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Report

Reduced Neural Integration of Letters and Speech Sounds Links Phonological and Reading Deficits in Adult Dyslexia

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Summary

Developmental dyslexia is a specific reading and spelling deficit [1] affecting 4% to 10% of the population [2, 3]. Advances in understanding its origin support a core deficit in phonological processing [4–6] characterized by difficulties in segmenting spoken words into their minimally discernable speech segments (speech sounds, or phonemes) [7, 8] and underactivation of left superior temporal cortex [9, 10]. A suggested but unproven hypothesis is that this phonological deficit impairs the ability to map speech sounds onto their homologous visual letters, which in turn prevents the attainment of fluent reading levels [7, 11]. The present functional magnetic resonance imaging (fMRI) study investigated the neural processing of letters and speech sounds in unisensory (visual, auditory) and multisensory (audiovisual congruent, audiovisual incongruent) conditions as a function of reading ability. Our data reveal that adult dyslexic readers underactivate superior temporal cortex for the integration of letters and speech sounds. This reduced audiovisual integration is directly associated with a more fundamental deficit in auditory processing of speech sounds, which in turn predicts performance on phonological tasks. The data provide a neurofunctional account of developmental dyslexia, in which phonological processing deficits are linked to reading failure through a deficit in neural integration of letters and speech sounds.

Results and Discussion

Successful acquisition of basic letter–speech-sound (LS) mappings is crucial for attaining fluent reading skills [12]. Functional magnetic resonance imaging (fMRI) in nonimpaired readers has identified heteromodal superior temporal sulcus and gyrus (STS and STG) as well as auditory cortex (heschl sulcus [HS] and planum temporale [PT]) as integration sites for letters and speech sounds [13, 14]. Reading problems in dyslexia have been primarily associated with a deficit in adequately representing the smallest speech segments (speech sounds, or phonemes) [7, 8], which in turn has been suggested to interfere with the acquisition of LS mappings and hence with the progression from letter-by-letter to fluent, automated reading [7]. The present fMRI study examined the neurofunctional correlates of LS integration as a function of reading ability. Thirteen nonimpaired readers and 13 dyslexic readers, matched for educational level, age, handedness, and IQ (Wechsler Intelligence Scale for Adults, standard scores for nonimpaired = 11.15, for dyslexic = 10.42), were tested on a battery of measures for reading status. All dyslexic readers showed impaired reading (within the lower tenth percentile on a standardized test of word reading) and poor performance on subtests involving phonological awareness, phonological decoding, and spelling (see Supplemental Data available online). Letters and speech sounds were presented during scanning in four experimental conditions: visual, auditory, audiovisual congruent, and audiovisual incongruent.

In the first step of the fMRI analysis, we assessed the relative contribution of unisensory auditory and visual conditions against the baseline by using a multisubject general linear model (*GLM 1*) for each reading group.

Figure 1 demonstrates that dyslexic and nonimpaired readers activated a comparable network of brain regions in response to unisensory presented letters (occipito-temporal cortex and inferior-parietal lobule, shown in green) and unisensory speech sounds (HS, PT, and STG, shown in red). Furthermore, cortical sites that were activated for both unisensory stimuli in fluent and dyslexic readers were found in the lower bank of STG and STS, structures previously implicated in LS convergence and integration [14] (see Supplemental Data).

In the second step, we examined potential group differences in LS processing between dyslexic and fluent readers by computing the interaction between "reading status" and "experimental condition" with a mixed 2 × 4 factorial model (*GLM2*). No main effect of reading status was found, but the interaction with condition revealed an STG bilateral cluster anterior-lateral to primary auditory cortex (Figure 2A; $F_{3, 72}$ = 14.3, p = .000 left, $F_{3, 72}$ = 7.3, p = .000 right Talairach coordinates, x = −46, y = −26, z = 6 (left) and x = 45, y = −22, z = 7 (right)). Here, the BOLD responses in the dyslexic group were reduced for unisensory presentations of speech sounds (t_{24} = 4.99, p = .000 [left] and t_{24} = 3.79, p = .001 [right]) and congruent LS pairs (t_{24} = 3.85, p = .001 [left] and t_{24} = 2.59, p = .016 [right]) (Figure 2B). Although these differential effects seemed slightly lateralized to the left hemisphere, the statistical interaction with the hemisphere in STG did not reach significance.

To assess whether the activation differences in STG reflect discrepancies in multisensory LS integration between dyslexic and nonimpaired readers, we used two complementary statistical criteria. The congruency criterion, which indexes integration through stronger responses to congruent than to incongruent LS pairs (represented as AV congruent > AV incongruent) directly evaluated the processing of the learned

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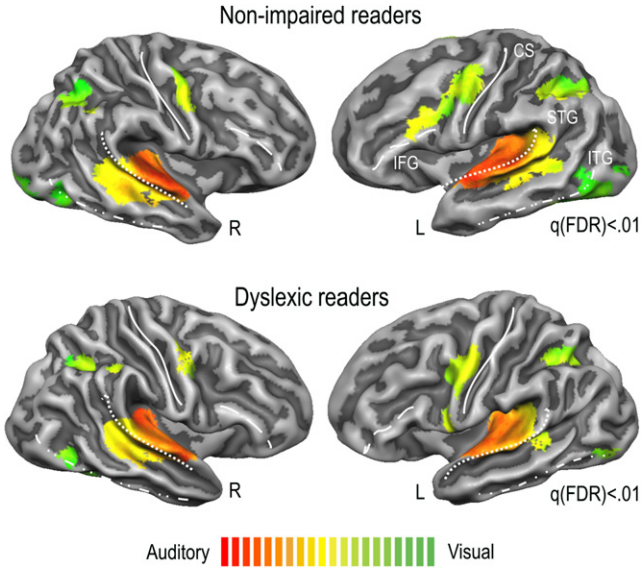

Figure 1. Activation for Letters and Speech Sounds

Response pattern for regions processing speech sounds (red), letters (green) or both unisensory conditions (yellow) in non-impaired (upper panel) and dyslexic readers (lower panel).

audiovisual relatedness between letters and speech sounds. Consistent with previous results [14, 15], we found that nonimpaired readers showed stronger activation for congruent than incongruent LS pairs in bilateral STG (t_{12} = 5.53, p = .000 left, t_{12} = 6.72, p = .000 right). In contrast, dyslexic readers showed no such activation difference, indicating reduced LS integration. Importantly, this effect cannot be explained by dyslexic readers' insufficient knowledge about LS mappings because they were highly accurate in judging the congruency of LS pairs in offline behavioral tasks (see Supplemental Data). Yet, dyslexic readers were significantly slower than nonimpaired readers, indicating less automatic processing of LS mappings [15, 16].

The second criterion we used to determine LS integration in STG was the multisensory interaction index (MSI) [17]. The MSI represents the multisensory response (MS) relative to the maximally unisensory response (US_{max}), where positive MSI values indicate response enhancement and negative values indicate response suppression (MSI = ([MS − US_{max}]/US_{max}) × 100). Using the MSI in addition to the congruency criterion is particularly useful in the present study, where dyslexic readers showed reduced activation for unisensory presentations of speech sounds, because it accounts for individual differences in unisensory response strength when one is classifying an area as an integration site. We found that nonimpaired readers exhibited response suppression in bilateral STG for incongruent LS pairs in comparison to the maximal unisensory response (t_{12} = −3.92, p = .002 [left] and t_{12} = −4.09, p = .002 [right]), whereas dyslexic readers failed to show such a suppression effect (Figure 2C) (nonimpaired versus dyslexic readers: t_{24} = −3.19, p = .004 [left] and t_{24} = −2.75, p = .011 [right]). In contrast, dyslexic and nonimpaired

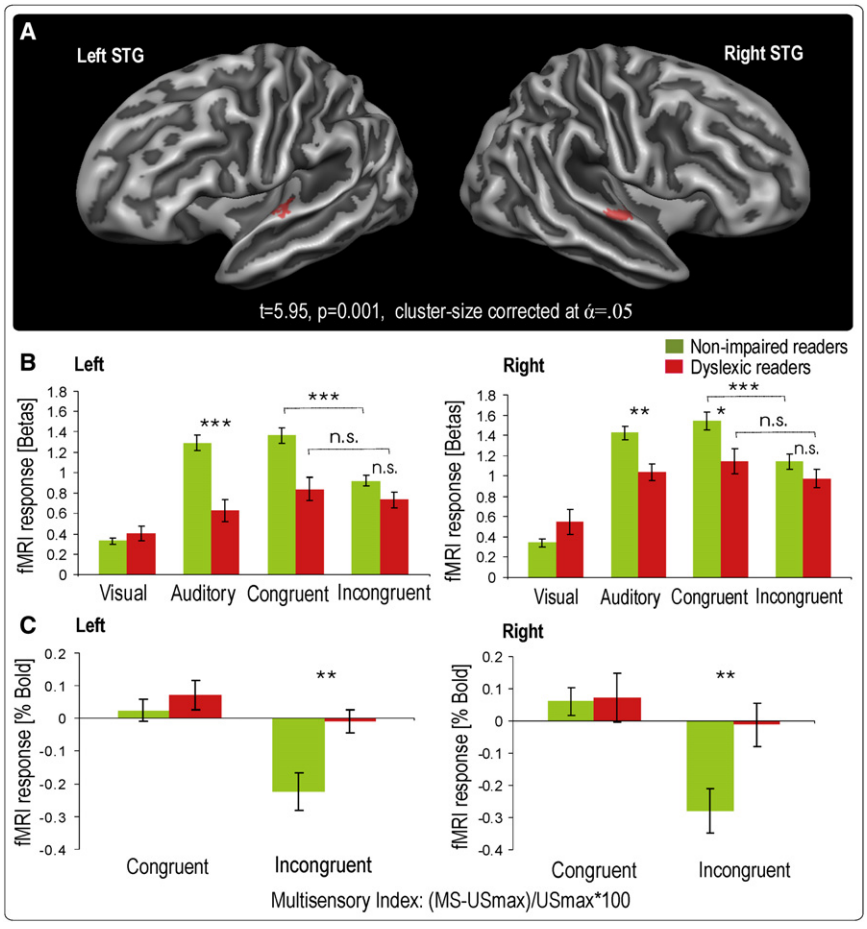

Figure 2. Interaction between Reading Ability and Condition

Group results for the "reading status*condition" interaction analysis (corrected for cluster-size at alpha = .05) projected on inflated cortex-based aligned group map showing clusters in bilateral STG (A). Mean BOLD response and standard error of the mean (SEM) for both reading groups indicates a reduced response to speech sounds and congruent LS pairs in dyslexia (B) and a reduced suppression of incongruent LS pairs relative to the maximal unisensory response (USmax) (C).

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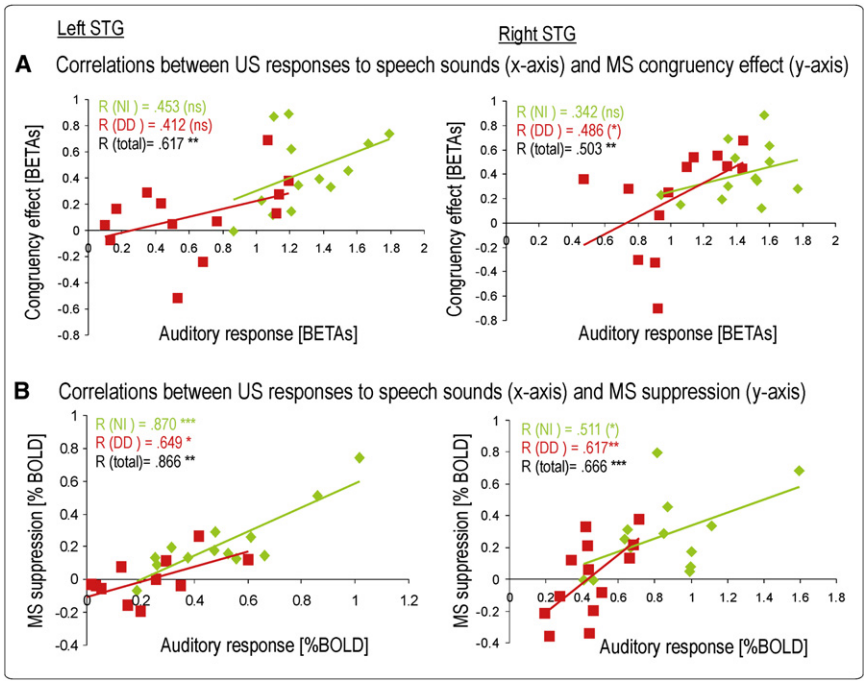

Figure 3. Correlations between the Auditory and Integration Responses

Pearson's correlation coefficients for the unisensory auditory response to speech sounds (*x* axis) and the congruency effect (congruent > incongruent, *y* axis) (A), and the unisensory auditory response to speech sounds (*x* axis) and the multisensory suppression effect (([MS-US_{max}]/US_{max})*100, *y* axis) (B). Note that while the fMRI signal in (A) is expressed in z-normalized beta values, in (B) it is expressed as relative change in BOLD signal in order to avoid the MSI to reach extremely high values for occasionally very low maximal unisensory responses (see methods).

readers showed a comparable weak enhancement for congruent LS pairs. In other words, dyslexic readers failed to modulate the response to speech sounds when those sounds were presented together with both congruent and incongruent visual letters, indicating the weak or absent integration of LS in line with the previous (congruency) analysis.

The absence of multisensory enhancement effects for congruent LS pairs relative to speech sounds might be due to response saturation for processing speech sounds in unisensory conditions, similar to reports from monkey electrophysiology [18]. Although an earlier study reported multisensory enhancement effects for congruent LS pairs in nonimpaired readers [14], the absence of such an effect in the present study is likely to be a consequence of differences in the analysis approach used. Importantly, the congruency effect and the demonstrated suppression effect for incongruent LS pairs are in line with those previous findings, supporting the same overall conclusion that STG is involved in LS integration.

Because dyslexic readers exhibited reduced responses to speech sounds and reduced indices of LS integration in STG, we evaluated how these two measures are related. Unisensory responses to speech sounds correlated positively with the congruency effect in bilateral STG across reading groups (Figure 3A) and with multisensory suppression for incongruent LS pairs across and within reading groups (Figure 3B). Thus, responses to speech sounds correlated with LS integration independently of the statistical criterion used for defining LS integration (congruency versus MSI). Multisensory enhancement effects showed a significant negative correlation with the speech response in the left STG in nonimpaired readers ($R = -.576$, $p = .039$; data not shown), indicating that saturation effects may have prevented the observation of MS enhancement effects. These findings indicate a linear dependence between multisensory integration effects and unisensory responses to speech. The relevance of speech-sound processing in STG for perception and/or behavior was indicated by significant correlations with speed and accuracy of phoneme deletion within the dyslexic group (speed only: $R = -.757$, $p = .003$) and across reading groups ($R = -.651$, $p = .000$) but not within the nonimpaired reading group (see Supplemental Data). Because phoneme deletion is a major diagnostic index of reading problems in dyslexia, this brain-behavior correlation suggests that STG responses to speech sounds are linked to the severity of phonological-awareness deficits in dyslexic individuals.

To further specify the group effects for speech sounds and LS congruency beyond the region of interest revealed in the interaction analysis, we introduced STG position as a variable in the group analysis. This analysis was motivated by models of auditory processing that imply that regions anterior-lateral to primary auditory cortex become gradually more sensitive to speech than to non-speech sounds (from posterior to anterior) [19]. Cortical responses to speech sounds versus the baseline showed a main effect of STG position ($F_{1, 15} = 16.23$, $p = .000$) (Figure 4A), best described as a quadratic trend in both reading groups (nonimpaired: $F_{1, 12} = 52.45$, $p = .000$. Dyslexic: $F_{1, 12} = 108.73$, $p = .000$). t tests comparing the response to speech sounds between groups at each STG location did not reveal significant differences for the functional clusters with two exceptions (y = −31, z = 9, light blue cluster; and y = −45, z = 21, dark blue cluster). The cluster located at the middle of the sampled distribution approximately corresponded to the superior temporal region, as revealed by the group-by-condition interaction analysis (Figure 2A).

The congruency effect showed a main effect of STG position against the baseline ($F_{1, 15} = 3.56$, $p = .024$) and a tendency for a significant interaction of reading group and STG position ($F_{2, 15} = 1.57$, $p = .08$) (Figure 4B). Nonimpaired readers showed an increased congruency effect at anterior STG sites; this effect diminished at more posterior sites (quadratic trend, $F_{1, 12} = 29.18$, $p = .000$) and was not found in the dyslexic group. Group differences for the congruency effect were significant in a range of functional clusters on anterior STG (from y = −24, z = 7 to y = −41, z = 16), showing a weaker congruency effect in dyslexia. Overall, nonimpaired and dyslexic readers showed a rather localized difference in functional sensitivity for speech sounds but differed to a greater extend in functional sensitivity for LS congruency.

The present fMRI study revealed that adult dyslexic readers differ from nonimpaired readers in the neural integration of

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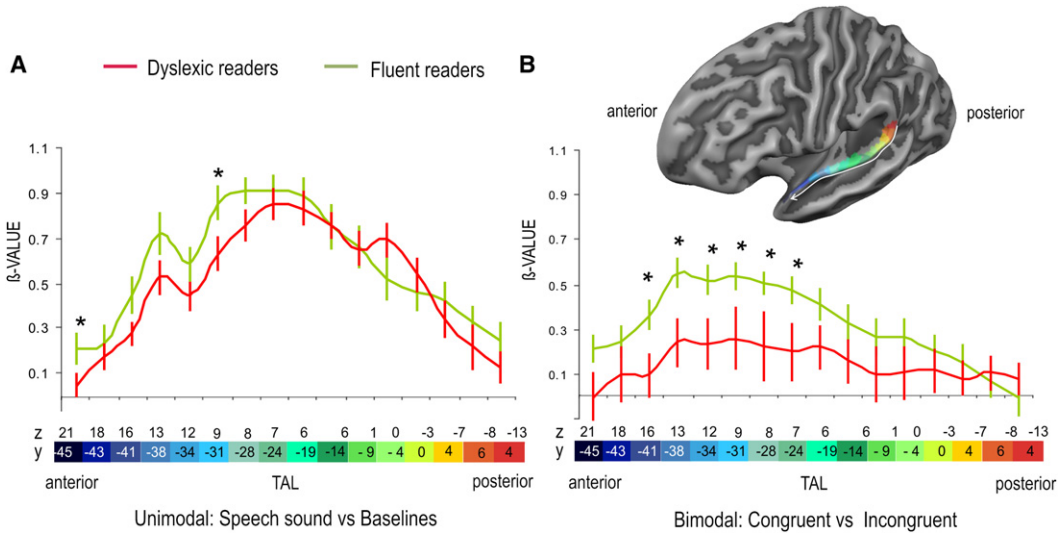

Figure 4. Functional Gradient for Processing Speech Sounds and Letter-Speech Sound Pairs

Mean BOLD response (beta value) and SEM to speech sounds versus baseline (A) and congruent versus incongruent LS pairs (B) as a function of position on left STG from posterior (red) to anterior (blue) (lines: dyslexic readers = red; nonimpaired readers = green).

basic LS pairs within superior temporal brain regions. In line with previous neuroimaging findings in nonimpaired readers [14, 20], cortical responses to speech sounds in STG were modulated by LS congruency, an effect that was more pronounced for nonimpaired than for dyslexic readers. Because the congruency between letters and speech sounds cannot be established unless auditory and visual inputs have been successfully integrated, a reduced congruency effect in dyslexia is likely to reflect less successful LS integration. The gradual rise and fall of the congruency effect along the STG axis for nonimpaired readers furthermore indicates the existence of a functional gradient for processing learned audiovisual associations. This gradient was found to be absent in dyslexia. Whether the origin of this integration deficit is entirely speech specific [21, 22] or has nonlinguistic roots [23, 24] remains to be determined. In addition, recent findings indicate that the LS integration deficit in dyslexia might dissociate from deficits in integrating audiovisual speech [25]. Certainly, a failure to activate key brain structures for integrating information about letters and speech sounds is likely to interfere with the acquisition of automated LS mappings and hence with reading success. This is in line with the prediction that learning and automating LS mappings is a crucial step in literacy acquisition [12] and that this ability is impaired in dyslexia [7].

The present finding that dyslexic readers did not suppress STG activity to incongruent LS pairs supports and extends this conclusion. Suppressive multisensory interactions reflect the downregulation of activity in one sensory modality by cross-modal inputs and have been reported previously for audiovisual speech in studies using fMRI [26] and event-related potentials (ERP) [27]. Decreased responses to incongruent LS pairs relative to speech sounds in nonimpaired readers most likely relate to their evaluation as being nonexisting audiovisual pairs in their language (not associated through learning). Consequently, a failure to suppress incongruent LS pairs in dyslexia indicates the less efficient discrimination of those stimuli from existing audiovisual pairs, which might provide a way to selectively filter distracting orthographic inputs in favor of processing relevant ones. This way of prioritizing relevant information is a core feature of theories on selective attention [28] and has, within modalities, been related to the impaired filtering of behaviorally irrelevant visual information in dyslexia [29].

Importantly, dyslexic readers also showed strongly reduced STG responses to speech sounds, suggesting a deficit in phonetic and/or phonological processing of speech input, which is in line with previous neuroimaging findings [9, 10, 30–32], although the activation focus in the present study was slightly more anterior. Moreover, cortical activity for speech sounds in dyslexic readers correlated strongly with their performance on a classical measure of phoneme awareness (phoneme deletion), which is one of the major indices of reading problems in dyslexia. This finding provides an interesting empirical link between behavioral measures of reading success and cortical processing of speech sounds in superior temporal brain regions.

Correlations between deviant responses to speech sounds and reduced LS integration indicate that these two "deficits" are related, but they raise questions about the nature of this relationship. One possible interpretation is that a phonological-processing deficit in dyslexia precedes a deficit in LS integration, which in turn causes difficulties in learning to read. This precedence of phonological deficits is supported by behavioral studies showing that the phonological skills a person possesses before learning to read predict later reading achievements [33, 34].

Alternatively, LS integration deficits may influence phonological processing of speech. This is supported by the finding that written language learning strongly interacts with phonological perception during development [35] and that LS mapping tasks but not phonological tasks predict later reading deficits in preschool children genetically at risk for dyslexia (G. Willems, H. Poelmans, U. Richardson, and L.B., unpublished data).

Clearly, these explanations are not mutually exclusive. Future LS training and longitudinal developmental studies as well as investigations of multisensory processing of larger linguistic units are necessary to distinguish which deficit

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represents "cause" and "effect" and how this is reflected in the differential recruitment and connectivity of relevant brain regions.

In sum, the present data provide neurofunctional evidence that a basic deficit in the integration of letters and speech sounds in adult dyslexia is one of the proximate causes of reading and spelling failure and may bridge the gap between phonological processing deficits and problems in learning to read.

Experimental Procedures

Thirteen dyslexic readers (mean age = 23.5, standard deviation [SD] = 3.7, 1 female) and 13 nonimpaired readers (mean age = 26.8, SD = 5.4, 4 females) participated in the experiment (a description of the dyslexic sample is available in the Supplemental Data), which was voluntary and in accordance with the Maastricht University ethical guidelines.

The stimuli and presentation design were adapted from [14]. Stimuli were visual letters and auditory speech sounds corresponding to Dutch single letters. Stimuli were presented with Presentation software (Neurobehavioral Systems, Inc.) in blocks corresponding to four experimental conditions: unisensory letters (L), unisensory speech sounds (S), multisensory congruent LS pairs, and multisensory incongruent LS pairs. One block was 20.8 s long, divided into four mini-blocks (5.2 s). During multisensory stimulation, stimuli were presented simultaneously. Subjects passively listened to and/or viewed the stimuli. The experiment included four experimental runs, each composed of eight blocks and alternating fixation periods. Each condition (40 trials) was repeated twice per run. The order of blocks was pseudorandomized within runs, and the order of runs was counterbalanced across subjects.

Blood-oxygen-level-dependent (BOLD) signals were measured with a 3 Tesla Siemens headscanner (Siemens, Erlangen, Germany). Functional MRI data were acquired with a T2*-sensitive gradient echo planar imaging (EPI) sequence covering the whole brain (24 slices, slice thickness 4.5 mm, 3 × 3 in plane resolution, repetition time (TR) = 5.2 s, TRslice/echo time (TE) = 63/32 ms, field of view (FOV) = 192 mm^2, matrix = 64 × 64 × 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 TR of 5.2 s. A high-resolution T1-weighted anatomical image was acquired for each subject (MP-RAGE sequence, 176 slices, 1 mm slice thickness, 1 × 1 in plane resolution, TR = 7.9 s, TE = 2.4 ms, matrix size = 256 × 256).

Imaging data were analyzed with BrainVoyager QX (Brain Innovation, Maastricht, Netherlands [36]). We processed functional data to correct for differences in slice scanning time, 3D motion artifacts, linear drifts, and low-frequency nonlinear drifts (high-pass filter $\leq$ 3 cycles/time course). Functional data were then coregistered with the in-session anatomical volume and transferred into standard stereotaxic space with Talairach normalization [37]. In addition, anatomical and functional images were aligned on the basis of individual curvature information reflecting the gyral and sulcal folding pattern (cortex-based alignment [36]), and shape-averaged folded cortical meshes were created for both hemispheres and groups. We generated multisubject general linear modal (GLM) statistics by modeling the evoked hemodynamic response for all four conditions as boxcars convolved with a two-gamma hemodynamic response function. Population-level inferences were based on second-level random-effects contrasts with predictors separated for each subject. In a first global analysis, unisensory auditory and visual conditions were contrasted against baseline conditions (*GLM 1*), and a relative contribution value was calculated in each voxel for the auditory versus visual predictors $(b^v - b^a)/(b^v + b^a)$. In a second analysis, "reading status" (nonimpaired or dyslexic), "stimulation condition" (L, S, LS, congruent, or LS incongruent; *GLM 2*), and interactions between these two factors were specified.

The false-discover rate (FDR [38]) was used for thresholding multisubject statistical maps for *GLM 1* (Figures 1 and 2). Cluster-size thresholding [36, 39], where setting an initial voxel-level threshold to .001 (t = 4.25) uncorrected resulted in a cluster level of 160 mm^3 after 1000 iterations and a corresponding corrected false-positive probability of 5% or less, was used for *GLM2* (Figures 3 and 4).

Statistical comparisons between conditions within regions of interest were based on z-normalized beta values ($y_{new}[t] = y[t] - mean/SD$) except for the computation of the multisensory interaction index (MSI: ([MS − USmax]/USmax) × 100) [17, 40], which was based on total, baseline-uncorrected percent signal values (baseline (100%) + signal change (e.g., 1.4%) = e.g., 101.4%) so that the MSI would not reach extremely high values for occasionally very low maximal unisensory responses [41] (also see Supplemental Data for a more detailed description of the methods).

Supplemental Data

Supplemental Data include Supplemental Experimental Procedures, two figures, and two tables and can be found with this article online at http://www.current-biology.com/supplemental/S0960-9822(09)00724-6.

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