Altering the Brain Circuits for Reading Through Intervention: A Magnetic Source Imaging Study

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Intervention-related changes in spatiotemporal profiles of regional brain activation were examined by whole-head magnetoencephalography in 15 children with severe reading difficulties who had failed to show adequate progress to quality reading instruction during Grade 1. Intensive intervention initially focused on phonological decoding skills (for 8 weeks) and, during the subsequent 8 weeks, on rapid word recognition ability. Clinically significant improvement in reading skills was noted in 8 children who showed “normalizing” changes in their spatiotemporal profiles of regional brain activity (increased duration of activity in the left temporoparietal region and a shift in the relative timing of activity in temporoparietal and inferior frontal regions). Seven children who demonstrated “compensatory” changes in brain activity (increased duration of activity in the right temporoparietal region and frontal areas, bilaterally) did not show adequate response to intervention. Nonimpaired readers did not show systematic changes in brain activity across visits.

Keywords: Magnetoencephalography, functional brain imaging, dyslexia, phonology, training

Supplemental material: http://dx.doi.org/10.1037/0894-4105.21.4.485.supp

Developmental reading disability is most frequently manifested as a persistent difficulty in acquiring key component skills that normally ensure accurate and fluent word recognition. These skills include phonological processing of spoken language, graphemic analysis, familiarity with the alphabetic principle, phonological decoding, and memory of word forms. This difficulty is typically resistant to regular classroom instruction, yet intensive tutoring or small group instruction has been shown to be very effective in improving reading skills (Lyon, Fletcher, Fuchs, & Chalbro, 2006).

There have been several reports of neurophysiological indices of impaired auditory and visual (print) processing among children and adults with (or at risk for) dyslexia (Breznitz, 2003; Helenius et al., 2002; Molfese et al., 2006). A large number of studies utilizing a variety of brain imaging techniques have demonstrated evidence of reduced engagement of posterior left-hemisphere regions in children with word-level reading disabilities (RDs), along with evidence of increased involvement of frontal lobe and posterior right hemisphere regions (see reviews in Alexander & Slinger-Constant, 2004; Moats, 2004; Noble & McCandliss, 2005; S. E. Shaywitz & Shaywitz, 2004). Given that these differences appear to be present early during the reading acquisition process, often in spite of adequate classroom reading instruction (Simos, Fletcher, Sarkari, et al., 2005), it is imperative to assess whether the aberrant developmental trajectory of the brain mechanism for reading can be altered in RD.

Studies using hemodynamic measures of brain activity in reading tasks before and after brief interventions report both “normalizing” and “compensatory” changes (Aylward et al., 2003; Eden et al., 2004; B. A. Shaywitz et al., 2004; Temple, Deutsch, & Poldrack, 2003). It is important to note that these terms are henceforth used to describe the status of the brain mechanism responsible for reading rather than the phenomenon for which this mechanism is responsible (see Temple et al., 2003). In this framework, normalizing changes were considered to be those that appeared to “restore” the functionality of brain circuits for reading to resemble that observed in typical readers without a history of dyslexia, consisting mainly of increased temporoparietal activity. Compensatory changes were considered to be those indicative of the institution of alternate circuits for reading, consisting mainly of increased hemodynamic responsivity in right temporoparietal and inferior frontal regions.

Although these findings provide very useful insights into the type of functional brain reorganization that takes place in response to systematic reading instruction, they provide little information...
regarding the relative timing of neurophysiological activity. This activity takes place within the first few hundred milliseconds following the presentation of a printed stimulus leading up to the point when a verbal or manual response is produced by the participant. This issue has been addressed in two recent studies with magnetoencephalography (MEG), a method that possesses adequate spatial and temporal resolution and accuracy to meet the aforementioned goal.

In the earlier study conducted with MEG (Simos et al., 2002), 8 children with severe RD 7–17 years of age were tested before and after an 8-week intensive intervention program that focused on the development of phonological awareness and decoding skills (Phonographix; McGuiness, McGuiness, & McGuiness, 1996). All children who had severe reading difficulties showed a clinically significant improvement in reading skills, scoring within the average range on standardized measures of phonological decoding. Neurophysiological changes were also dramatic, consisting primarily of normalizing trends, so that children with RD did not differ from controls in the degree of left temporoparietal activity at the end of the study period. However, the type of whole-head magnetometer device used in that study may not have been sufficiently sensitive to reveal (a) compensatory changes, especially those involving increased activity in inferior frontal regions, and (b) the detailed temporal progression of brain activity among active regions. Moreover, the limited sample did not permit examination of systematic individual differences in the pattern of change in brain activity.

In the second study, spatiotemporal profiles of brain activity were obtained during performance of a reading task involving high-frequency words before and after intensive reading intervention. Participants were 15 Grade 2 children who had failed to show adequate progress in basic reading skills in response to supplemental instruction during Grade 1 (Simos et al., 2007). Before the intervention, brain activity was detected primarily in ventral and lateral extrastriate areas, in the posterior portion of the middle temporal gyrus (Brodmann’s area [BA] 21), and in the inferior frontal and premotor regions, bilaterally. Across three visits, the duration of magnetic activity in BA 21 increased linearly. Moreover, systematic changes were detected in the onset latency of regional activity that were essentially normalizing: There was an increase in onset latency in premotor regions and a decrease in the onset of activity in BA 21 and extrastriate areas, establishing the temporal progression of activity that is typical of nonimpaired readers.

The present study extends these magnetic source imaging (MSI) results by examining a sample of children who were demonstrably inadequate responders to effective reading intervention. These children received a more comprehensive two-stage intervention focusing during the first 8 weeks on phonological decoding skills and during the subsequent 8 weeks on rapid word recognition, and allowing for two post-intervention scans. A state-of-the-art neuro-magnetometer was used, affording greater sensitivity in examining temporal as well as regional anatomical features of task-specific activation profiles. We examined individual differences in response to intervention as a function of the specific changes that the spatiotemporal profile of brain activation had undergone, hypothesizing specifically that profiles associated with a positive response to intervention would resemble those of typically achieving readers and that profiles for inadequate responders would show less change and parallel those observed in children and adults with RD.

Method

Participants

This study involved a group of children who had been identified as at-risk for reading difficulties at the end of kindergarten and received a Grade 1 intervention (reported in Mathes et al., 2005). They were selected from the population of six non–Title 1 schools in a large urban school district in Texas. These schools were selected because of evidence indicating that they had adequate core reading programs. The risk status of all children in kindergarten in these schools was evaluated with the teacher-administered Texas Primary Reading Inventory (TPRI; Fletcher et al., 2002). Those children who were identified as at risk on the basis of the screening section from the TPRI received additional standardized assessments of word recognition and text reading to eliminate potential false positives, as the TPRI was designed to minimize the risk of missing children who might have reading problems, with the expected consequence of higher rates of false positives.

The 298 at-risk students were randomly assigned to three reading interventions in Grade 1 (Mathes et al., 2005) consisting of (a) enhanced classroom reading instruction in which classroom teachers were receiving extensive professional development in reading instruction, with monitoring of oral reading fluency (n = 114) or (b) one of two different daily small-group supplemental interventions (n = 92 each) for 40 min a day over 30 weeks. In an evaluation of these reading interventions, Mathes et al. (2005) reported that students who received either of the two supplemental interventions performed significantly better on several measures of reading achievement at the end of Grade 1, as compared with students who were at risk but only received enhanced classroom instruction. Across all three interventions, 7% of the participants had scores below the 31st percentile on measures of word decoding, which was less than 2% of the student population. These students, who represented inadequate responders to reading instruction that was effective for most participants, were the focus of another intervention in Grades 2 and 3 (Denton, Fletcher, Anthony, & Francis, 2006). Both accuracy and fluency criteria were used to determine eligibility for the intervention study on the basis of grade-level benchmarks (Basic Reading Composite < 30th percentile; reading fluency on a progress monitoring fluency probe < 40 words per minute). The 27 students who met the inclusion criteria received a 16-week intervention package that was entirely different than the intervention they had received during Grade 1 in both content and intensity. During the first 8 weeks, intervention focused on the development of decoding skills (based on the Phonographix program; McGuiness et al., 1996) and was provided for 2 hr per day for 8 weeks. During the next 8 weeks, intervention varied by providing instruction aimed at the development of efficient word recognition skills. This second program was based on the Read Naturally program (Ihnot, Mastoff, Gavin, & Hendrickson, 2001) and involved 1 hr of daily instruction. A subset of these students volunteered for a MEG imaging study, which took place before the 16-week intervention and after each of the two intervention phases, with 15 students providing adequate MEG recordings at all three time points. Of the other 12 students, most had dental work that precluded participation, and one did not return for all the recording sessions. Hence-
forth, the term intervention refers to the 16-week intervention program which is the primary focus of this study. The effects of the supplemental instruction during Grade 1 are described in detail elsewhere (Mathes et al., 2005; Simos et al., 2005).

Table 1 displays group scores on the Sight Word and Pseudoword Efficiency subtests of the Test of Word Reading Efficiency (TOWRE; Form A; Torgesen, Wagner, & Rashotte, 1999) and the Word Attack and Letter–Word Identification subtests of the Woodcock–Johnson III Psychoeducational Battery (Woodcock, McGrew, & Mather, 2001), collected independently of the intervention study. Baseline scores prior to intervention indicate group mean performance that was at least one standard deviation below average on untimed measures of word and pseudoword reading accuracy, with particularly low performance on oral reading efficiency.

Individual differences in response to intervention were assessed on a group basis with change in standard score on the Basic Reading Composite between baseline and last visit as an index (a 10-point difference cutoff was used, representing the median amount of change). This measure was used because few students achieved grade-level fluency benchmarks and because it is generally more stable than scores on either Word Attack or Letter–Word Identification subtests alone. Among the sample, 8 children were classified as responders, demonstrating a mean improvement on the Basic Reading Composite of 15 ± 3 points, and 7 were classified as nonresponders, improving by only 4 ± 3 points. Although Table 1 shows that the responder and nonresponder groups were not comparable at baseline on reading measures (see Table 1), which is not surprising given that they differed in responder status at the end of the study, their brain activation profiles were similar, as described in greater detail below.

A second group of 10 non–reading impaired children who had never experienced difficulties in learning to read were tested on three occasions over a 6-month period on the same activation tasks to ensure that any changes observed over time in the RD group were not due to confounding factors such as maturation, repeated exposure to the stimuli, or habituation to the testing procedures. The RD group included 6 boys and 9 girls ages 93–116 months (M = 105 months), with 10 children of African American descent, 2 Hispanic children, and 3 Caucasian children. Most were in Grade 3 (n = 8), with 5 in Grade 2, and 2 retained in Grade 1. Among the participants, 12 had previously received enhanced classroom instruction, whereas 3 had received both enhanced classroom instruction and a supplemental intervention. There were 7 boys and 3 girls in the non–reading impaired group, ages 94–122 months (M = 103 months), with 2 of African American descent, 5 Hispanic children, and 3 Caucasian children. All children spoke English as their primary language. Statistical comparisons for age, gender, and ethnicity were not significant, but the samples are small. Although the groups were comparable in age, the non–reading impaired group tended to have more girls and more Hispanic than African-American children. We have not observed effects of ethnicity or gender in previous MEG studies of reading.

**Procedure**

MSI scans were acquired while children performed a pseudoword reading task, with three-letter pronounceable nonwords (e.g., lan) subtending 2.0° of visual angle. The printed stimuli were projected centrally for 1,500 ms, one at a time (with a randomly varied interstimulus interval of 3–4 s) through an LCD projector (Sharp Model XG-E690U) on a back-projection screen located approximately 60 cm in front of the participant. The children were instructed to read the “made-up” words as soon as they disappeared from the screen to avoid contamination of the MEG data segments by movement-related magnetic artifacts. Stimuli for each task were arranged randomly into four blocks of 25 items. The stimuli for the activation task were initially chosen in order to ensure relatively high performance level for all participants and prevent floor effects by RD children at baseline while still requiring phonological decoding processes.

MSI scans were obtained with a whole-head neuromagnetometer array (4-D Neuroimaging, Magnes WH3600), which consisted of 248 first-order axial gradiometer coils, housed in a magnetically shielded chamber and arranged to cover the entire head surface. The methods used for signal processing, source localization, and precise co-registration with the patient’s structural MRI scans are described in detail elsewhere (Simos et al., 1999). Briefly, the magnetic flux measurements were filtered with a bandpass filter between 0.1 and 20 Hz and digitized at 250 Hz. The single-trial event-related field segments (ERFs) in response to 50–70 stimulus presentations were averaged after excluding those containing eye movement or other myogenic or mechanical artifacts. The resulting averaged ERFs, in all cases, consisted of an

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<td><strong>Standardized Measures of Reading Skill at the First and Last Magnetoencephalography Recording Sessions</strong></td>
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*Note.* WJ-III = Woodcock-Johnson III Achievement Battery; TOWRE = Test of Word Reading Efficiency.
early portion (typically between 30- and 150-ms post-stimulus onset) and a late portion (typically between 150 and 1,000 ms post-stimulus onset). To identify the intracranial origin of ERFs, we analyzed the magnetic flux distribution that had been recorded simultaneously over the entire head surface at successive points (4 ms apart), thus preserving the temporal information that is inherent in the MEG methodology.

The analysis consisted of the application of a mathematical model that considered the intracranial activity sources (sets of active neurons) as equivalent to physical current dipoles embedded in a spherical conductor approximating the local skull curvature (Sarvas, 1987) and was intended to provide estimates of the location and strength of these sources, the activity of which had produced the recorded magnetic flux at each time point. Occasionally, two distinct dipolar distributions were visually identified at a single time point over a given hemisphere. In those instances, source estimation was performed independently with data from a subset of magnetic sensors covering both extrema of each dipolar distribution. In order to avoid localization errors produced by smearing of the magnetic flux from one source by the flux induced by the other source, we retained two simultaneous source solutions only if the corresponding dipoles were at least 5 cm apart. With this method, no more than two sources, located in different anatomical regions, can be computed in each hemisphere at each 4-ms time bin. Therefore, a maximum number of (970 ms / 4 ms) × 2 sources = 484 sources could be computed for each hemisphere during each epoch for the time period included in the analysis.

The location estimates of each "dipolar" source were specified with reference to a Cartesian coordinate system and anchored on three fiducial points on the head (the nasion and the external meatus of each ear). The same fiducial points were marked with vitamin pills, thus enabling precise registration of the location of each dipolar source on the participants’ high-resolution, T1-weighted MRI scans. Activity sources were found in a significant proportion of participants during at least one visit (80/150 hemispheres [25 participants × 3 visits × 2 hemispheres], binomial test \( p < .05 \) in the following areas: posterior portion of the superior temporal gyrus (BA 22), supramarginal gyrus (BA 40), angular gyrus (BA 39), inferior frontal gyrus (BA 44/45), premotor cortex (BA 6), ventral occipitotemporal cortex (BA 37), lateral occipitotemporal cortex (BA 19), middle temporal gyrus (BA 21), and mesial temporal cortex (hippocampus and parahippocampal gyrus). Activity sources in mesial temporal cortices may reflect the involvement of short-term memory processes associated with the requirement for brief maintenance of the phonological/articulatory representation of the pseudoword stimuli before producing a (delayed) response.

Spatiotemporal profiles of brain magnetic activity were quantified by two complementary variables that were analyzed separately. One was the number of dipolar sources that were consistently localized in a particular area for longer than 12 ms at a time. Activity sources meeting this criterion were consistently identified, across participants, in the nine areas listed above. This measure was used as an index for the total duration of neurophysiological activity that takes place during stimulus processing and prior to the initiation of an overt behavioral response (pronunciation of the word). In the context of large-scale studies with both neurologically intact volunteers and patients, this measure has been found to be the most reliable and valid index of the degree of regional cerebral activation that is specific to various language functions (Maestú et al., 2002; Papanicolaou et al., 2004; Szymanski et al., 2001). For the purposes of the parametric analyses, the data were normalized separately for each participant on the basis of the total number of activity sources found anywhere in the brain for a given recording session. This was done to control for potential fluctuations in the signal-to-noise ratio of MEG recordings across sessions, which could affect the likelihood of obtaining satisfactory dipole fits. The second measure used in the present study reflected the onset of regional activity in each area, in milliseconds after stimulus onset.

Data on the number of activity sources (or total duration of regional activity) were submitted to a multivariate analysis of variance (MANOVA) with visit (3) and hemisphere (2) as the within-subject variables and group (responder, nonresponder, and non–reading impaired) as the between-subjects variable. Data from each of the nine consistently active regions were treated as different, yet potentially intercorrelated, measures. Conversely, regional differences in the onset of brain activity reflect the relative timing of engagement of different areas that serve as components of the brain mechanism supporting the cognitive function exemplified by the experimental task. In order to preserve this information in the analyses, onset latency data was initially submitted to an analysis of variance (ANOVA) that included area (with nine levels), visit (1st, 2nd, 3rd), and hemisphere (left, right) as the within-subject variables. Group was again used as the between-subjects variable, as described above.

In the second set of analyses, the temporal progression of regional activity at each visit was examined, first by ranking the 18 anatomical locations where activity sources were found consistently (nine regions × two hemispheres) according to the mean onset latency of activity in each region. Next, a series of dependent-sample \( t \) tests were computed between anatomical areas that first became active in close succession, in order to test the hypothesis that regional onset latency differences were statistically significant. In order to control for Type I error for multiple comparisons, we evaluated all tests at an alpha of .001. This procedure was performed separately for each visit and for each of the three groups of participants.

**Results**

Performance on standardized tests. Significant interactions between visit and RD subgroup (responder vs. nonresponder) were found for Word Identification scores, \( F(1, 13) = 49.17, p < .0001, \) and Word Attack scores, \( F(1, 13) = 31.30, p < .0001 \), indicating greater improvement for responders across visits. The two subgroups differed only on Word Attack scores at baseline, \( F(1, 13) = 6.57, p < .024 \). Subgroup did not mediate the degree of improvement on word and pseudoword reading efficiency measures; main effects of visit: \( F(1, 13) = 60.18, p < .0001 \) and \( F(1, 13) = 22.29, p < .0001 \), respectively. As the effects of the intervention at the behavioral level were essentially identical to those observed in the larger intervention study, the reader is referred to Denton et al. (2006) for more details.

**In-Scanner Task Performance**

On average, children showed significant gains in decoding accuracy across the three visits, as indicated by main effects and
linear trends, $F(1, 13) = 5.24, p < .019$ (see Figure 1). There were no main effects or interactions with RD subgroup.

**Brain Activation Profiles at Baseline**

At baseline the typical spatiotemporal brain activation profile for the group of impaired readers involved early activity in lateral and ventral occipitotemporal areas in both hemispheres. Extrastriate activity was followed by magnetic sources in inferior frontal, angular, and superior temporal regions in the right hemisphere; sources in the left supramarginal gyrus in the left hemisphere; and magnetic activity in middle and mesial temporal cortices, bilaterally. On average, the degree of activity was bilaterally symmetric in all areas (including BA 22). For BA 22, in particular, 13 of 15 participants showed predominantly right hemisphere or bilaterally symmetric activity. There were no notable differences between responders and nonresponders at baseline.

As expected on the basis of previous MSI studies (Simos, Breier, Fletcher, et al., 2001; Simos et al., 2005), spatiotemporal activation profiles for the group of nonimpaired readers were notably different following the early activation of extrastriate areas in the left hemisphere. In this group, activity was next observed in homologous extrastriate areas in the right hemisphere and temporoparietal areas (BA 22, BA 39, BA 40) predominantly in the left hemisphere, followed by activity in frontal regions (BA 44/45, BA 6) bilaterally. On a group basis, significantly greater activation was found for non–reading impaired as compared with RD children in the angular gyrus and ventral occipitotemporal cortices in the left hemisphere, $F(1, 23) = 5.17, p < .03$ and $F(1, 23) = 5.91, p < .02$, respectively. Nonsignificant trends in the same direction were noted for activity in BA 22 and lateral occipitotemporal cortices bilaterally. Nonsignificant differences in the opposite direction (greater activity for the RD group) were found in left BA 44/45 and in right BA 40.

**Degree (or Duration) of Magnetic Activity**

Significant changes across visits were noted for activity in temporoparietal and inferior frontal regions, with notable differences between responders and nonresponders. Responders’ data demonstrated a Visit × Hemisphere interaction for BA 22, $F(2, 14) = 4.26, p < .036$, with a significant simple main effect in the left hemisphere, $F(2, 14) = 9.69, p < .002$, but not in the right hemisphere ($p > .05$). As shown in Figure 2, the duration of activity in the left BA 22 (corrected for changes in total brain activity) increased linearly over the 4-month period of the study: linear trend across three visits: $F(1, 7) = 13.74, p < .009$. Planned trend analyses revealed similar effects for BA 40, $F(1, 7) = 7.54, p < .025$, and BA 39, $F(1, 7) = 12.83, p < .009$, both in the left hemisphere ($p$ values for corresponding analyses in the right hemisphere were all $> .1$). A Visit × Hemisphere interaction for activity in BA 22 was also found for nonresponders, $F(2, 12) = 5.81, p < .017$, but in this group follow-up tests indicated that the quasi-linear increase in the duration of activity apparent in Figure 2 was significant only in the right hemisphere, $F(1, 6) = 6.55, p < .043$ (left hemisphere: $p > .1$). The duration of activity in BA 44/45, bilaterally, showed a trend in the same direction (increasing activity over time), as indicated by a visit simple main effect, $F(2, 12) = 4.77, p < .034$, and significant linear trends in the left hemisphere, $F(1, 6) = 8.40, p < .026$, and in the right hemisphere, $F(1, 6) = 9.58, p < .021$. No effects involving visit were noted for nonimpaired readers ($p > .1$), indicating overall stability of activation profiles over time.

**Onset Latency of Regional Activity**

A nonsignificant tendency for (a) reduced onset latency of activity in BA 22 and (b) increased onset latency in BA 44/45 was noted for both subgroups of impaired readers. Subsequent analyses performed on data collapsed across subgroups revealed significant main effects of visit in BA 22, $F(2, 28) = 6.65, p < .004$, and BA 44/45, $F(2, 28) = 5.53, p < .01$. Significant quadratic trends in both cases, $F(1, 14) = 9.46, p < .008$, and $F(1, 14) = 13.22, p < .003$, respectively, indicated that changes took place predominantly between the first and second visits (increased latency for frontal activity and decreased latency for superior temporal activity) as shown in Figure 3.

Perhaps the most conspicuous finding consisted of a change in the relative timing of regional activity among extrastriate, superior temporal, and inferior frontal regions. For nonimpaired readers, onset latency data were collapsed across visits given the absence of notable differences in the spatiotemporal profiles of activity. Although the general outline of the temporal progression of activity during the first 700 or so milliseconds after stimulus onset has been described in the previous paragraph, a closer view indicated statistically reliable temporal differentiation in the onset of activity (revealed by significant, $p < .001$, differences in onset latency outlined in Table 2) among three sets of brain regions: extrastriate, temporoparietal, and frontal. Specifically, the onset of activity in left occipitotemporal regions (which, on average, occurred at 150 ms) was significantly earlier than the onset of activity in any other brain region (including the corresponding regions in the right hemisphere). Activity in the left superior, middle temporal, and angular gyri took place next and significantly earlier than activity in the supramarginal gyrus and frontal regions, bilaterally. Finally,
Figure 2. Average degree of activity (number of consecutive magnetic activity sources) in temporoparietal (Brodmann’s area [BA] 22, BA 39, BA 40) and frontal (BA 44/45) regions recorded at each visit (baseline, 2nd, 3rd) for the entire group of impaired readers. Regions are shown for a given subgroup of children with reading disabilities only if significant simple main effects or linear trends for visit were found (indicated by asterisks). Vertical bars represent standard error of the mean.
the onset of activity in the left supramarginal gyrus was first noted at approximately the same latency as activity in the left inferior frontal gyrus and premotor region but significantly earlier than activity in the corresponding regions in the right hemisphere.

In contrast to nonimpaired readers (Figure 4), a clearly distinct temporal profile of activity was noted at baseline for the entire group of impaired readers, with essentially no differences between responders and nonresponders. This profile, which is presented schematically in Figure 5, featured activity in only 10 brain regions (compared with 16 in the group of nonimpaired readers). Initially activity sources were found in extrastriate cortices (with no reliable difference between hemispheres) followed by essentially simultaneous onset of activity in the middle temporal gyrus, bilaterally, in the right angular, superior temporal, and inferior frontal gyri, and in the left supramarginal gyrus. Significant temporal differentiation was found only between extrastriate areas and the rest of the active brain regions ($p < .001$; see Table 3).

The temporal progression of activity for responders following intervention (on the third visit) was similar to the profile that was characteristic of the group of nonimpaired readers as shown in Figure 6 and Table 4, featuring a reliable temporal differentiation of activity among extrastriate, temporoparietal, and frontal areas. Specifically, initial activation of left hemisphere extrastriate cortices was first noted earlier than activity in any other brain region (including corresponding right hemisphere areas). Activity in the left supramarginal gyrus, the right angular gyrus, and the superior and middle temporal gyri (in both hemispheres) took place next and significantly earlier than activity in frontal regions, bilaterally.

Figure 7 and Table 5 reveal a different temporal profile for the group of nonresponders. In this group there was (a) lack of a clear temporal differentiation between hemispheres in the onset of activity in extrastriate areas, (b) no clear temporal differentiation between the onset of activity in left hemisphere temporoparietal areas and the onset of activity in frontal regions, and (c) a signifi-

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**Table 2**

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*Note.*  
R = right hemisphere; L = left hemisphere; BA = Brodmann’s area; MTL = medial temporal lobe. Data were collapsed across all visits.  
* * $p < .001$.  

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Figure 3. Change in average onset latency of activity (in milliseconds after stimulus onset) across visits (baseline, 2nd, 3rd) in temporoparietal (Brodmann’s area [BA] 22, BA 39, BA 40) and inferior frontal regions (BA 44/45), collapsed across hemispheres. Vertical bars represent standard error of the mean.
significant difference in onset latency between BA 22 in the right hemisphere and BA 6, 44, and 45, in both hemispheres.

Discussion

The data presented here corroborate previous MSI (Simos et al., 2002) and fMRI findings (e.g., Eden et al., 2004; Temple et al., 2003) in showing that completion of an intensive instruction program focusing on the development of phonological awareness and decoding skills is often accompanied by increased neurophysiological activity in temporoparietal cortices in the left hemisphere during performance of reading tasks that require phonological decoding. The novel finding that emerged from the present data is that adequate response to this instruction is contingent on: (a) increased duration of neurophysiological activity in the posterior portion of the superior temporal gyrus, the supramarginal and angular gyri in the left hemisphere, and (b) change in the sequence of regional activity between left temporoparietal and frontal regions. For the subgroup of initially impaired readers who subsequently scored in the average range of standardized tests of word and pseudoword reading accuracy (responders), these changes can be considered as normalizing, rendering the spatiotemporal activation profiles more similar to the activation profiles of age-matched children who never experienced difficulties in learning to read. In contrast, for the subgroup of children who showed small and clinically insignificant improvement in basic reading skills (nonresponders), the observed neurophysiological changes indicated increased reliance on alternate brain regions to support phonological decoding.

Interestingly, the distinct neurophysiological profiles of responders and nonresponders were obtained while performing a phonological decoding task, the difficulty level of which was titrated to ensure that both groups would be able to perform at comparable levels before, during, and after the intervention. This can probably account for the fact that responders showed significant improvement on norm-referenced measures of reading accuracy (involving stimuli of increasing length and complexity), whereas subgroup differences in the rate of improvement on performance of the in-scanner task were minimal. This suggests that neurophysiological differences between the two groups did not reflect different performance levels but rather more basic aspects of the brain circuits that engage during decoding tasks. Moreover, the fact that neurophysiological changes were observed only in the RD children and not in the control group suggests that they were associated with supplemental instruction and were not simply the result of developmental changes that normally take place during the course of regular classroom instruction.

Evidence regarding the actual role of alternate regions (right temporoparietal and inferior frontal cortex) in the brain circuits for reading is mostly indirect. Some brain imaging studies on dyslexia have reported increased activity in these regions during performance of a variety of reading tasks (Brunswick, McCrory, Price, Frith, & Frith, 1999; S. E. Shaywitz et al., 1998). Damage to these regions, however, does not regularly cause deficits in single word reading. Moreover, MSI studies with more experienced nonimpaired readers, both children and adults, clearly show that activation of inferior frontal cortices occurs at a latency when word recognition and lexical access has already taken place (between 500–700 ms after stimulus onset; Simos, Breier, Fletcher, et al., 2001; Simos et al., 2007). A plausible explanation for the putative hyperactivation of inferior frontal regions suggests that these areas are involved in the mapping of the sound structure of the printed stimuli via activation of articulatory patterns (S. E. Shaywitz & Shaywitz, 2004). At the psychological level, this process is not as efficient for fluent reading as the more direct mapping of print to sound (either at the word or the subword level), but when the latter process is deficient, children with severe reading difficulties may inadvertently rely on this alternative strategy. Along the same

Figure 4. Nonimpaired readers (data collapsed across the three visits): Temporal progression of magnetic activity on schematic views of the lateral surface of the left (L) and right (R) hemispheres. Mean onset latency of activity in each active region is shown in milliseconds after stimulus onset. Areas with significantly different onset latencies are shown in different colors.

Figure 5. Reading-impaired children at baseline: Temporal progression of magnetic activity on schematic views of the lateral surface of the left (L) and right (R) hemispheres. Mean onset latency of activity in each active region is shown in milliseconds after stimulus onset. Areas with significantly different onset latencies are shown in different colors.
lines, increased engagement of right hemisphere temporoparietal regions during reading in children with dyslexia may correspond, at the psychological level, to increased reliance on (visual) perceptual processes to compensate for poor phonological decoding skills. It should be noted, however, that increased activation of inferior frontal regions in children with dyslexia versus controls is not a universal finding (see, for example, Eden et al., 2004), and there is some evidence that this activity may serve to compensate for disrupted posterior brain systems.

In the present study, changes in spatiotemporal profiles of activation were observed during performance of a task that posed significant demands on phonological decoding processes (pseudoword reading). Despite the fact that RD children had received supplemental instruction during Grade 1 (prior to the baseline scan), their activation profiles showed some of the commonly observed differences from those of nonimpaired readers, namely, reduced activity in temporoparietal and occipitotemporal regions in the left hemisphere and increased activation of inferior frontal cortices.

At the behavioral level, the two-stage intervention influenced both accuracy and reading efficiency measures (Denton et al., 2006), yet there was a tendency for greater improvement of basic reading skills (word and pseudoword reading accuracy) and reading speed during the first 8 weeks of the program, which focused on phonological decoding skills. At the neurophysiological level, the trajectory of changes in activation during performance of the pseudoword reading task did not appear to be in phase with the type of intervention. Changes in the duration of activity took place with similar intensity during the two phases of the program, whereas changes in onset latency were more prominent during the first phase of the program. A similar trend was observed in Simos et al. (2007), where the most evident changes in activation patterns during performance of a sight-word reading task took place during the first 8 weeks of the intervention program. These findings may reflect an essential temporal uncoupling of instruction effects at the psychological and brain level, a peculiarity of the particular intervention programs used in the study, or the effects of individual variability in response to instruction made more prominent in the results by the small sample size.

In an earlier MSI study, increased activity and reduced onset latency of activation were observed in the middle temporal gyrus and extrastriate (occipitotemporal) areas during performance of a task that posed lesser demands for decoding and increased demands for rapid recognition of (mostly familiar) word forms (Simos et al., 2007). This finding is in partial agreement with results from a large scale functional magnetic resonance imaging study comparing children who received intensive intervention for a period of 8 months (focusing on phonological decoding, word recognition, and text comprehension skills) with children who received less systematic interventions within the school setting (B. A. Shaywitz, Shaywitz, Blachman, et al., 2004). Persistent changes in the degree of regional activation observed during performance of a cross-modal letter name identification task were
found in occipitotemporal and inferior frontal areas. Therefore, data from studies conducted with a variety of cognitive tasks and imaging methods are in agreement with suggestions that specific task demands (which are in part determined by the nature of the printed stimuli used) affect the layout and organization of the brain circuit that is engaged to perform each task (Bentin, Kutas, & Hillyard, 1995; Ruz, Wolmetz, Tudela, & McCandliss, 2005).

In comparison with an earlier MSI investigation on the effects of intensive instruction on the profile of activity associated with the performance of a phonological decoding task (Simos et al., 2002), the design of the present study has incorporated a number of improvements. First, it included a larger sample of children selected to ensure a wider representation of participants based on initial standardized scores and socioeconomic status (SES) and home characteristics. The present sample was more uniform with respect to age and instructional experiences, permitting the examination of individual differences in response to intervention. Second, on average, children in the present sample had less severe RD (mean Word Attack standard score \( \text{H11005} \approx 80 \text{ vs. 72} \text{ H11006} \approx 7.4 \text{ in the previous study}). In the present study, only 7 of 15 children scored below the 10th percentile (i.e., had a standard score \( \text{H11021} \approx 80 \)) on the Word Attack subtest of the Woodcock–Johnson battery. In our previous study 6 of 8 children scored in that range. Third, intervention was performed at the school by specially trained teachers, and not at a reading clinic, with close supervision and the capability to customize the instructional sequence to fit the student’s rate of progress. Fourth, there was a second follow-up approximately 2 months after the initial intervention. During that period children received structured teaching to improve word recognition and fluency skills. Fifth, we used a different neuromagnetometer sensor, which was equipped with 248 first-order gradiometer coils (compared with only 148 magnetometer coils in our previous study), which affords significantly improved signal-to-noise ratio and denser coverage of the head surface. The inclusion of a larger, more homogeneous sample of RD children, and the improved sensitivity of the magnetic scanning device used in the present study (which is crucial for detecting magnetic activity emanating from frontal cortices) may account for the present study’s success in identifying systematic individual variability in intervention-related changes in neurophysiological activity for reading.

In conclusion, the present findings demonstrate that remediation can be associated with changes in the relative timing of activity in key brain regions and, often, with quite dramatic changes in the sequence of neurophysiological events that comprise the neural signature of the brain mechanism for reading. Successful intervention (evidenced in the group of responders) was associated with establishment of a brain circuit for reading that was structurally

### Table 4

**Significant Differences in Mean Onset Latency Among 16 Brain Regions for the Group of Responders**

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*Note.* R = right hemisphere; L = left hemisphere; BA = Brodmann’s area; MTL = medial temporal lobe. Data were collapsed across the 2nd and 3rd visits. \( p < .001. \)

**Figure 7.** Non-responders post-intervention: Temporal progression of magnetic activity on schematic views of the lateral surface of the left (L) and right (R) hemispheres. Mean onset latency of activity in each active region is shown in milliseconds after stimulus onset. Areas with significantly different onset latencies are shown in different colors. The temporal profile of activity was essentially identical for the 2nd and 3rd visits and data were collapsed across the two visits.
similar to, and operated like, the brain mechanism characteristic of nonimpaired readers (normalizing changes at the neurophysiological level). Conversely, when intervention failed to have a significant impact at the behavioral level, it was associated with neurophysiological changes suggestive of the establishment of alternative brain circuits for reading (compensatory changes). The nature of intervention-related changes in the profile of regional brain activation is consistent with the notion that dyslexia is associated with a functionally impaired brain circuit for reading, which, in turn, may be caused by inefficient or inadequate neuronal connections between key brain areas that normally participate in this circuit (Beaulieu, Plewes, Paulson, et al., 2005; Deutsch et al., 2005; Eckert et al., 2005; Klingberg et al., 2000; Horwitz, Rumsey, & Donohue, 1998; Niogi & McCandliss, 2006; Pugh, Mencl, Shaywitz, et al., 2000; Stanberry et al., 2006). The data presented here provide more direct evidence for changes in the relative timing of neurophysiological activity among various components of the brain circuit for reading, indicating substantial changes in the pattern of functional corticocortical connections that support this circuit.

Whereas the relatively small sample of the present study may not be sufficient to draw definite conclusions regarding the nature of changes in neuronal circuitry in response to systematic instruction, data are consistent with the prevalent notion regarding the pathophysiology of dyslexia (at least at the macroscopic level). Our findings are also clearly indicative of systematic individual differences in the type of changes, at the neuronal level, that appear to reflect a child’s degree of response to intervention. It should be emphasized, however, that conclusions based on the present findings are necessarily limited to the task used, the brain imaging method used, and the characteristics of the participants. Future investigations, with larger samples of RD children, should systematically examine factors that may influence response to intervention, which may include, but are not limited to, individual reading skill profiles, developmental histories, genetic predisposition, and factors related to the intensity, duration, and content of the intervention itself. The role of practices targeting motivation and self-monitoring ability appears to be a particularly important but often overlooked area in intervention research (e.g., Eckerd, Ardoin, Daly, & Martens, 2002; Morgan & Sideridis, 2006). It should also be noted that the small numbers of responders and nonresponders in our study did not permit a detailed account of the extent to which the second part of the intervention, focusing on the development of rapid word recognition skills, contributed to further changes in brain activation profiles. In future studies nonresponders could be randomly assigned to different treatments in order to assess the relative impact of different components of the intervention program.

References


