \times 1$ mm³) was acquired for each subject using a three dimensional gradient echo sequence (Alzheimer's Disease Neuroimaging Initiative-magnetization prepared rapid gradient echo 192 slices, 1 mm slice-thickness, repetition time = 2.25 s, echo time = 2.6 ms, flip angle = 9 degrees, matrix size: 256×256) optimized for morphometric analyses of MRI data across platforms (Jack *et al.*, 2008).

fMRI data analysis and statistics

Imaging data were analysed using BrainVoyager QX (Brain Innovation, Maastricht, the Netherlands). Functional data were preprocessed to correct for slice scan time differences (using sinc interpolation), 3D motion artifacts (trilinear interpolation), linear drifts, and low-frequency non-linear drifts (high pass filter ≤ 3 cycles/time course). No spatial or additional temporal smoothing was applied. Functional data were then co-registered with the anatomical volume and transferred into standard stereotaxic space using Talairach normalization (Talairach and Tournoux, 1988).

Table 1 Offline behavioural performance

	Phoneme deletion				Phonological decoding				Reading				Letter–speech sound matching			
	Cont	Dys	t^a	Sig.	Cont	Dys	t^a	Sig.	Cont	Dys	t^a	Sig.	Cont	Dys	t^a	Sig.
Accuracy (sum score)	84	57	3.9	0.00	89	69	5.1	0.00					91	90	0.7	0.49
Speed (seconds)	2.6	6.1	−6	0.00	2.4	3.9	−5.4	0.00					1.4	1.9	−3.6	0.00
Accuracy + speed ^b (percentile score)									64	7.0	8.1	0.00				

a Between-group t -values are reported at $df = 32$; Cont = fluent readers; Dys = dyslexic readers.

b Percentile scores are based on Dutch norms for elementary-school children (Blomert and Vaessen, 2009).

Statistical maps were generated by modelling the evoked haemodynamic response for all four conditions (letters, speech sounds, congruent letter–speech sound pairs, incongruent letter–speech sound pairs) as boxcars convolved with a two-gamma haemodynamic response function in the context of the general linear model. Population-level inferences concerning blood-oxygen-level-dependent signal changes between the experimental conditions were based on a random effects model with predictors separated for each subject. Statistical comparisons between conditions were based on percentage-normalized beta values.

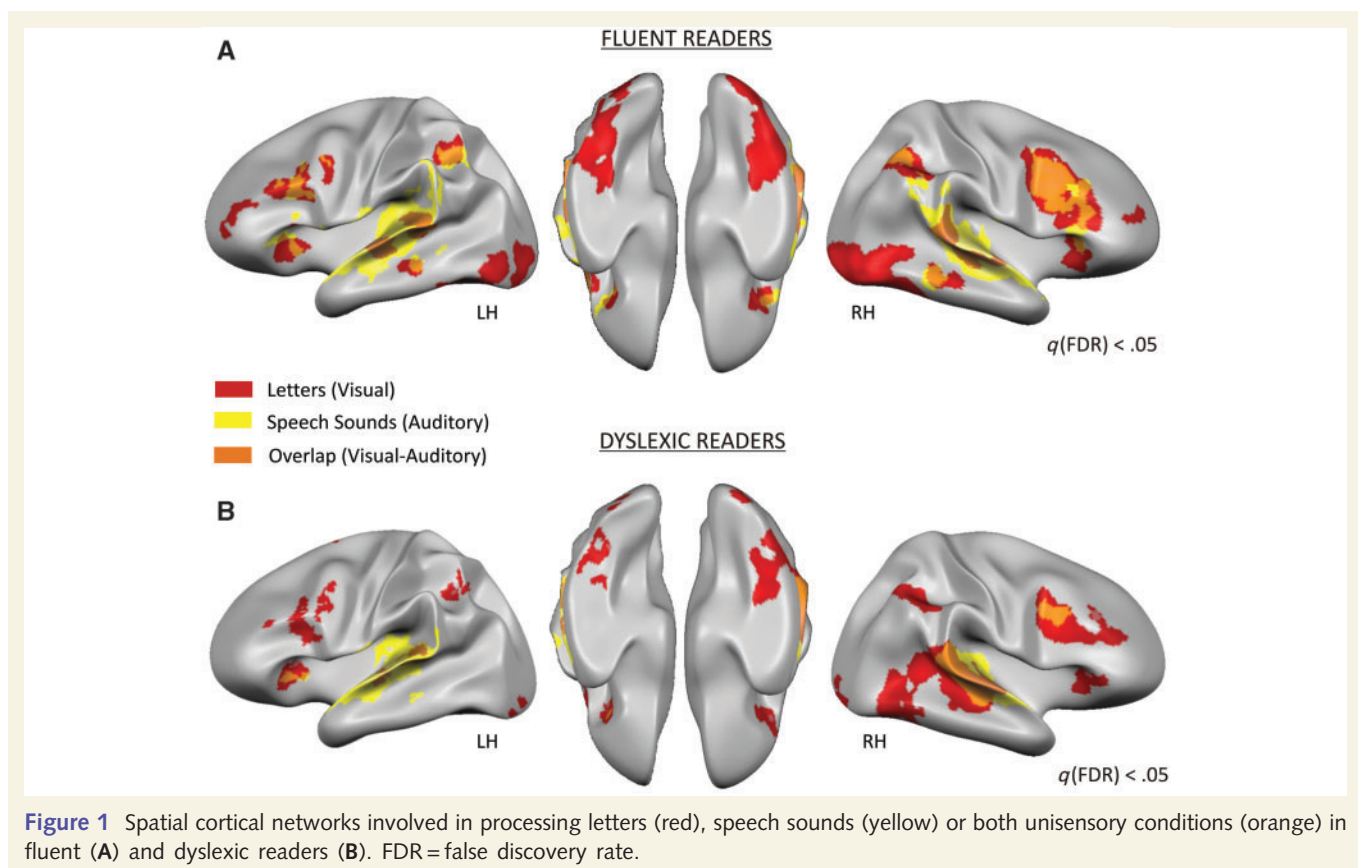
The first general linear model (GLM1) was a single-factor model including the four conditions as separate predictors used to determine brain regions involved in processing unisensory and multisensory processing across all subjects. Moreover, two separate general linear models were computed for fluent and dyslexic readers in order to evaluate the spatial pattern of activation in each reading group separately (GLM2 and GLM3, Fig. 1). The beta values from GLM1 served as input for the calculation of statistical comparisons based on reading ability. Brain regions sensitive to the interactions between reading status and letter–speech sound congruency were of particular interest as they reflect the differential processing of the learned letter–speech sound association between fluent and dyslexic readers. To test this hypothesis, a 2×2 factorial model including ‘reading status’ (fluent, dyslexic) and ‘multisensory condition’ (congruent, incongruent) was computed including the interactions between the two factors (GLM4). A corresponding analysis including the ‘unisensory conditions’ was used to compare dyslexic and fluent readers on the processing of letters and speech sounds in isolation (GLM5). All between-group comparisons were restricted to voxels activated by either of the unisensory conditions (visual > baseline or

auditory > baseline) by application of a functional mask. No voxels were exclusively activated by letter–sound pairs and not by isolated letters or sounds.

In order to identify an area as the multisensory integration site we used the congruency effect, defined as the difference between congruent and incongruent letter–speech sound pairs (van Atteveldt *et al.*, 2007; Doehrmann and Naumer, 2008).

Depending on the specificity of the contrast, multisubject statistical maps were corrected for multiple comparisons using the false-discovery rate (Genovese *et al.*, 2002) or cluster-size thresholding (Forman *et al.*, 1995; Goebel *et al.*, 2006). For GLM4 (i.e. the interaction between ‘multisensory condition’ and ‘reading status’), an initial voxel-level threshold was set to $P < 0.01$ ($t = 5.1$) uncorrected resulting in a cluster level of 115 mm^3 (four contiguous voxels) after 1000 iterations and a corresponding corrected false-positive probability of 5% or less. For GLM5 (i.e. the direct comparisons between control and dyslexic readers on the auditory or visual condition), an initial voxel-level threshold was set to $P < 0.01$ ($t = 2.5$) uncorrected, resulting in a minimum cluster of 168 mm^3 (five contiguous voxels) at a false-positive probability of 5% or less.

Behavioural data used for correlation-analysis were corrected for outliers, defined as values deviating more than two standard deviations from the mean (Moore and McCabe, 1999). Rejected data points were replaced by the closest maximum or minimum value. Unless otherwise indicated all correlation coefficients were calculated using linear correlation statistics (Pearson’s R). In addition, we used stepwise multiple linear regressions in order to determine which of the fMRI group effects explain a significant portion of independent variance in reading performance. Independent variables in this analysis were percentage signal change values related to (i) the congruency effect



in planum temporale/Heschl sulcus and superior temporal sulcus, (ii) the response to speech sounds in anterior superior temporal gyrus, planum temporale/Heschl sulcus and superior temporal sulcus and (iii) the response to visual letters in fusiform gyrus. Only brain regions showing a differential response between dyslexic and fluent readers were included in the analysis to investigate the effect of reading ability on the link between performance measures and cortical responses. Given the left-lateralization of the effect in planum temporale/Heschl sulcus, we furthermore restricted this analysis to regions of interest in the left hemisphere.

In order to assess co-linearity, the variance inflation factor was computed for each variable. For all independent variables the variance inflation factor was between 1.05 and 2.29 and hence multi co-linearity was considered of no concern for the present model.

Results

Attention task

Both reading groups performed at ceiling for the detection of visual, auditory and audiovisual attention control stimuli (fluent: mean = 97.91, SEM = 1.55; dyslexic: mean = 99.08, SEM = 0.55). In addition, non-impaired and dyslexic readers responded equally fast to attention stimuli (fluent: mean = 575 ms, SEM = 16.1; dyslexic: mean = 609 ms, SEM = 14.0; $P = 0.10$), indicating that attention levels were comparable across reading groups.

Offline behaviour/diagnostic testing

As can be seen in Table 1, the performance of dyslexic children on reading-related tasks outside the scanner was poor compared to their fluently-reading peers. Specifically, dyslexic readers showed impaired reading (within the lower 10th percentile on a standardized test of word reading) and poor performance on subtests involving phonological awareness and phonological decoding (Table 1).

fMRI results

Unisensory activations

In order to assess the basic networks involved in the processing of speech sounds and letters presented in isolation, we compared visual and auditory conditions against baseline in each reading group. Figure 1 provides an overview of the spatial cortical network involved in viewing letters (red) and listening to speech sounds (yellow) for fluently reading and dyslexic children. Orange brain regions represent convergence zones where activity for visual and auditory stimuli overlapped.

Between-group statistical comparisons revealed two brain regions that were differentially activated for processing unisensory stimuli in fluent compared to dyslexic readers (Fig. 2). Dyslexic children showed weaker activity for processing speech sounds in the anterior superior temporal gyrus (Fig. 2A) and for processing

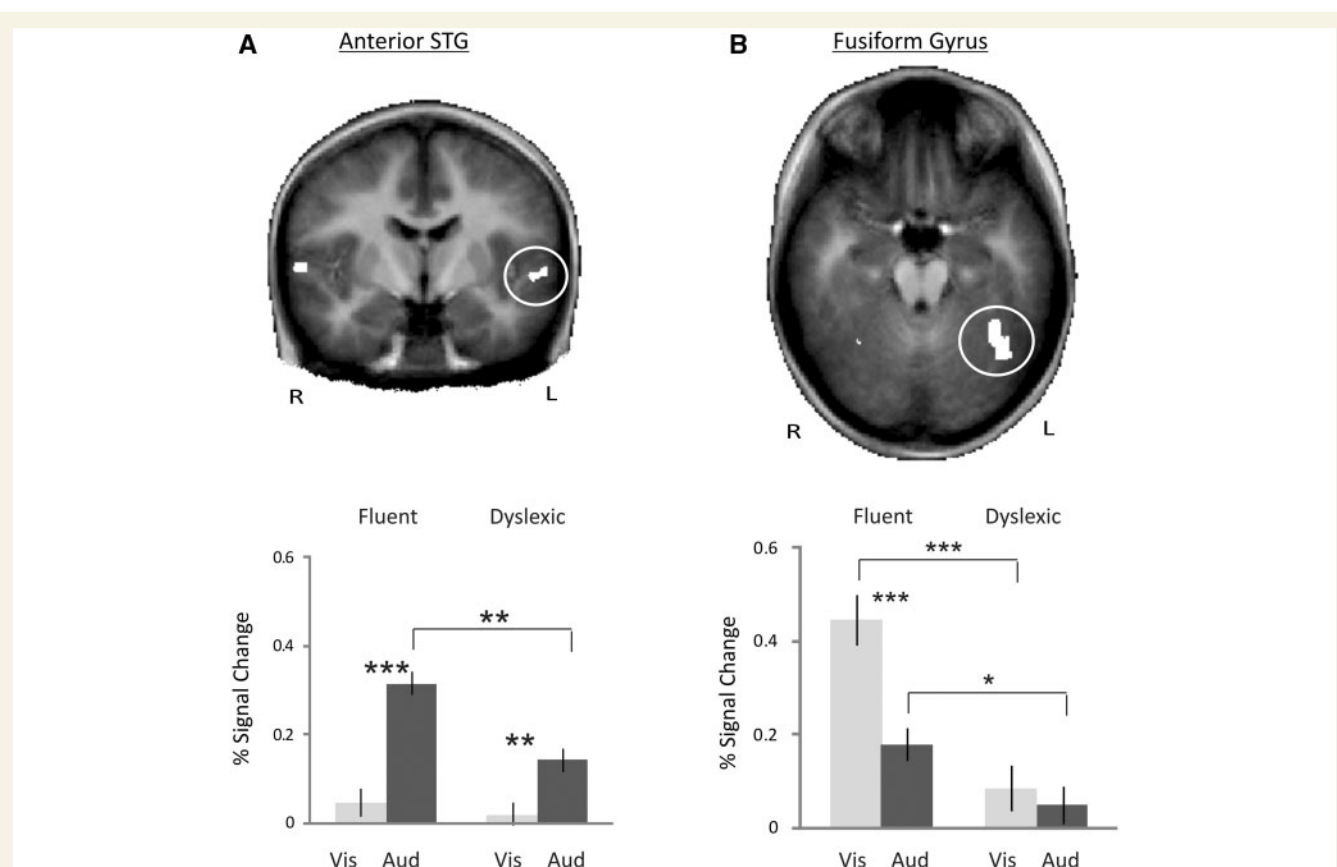


Figure 2 Mean percent signal change and standard error of mean (SEM) are shown for the unisensory group effects in the left anterior superior temporal gyrus (STG) (A), and the left fusiform gyrus (B) projected on the average anatomy ($n = 34$). Vis = visual; aud = audio.

Table 2 Region of Interest details and statistics per analysis

Brain area	Hemisphere	Talairach coordinates			Voxels	Effect size		Statistical test ^b
		X	Y	Z		F, t-value ^a	P-value	
PT/HS	Left	−42	−28	13	117	16.7	0.00	Interaction group × Congruency
STS	Left	−56	−33	4	171	7.73	0.01	
STS	Right	58	−33	3	225	8.34	0.01	
aSTG	Left	−51	−8	1	171	2.89	0.01	Control AUDITORY – Dyslexic AUDITORY
aSTG	Right	57	−8	7	169	2.8	0.01	
FG	Left	−36	−51	−17	315	3.83	0.00	Control VISUAL – Dyslexic VISUAL
FG	Right	36	−55	−11	268	4.51	0.00	

Abbreviations: PT/HS = planum temporale/Heschl sulcus; STS = superior temporal sulcus; aSTG = anterior superior temporal sulcus; FG = fusiform gyrus.

a Average *t*-value and *P*-value across all voxels in a region of interest.

b Statistical tests used for region of interest selection (corrected for cluster size at alpha = 5%).

letters in an area around the fusiform gyrus bilaterally (Table 2 and Fig. 2B). Interestingly, dyslexics also displayed less activity for speech sounds in this same fusiform gyrus (visual letter) area. No other area of activation survived the correction for cluster size.

Multisensory activations

The further goal of the analysis was to identify areas for the integration of letters and speech sounds in dyslexic versus fluent readers by computing the interaction between ‘reading status’ and ‘multisensory condition’ (congruent versus incongruent letter–speech sound pairs). The results revealed a significant interaction in the dorsal part of the left superior temporal gyrus (planum temporale) in close proximity to primary auditory cortex (Heschl sulcus) (Table 2). An investigation of the time courses in planum temporale/Heschl sulcus revealed the presence of a strong effect of multisensory congruency in fluent readers (Fig. 3, top right). This effect was absent in the dyslexic group.

Next, we assessed how the unisensory conditions contributed to the observed between-group congruency difference. Figure 3A (bar graphs) shows the average fMRI signal change in the planum temporale/Heschl sulcus interaction cluster for the multisensory and unisensory conditions in both reading groups. The planum temporale/Heschl sulcus exhibits a clear auditory-specific activation profile in both reading groups. However, the absolute strength of the auditory response was reduced in dyslexia.

In addition to planum temporale/Heschl sulcus, a bilateral cluster in superior temporal sulcus showed a significant group-by-congruency interaction (Table 2). Both activation-clusters were located within the middle portion of the superior temporal sulcus (Fig. 3B). Comparable to planum temporale/Heschl sulcus, fluent readers activated the superior temporal sulcus more for the presentation of congruent as opposed to incongruent letter–speech sound pairs, while dyslexic readers showed no congruency effect. In relation to the auditory response, dyslexic readers did not show any significant modulation in the multisensory conditions based on letter–speech sound congruency. No main effect of reading ability was found for the processing of multisensory letter–speech sound pairs. Table 2 provides a summary of all group effects.

Correlation between unisensory and multisensory cortical responses

Unisensory responses to speech sounds correlated positively with the congruency in planum temporale/Heschl sulcus ($R_{\text{PARTIAL}} = 0.67$, $P = 0.000$) and the left superior temporal sulcus ($R_{\text{PARTIAL}} = 0.41$, $P = 0.019$) even after the factor reading ability was partialled out. Moreover, the visual response in left and right fusiform gyrus correlated with congruency effects in planum temporale/Heschl sulcus (left fusiform gyrus: $R = 0.38$, $P = 0.025$; right fusiform gyrus: $R = 0.37$, $P = 0.030$), with fluent readers showing stronger responses to letters and a stronger effect of letter–speech sound congruency. This effect was non-significant when the factor reading group was partialled out, indicating that it was dependent upon reading ability.

Correlations with performance

We calculated full and partial correlations (controlling for factor group) between performance measures on reading-related tasks and the fMRI response in brain regions showing a differential response between dyslexic and fluent readers in order to focus the analysis on the effect of reading ability. Given the left-lateralization of the effect in planum temporale/Heschl sulcus, we furthermore restricted this analysis to regions of interest in the left hemisphere. Two performance measures were selected for visualization: reading and speed on letter–speech sound matching. Both tasks reliably distinguished fluent from dyslexic readers (Table 1). Letter–speech sound matching was added to the reading measure because the stimuli corresponded closely to those presented during scanning. Furthermore, dyslexic readers were equally accurate on letter–speech sound matching but showed a reliable difference in processing speed. Based on the assumption that faster processing is one of the main indices for the automation of a cognitive process (Schneider and Chein, 2003), correlations of a reaction time measure with the fMRI response could provide evidence for differences in the automation of letter–speech sound integration between reading groups.

Figure 4 illustrates that the fMRI congruency response in planum temporale/Heschl sulcus and superior temporal sulcus correlated positively with accuracy on the reading task and negatively with reaction times on letter–speech sound matching

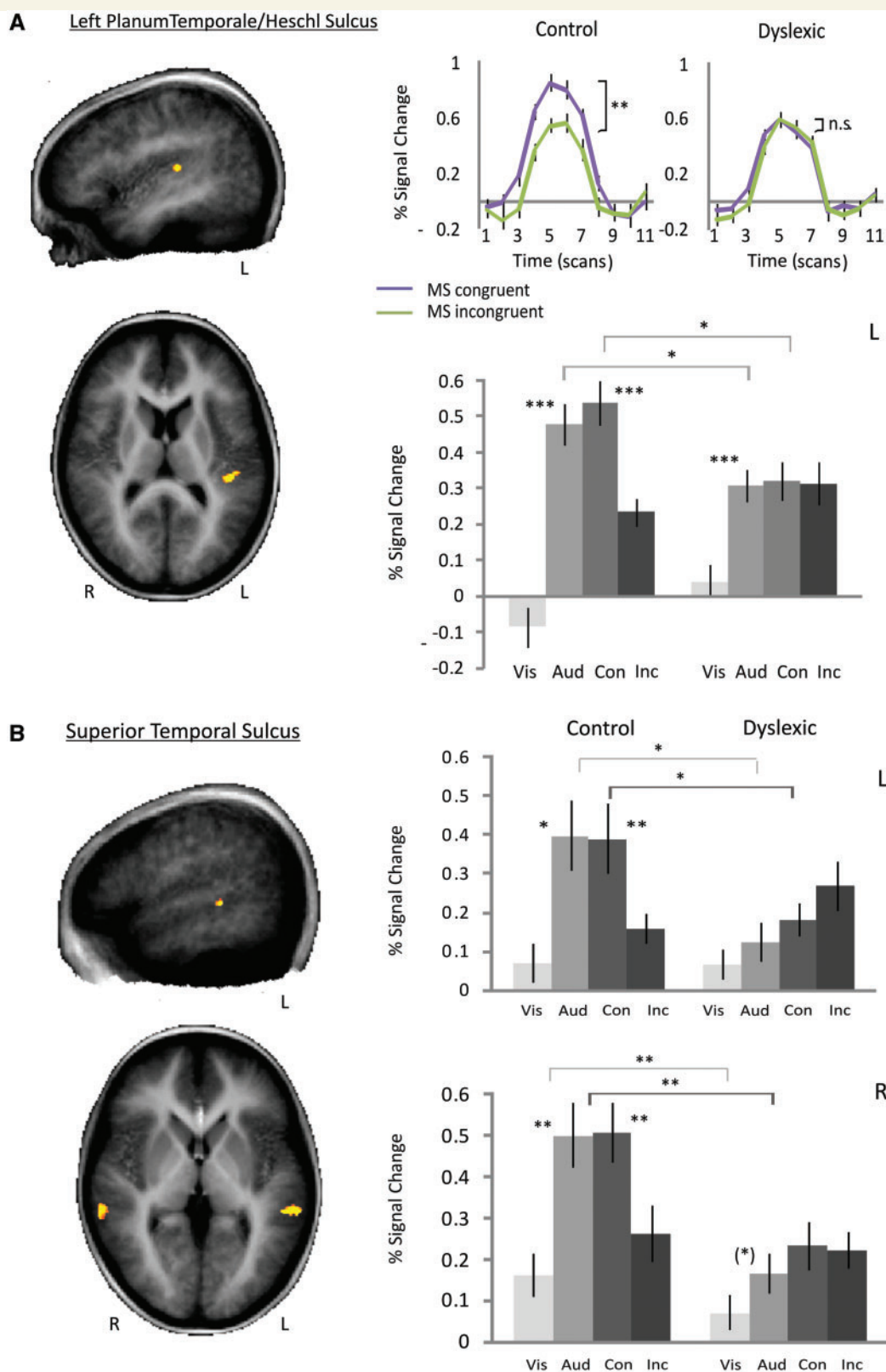


Figure 3 Interaction effect between 'reading group' and 'multisensory condition' (congruent, incongruent) in the planum temporale/Heschl sulcus of the left hemisphere (A) projected on the average anatomy. The right side of the figure depicts the percent signal change and corresponding SEM as a function of time for fluent and dyslexic readers in multisensory congruent (purple line) and incongruent (green line) conditions. Bar graphs illustrate the percent signal change and SEM for the multisensory and unisensory conditions in fluent (left) and dyslexic readers (right) (based on mean % signal change per subject). The interaction site in the left and right superior temporal sulci is shown in (B). Bar graphs illustrate the mean percent signal change in each condition for fluent (left) and dyslexic readers (right) corresponding to the left (top) and right hemispheres (bottom).

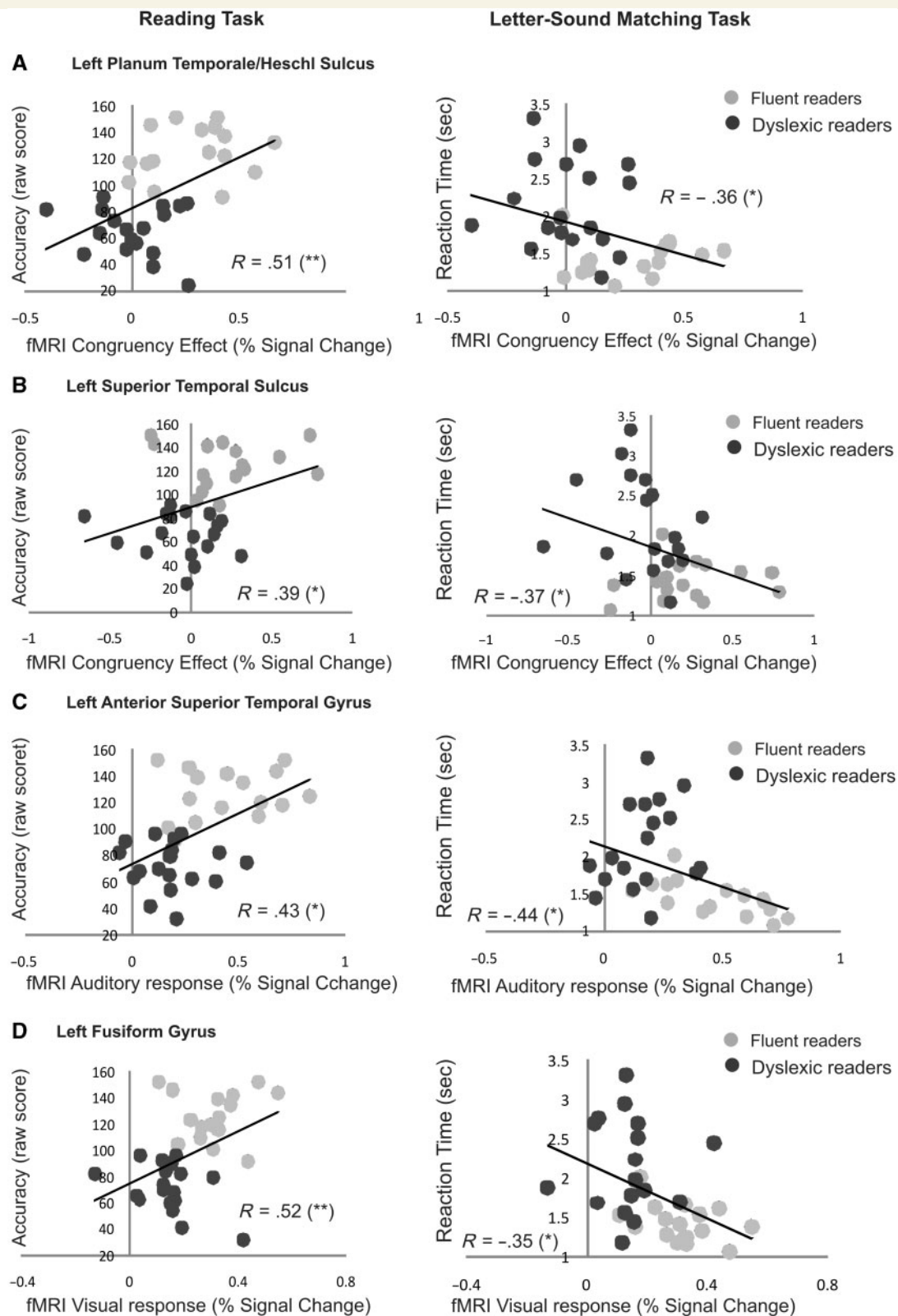


Figure 4 Correlations between reading accuracy as well as speed of letter-speech sound matching and the neural response to congruent versus incongruent letterspeech sound pairs in planum temporale/Heschl sulcus (fMRI congruency effect) (A), the fMRI congruency effecting superior temporal sulcus (B), the auditory response in the anterior superior temporal gyrus (C) and the visual response in fusiform gyrus (D).

(Fig. 4A and B). Moreover, the auditory response in the anterior superior temporal gyrus correlated with reading accuracy and the speed of letter–speech sound matching (Fig. 4C) as did the visual response in the fusiform gyrus (Fig. 4D). All reported correlations turned out to be non-significant when the factor reading group was controlled using partial correlations, suggesting that the brain–behaviour correlations were driven by group differences in reading ability.

We used stepwise and hierarchical multiple linear regression to evaluate further whether the neural responses that correlated strongest with reading performance were the same as the ones explaining independent variance in reading. This analysis included the percent signal change values of all relevant brain areas as predictor variables (Congruency effect: planum temporale/Heschl sulcus, superior temporal sulcus; Auditory response: planum temporale/Heschl sulcus, superior temporal sulcus, anterior superior temporal gyrus; Visual response: fusiform gyrus). In the absence of high co-linearity (see methods), the congruency effect in planum temporale/Heschl sulcus as well as the visual response in fusiform gyrus were both found to cause significant reductions in error variance on the reading task (planum temporale/Heschl sulcus: $R=0.51$, R^2 change=0.27, $F=12.04$; $P=0.002$; fusiform gyrus: $R=0.52$, Combined model: $R=0.62$; R^2 change=0.11, $F=5.73$; $P=0.023$). Together, these two neural effects explained almost 40% of the variance in reading performance ($R^2=0.39$). Auditory effects explained no additional variance that was not already explained by the effect of congruency in planum temporale/Heschl sulcus and superior temporal sulcus, while the congruency effect explained an additional 20% of the variance above and beyond the auditory response to speech. The visual response to letters in fusiform gyrus explained about 11% additional variance beyond the variance already explained through the auditory response and the congruency effect in planum temporale/Heschl sulcus.

Discussion

The main goal of the present study was to investigate whether dyslexic children differ from fluent readers in the processing of letters, speech sounds and their combination. In multisensory conditions, we found weaker effects of congruency in the planum temporale/Heschl sulcus and the superior temporal sulcus of dyslexic children, indicating less successful integration of letters and speech sounds. This effect was accompanied by weaker activation in response to unisensory speech sounds in dyslexic readers in the planum temporale/Heschl sulcus, superior temporal sulcus, anterior superior temporal gyrus and weaker activation to unisensory visual letters in the fusiform gyrus. The congruency effect in the planum temporale/Heschl sulcus and the visual response to letters were, moreover, both found to explain a significant and (largely) independent part of the individual variance in reading performance. Finally, we examined the relation between unisensory and multisensory group effects. We found that the response to speech sounds in the planum temporale/Heschl sulcus and superior temporal sulcus as well as the visual response in the fusiform

gyrus correlated with the strength of the congruency effect in the planum temporale/Heschl sulcus.

Multisensory processing of letters and speech sounds

The present neuroimaging study revealed that dyslexic children differ from fluently reading children in the neural integration of basic letter–speech sound pairs. Fluently reading children activate the planum temporale/Heschl sulcus and superior temporal sulcus more strongly for the processing of congruent compared to incongruent letter–speech sound pairs. In contrast, dyslexic children exhibit little or no modulation of cortical responses to speech sounds in the auditory cortex and superior temporal cortex as a function of audiovisual congruency. As indicated by their adequate accuracy on matching letters and speech sounds in offline behavioural tasks, this deficit could not be explained by dyslexic readers' insufficient knowledge about letter–speech sound correspondences. As the congruency between letters and speech sounds cannot be established unless auditory and visual inputs have been successfully matched (van Atteveldt *et al.*, 2007), reduced congruency effects in dyslexic children are likely to indicate less successful letter–speech sound integration. This finding is in line with more indirect measures of orthographic-phonological processing such as letter rhyming or nonword reading, which has also been linked to reduced activation in superior temporal and temporoparietal brain regions in dyslexic readers (Shaywitz *et al.*, 1998). It furthermore extends earlier neuroimaging investigations in adult dyslexic readers by showing that a deficit in letter–speech sound integration is an emergent property of learning to read and not the result of a lifetime of reading difficulties (Blau *et al.*, 2009), suggesting that the ability to integrate letters efficiently with speech sounds in the planum temporale/Heschl sulcus and superior temporal sulcus might be one of the direct neurofunctional correlates of reading failure.

Our finding that planum temporale/Heschl sulcus and superior temporal sulcus were involved in the integration of letters and speech sounds is in line with previous results in healthy adults (van Atteveldt *et al.*, 2004, 2007). However, the overall extent of activated regions seemed reduced in children, whereas both visual cortex as well as frontal areas were more active in children than in adults. One possible explanation for these 'apparent' differences might be the reduced experience with print in children compared to adults and associated reduced specialization for processing letters and letter-sound associations. This assumption, however, needs further empirical validation. While the superior temporal sulcus is a well-known heteromodal structure that receives input from multiple senses via cortical and subcortical connections (Beauchamp *et al.*, 2004; Macaluso *et al.*, 2004), planum temporale/Heschl sulcus activation has been generally associated with the processing of speech and complex sounds (Binder *et al.*, 1996; Seifritz *et al.*, 2002). In addition, activation in planum temporale has also been related to integration of spoken and written language (Nakada *et al.*, 2001; van Atteveldt *et al.*, 2004), and the learning of new audiovisual associations (Hasegawa *et al.*, 2004).

The present correlation between congruency effects in planum temporale/Heschl sulcus and left superior temporal sulcus and performance on reading-related tasks points to auditory and superior temporal brain structures as potential neuroanatomical correlates linking letter–sound integration and reading skill. More concretely, weaker congruency effects in planum temporale/Heschl sulcus as well as superior temporal sulcus of dyslexic children were associated with lower reading scores, while stronger congruency effects in fluent readers were associated with higher reading scores. These correlations turned out to be non-significant when the factor reading group was partialled out indicating that they indeed reflect an effect of reading ability. In addition, neural integration responses in planum temporale/Heschl sulcus and superior temporal sulcus correlated with the speed of performance on letter–speech sound matching, in the absence of accuracy differences for judging the congruency between letters and sounds. Given that the speed of processing is one of the major indices for automation of a cognitive process (Schneider and Chein, 2003), this finding indicates that a neural deficit in letter–speech sound integration reflects an inability to retrieve or apply knowledge about letter–speech sound associations quickly during reading. This is supported by findings from behavioural (Blomert and Vaessen, 2009) and electrophysiological studies (Froyen *et al.*, 2009) suggesting a dissociation between accuracy and speed in the learning of letter–speech sound associations during development. Although unstable letter–speech sound associations have been suggested as a potential key factor in dyslexia (Share, 1995; Ehri, 2005), this hypothesis has remained largely untested. The present study provides first time empirical support for the planum temporale/Heschl sulcus and superior temporal sulcus as neuroanatomical correlates for a failure to adequately automate letter–speech sound processing skills in dyslexic children.

Unisensory processing and effects of reading ability

Next to investigating the multisensory integration of letters and speech sounds, the present study examined whether dyslexic children differ from fluent readers for the processing of unisensory letters and speech sounds. Overall, our results demonstrate that both dyslexic and fluently-reading children activated a spatially similar network of brain regions for processing letters and speech sounds, in good agreement with previous findings (van Atteveldt *et al.*, 2004; Blau *et al.*, 2009). Nevertheless, group differences for processing unisensory stimuli between dyslexic and fluent readers were observed, localized to planum temporale/Heschl sulcus and superior temporal sulcus (interaction sites) and two additional processing regions in the anterior part of superior temporal gyrus and the fusiform gyrus. The finding that dyslexic subjects underactivate superior temporal brain regions when processing speech sounds is in line with previous paediatric neuroimaging studies that implicated perisylvian cortex including the left superior temporal gyrus (Temple *et al.*, 2001), middle temporal gyrus (Cao *et al.*, 2006; Hoeft *et al.*, 2007), and angular gyrus/supramarginal gyri (Shaywitz *et al.*, 2002) using more complex phonological tasks.

In addition, the neural responses to visual letters in the fusiform gyrus were less pronounced in the dyslexic group. The location of the fusiform gyrus activation was in close proximity to areas previously implicated for the processing of letters or words (Cohen *et al.*, 2002; McCandliss *et al.*, 2003; Cohen and Dehaene, 2004; Flowers *et al.*, 2004). In line with the present results, electrophysiological recordings in dyslexic adults and children have shown that responses for letter-strings in occipito-temporal cortex were reduced in dyslexic readers (Helenius *et al.*, 1999; Maurer *et al.*, 2007). It is interesting to note that in the present data-set, the relatively weak response to speech sounds in the fusiform cortex was also weaker in dyslexic subjects than in fluent readers.

Relation between unisensory and multisensory effects

Lastly, we examined whether unisensory and multisensory neural deficits in dyslexic readers are related in order to improve our understanding of their interactive contribution to reading skill. The present data revealed that the congruency effect in planum temporale/Heschl sulcus and superior temporal sulcus is positively correlated with the neural response to speech sounds, indicating the dependency between phonological processing of speech and letter–speech sound integration in beginning readers. Moreover, we also found significant correlations between the unisensory response to visual letters in fusiform gyrus and the congruency effect in planum temporale/Heschl sulcus that was dependent upon reading ability, suggesting a further association between visual responses to print and letter–speech sound integration. Together, the correlation of the visual response and the auditory response with letter–speech sound integration in planum temporale/Heschl sulcus as a function of reading ability make a case for the existence of an interactive cortical network involved in linking orthographic and phonological representations of print in early reading development. Therefore, we think that the present findings may be best accounted for by reading models that emphasize the reciprocal nature between reading and phonological development.

Strong supporting evidence for the relevance of visual and audiovisual neural responses for reading was gathered using multiple linear regressions. Together, the visual fusiform gyrus response to letters and the congruency effect in planum temporale/Heschl sulcus explained almost 40% of the variance in individual reading performance. The phonological response to speech sounds in planum temporale/Heschl sulcus in contrast was also relevant, but did not explain more variance in reading than the congruency effect alone or in combination with the visual response. In other words, the influence of the auditory response to speech sounds on reading performance was mediated through its relation to visual letters. While these linear regression results should be treated with caution because of the small sample size of neuroimaging studies, they certainly indicate a dominant role for letter–speech sound integration and visual processing in early reading performance.

Conclusion

In summary, the present data provide first evidence for a neural deficit in the integration of letters and speech sounds in dyslexic children localized to auditory cortex and the superior temporal sulcus. These neurofunctional effects closely resemble those seen in adult dyslexia. This suggests that letter-speech sound integration is an emergent property of learning to read that develops inadequately in dyslexic readers, presumably as a result of a deviant interactive specialization of neural systems for processing auditory and visual linguistic inputs.

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