Intensive Instruction Affects Brain Magnetic Activity Associated with Oral Word Reading in Children with Persistent Reading Disabilities

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Abstract

Fifteen children ages 7 to 9 years who had persistent reading difficulties despite adequate instruction were provided with intensive tutorial interventions. The interventions targeted deficient phonological processing and decoding skills for 8 weeks (2 hours per day) followed by an 8-week, 1-hour-per-day intervention that focused on the development of reading fluency skills. Spatiotemporal brain activation profiles were obtained at baseline and after each 8-week intervention program using magnetoencephalography during the performance of an oral sight-word reading task. Changes in brain activity were found in the posterior part of the middle temporal gyrus (Brodmann's Area [BA] 21: increased degree of activity and reduced onset latency), the lateral occipitotemporal region (BA 19/37: decreased onset latency of activation), and the premotor cortex (increased onset latency). Overall changes associated with the intervention were primarily normalizing, as indicated by (a) increased activity in a region that is typically involved in lexical–semantic processing (BA 21) and (b) a shift in the relative timing of regional activity in temporal and frontal cortices to a pattern typically seen in unimpaired readers. These findings extend previous results in demonstrating significant changes in the spatiotemporal profile of activation associated with word reading in response to reading remediation.

There have been several cognitive explanations of developmental reading disabilities (RD), each focusing on a specific aspect of the constellation of skills that appear to be impaired, including phonological processing (Liberman, Shankweiler, & Liberman, 1989; Ramus et al., 2003), rapid naming (Wolf, Bowers, & Biddle, 2000), and processing of rapidly changing visual (Livingstone, Rosen, Drislane, & Galaburda, 1991; Lovegrove, Bowling, Badcock, & Blackwood, 1980) or auditory (Tallal, 2000) stimuli. Currently, there is a consensus among researchers that the predominant underlying deficit in RD involving word recognition is the awareness that the letters and letter strings (i.e., orthography) represent the sounds of spoken language (phonology) and the ability to mentally manipulate speech-specific sound (phonological) representations. These abilities are considered to be necessary for learning the alphabetic principle (i.e., the concept that letters and short letter sequences represent distinct phonological elements; Bruck, 1992; Liberman et al., 1989; Wagner & Torgesen, 1987). This hypothesis is strongly supported by reports that systematic interventions that target phonological awareness and decoding skills significantly improve reading ability in children with severe RD (Berninger et al., 2003; Lovett, Barron, & Benson, 2003; National Reading Panel, 2000).

Partitioning words into orthographic segments and assembling a corresponding phonological representation is essential for successful reading acquisition, but the ultimate goal of reading is rapid, automatic recognition of words and comprehension of their meaning in connected text (Berninger et al., 2003; Gough & Tunmer, 1986). Some students with RD show difficulties in word recognition despite intact higher order cognitive and linguistic abilities, such as general intelligence and reasoning, vocabulary (Share & Stanovich, 1995), and syntax (Shankweiler et al., 1995). Such examples make it clear that higher level deficits in comprehension are the result of a breakdown in basic skills (i.e., phonological analysis of spoken and written language) that are necessary for the construction and maintenance of adequate

word-level representations (Gough & Tunmer, 1986; Liberman et al., 1989). Thus, the student's ability to identify a particular word is specifically hindered by difficulty in sounding out the word, leading to poor performance on comprehension tasks despite the fact that the student actually knows the meaning of that word.

The accumulation of data indicating that severe difficulty in learning to read words can occur in children with intact or even superior intelligence and other language skills supports the hypothesis that this form of RD is associated with a specific functional deficit in the brain circuits that normally support reading. Direct evaluation of this hypothesis using methods for functional brain imaging has shown reliable neural correlates of RD (Papanicolaou et al., 2004; S. E. Shaywitz & Shaywitz, 2004). Functional brain imaging methods measure various aspects of neurophysiological function (e.g., regional blood flow or metabolism, magnetic signals produced by increased neuronal signaling) during the performance of experimental tasks (e.g., word and pseudoword reading, spoken word segmentation) that require reading and reading-related skills, such as word recognition, phonological decoding, and phonological processing.

The results of this research tend to converge across methods and laboratories in good and poor readers (Eden & Zeffiro, 1998; S. E. Shaywitz & Shaywitz, 2004). These studies indicate that specific networks of brain areas mediate different word recognition processes as well as other processes involved in language and reading. These networks, however, vary with proficiency, showing different patterns of activation in poor readers than in more skilled readers. The areas most consistently involved in these networks include the temporo-occipital region, the temporoparietal region (including the posterior portion of the superior temporal gyrus and the angular and supramarginal gyri), and the inferior frontal regions, predominantly in the left hem-

isphere (Eden & Zeffiro, 1998; Papanicolaou et al., 2003; S. E. Shaywitz & Shaywitz, 2004). Considerably less attention has been devoted to a set of brain areas located in the posterior temporal/temporo-occipital cortex that according to recent models of the neurobiological basis of reading (e.g., Logan, 1997) may be specialized for the analysis of print at the whole-word level. For instance, activation of the ventral occipitotemporal region occurs consistently during the early stages of reading (between 150–200 ms after stimulus onset; Breier, Simos, Zouridakis, Constantinou, & Papanicolaou, 1998; Breier, Simos, Zouridakis, & Papanicolaou, 1999). The degree of this activity correlates positively with the growth of reading skills (McCandliss, Cohen, & Dehaene, 2003; B. A. Shaywitz et al., 2002).

In a more recent longitudinal magnetoencephalography (MEG) study, we found that the onset latency of activity in the ventral occipitotemporal region improved significantly (i.e., activity took place progressively earlier after stimulus onset) in children who showed substantial gains in reading skill during kindergarten (Simos et al., 2005). Furthermore, word reading tasks preferentially activated a cortical region located on the lateral surface of the temporal lobe in the posterior portion of the middle temporal gyrus (Simos, Breier, et al., 2002). This region has been implicated in lexicosemantic functions by lesion, cortical stimulation, and neuroimaging studies (Damasio & Damasio, 1989; Fiebach, Friederici, Muller, & von Cramon, 2002; Hagoort et al., 1999; Roux et al., 2004; Turkeltaub, Eden, Jones, & Zeffiro, 2002). Moreover, neuromagnetic studies have reported a positive correlation between the onset of neurophysiological activity in this region and oral reading speed for words, but not for pseudowords (Simos, Breier, et al., 2002).

Hemodynamic (e.g., functional magnetic resonance imaging; fMRI) and neuromagnetic (e.g., MEG) studies have revealed consistent hypoactiva-

tion of posterior temporal and temporoparietal cortices in children with RD coupled with compensatory increases in activity in homologous regions of the right hemisphere and bilaterally in inferior frontal cortices (Simos, Breier, Fletcher, Foorman, et al., 2000; Simos, Breier, Fletcher, Bergman, & Papanicolaou, 2000; B. A. Shaywitz et al., 2004). The MEG studies have supplied additional evidence regarding the intrinsic timing of regional activity within the reading circuit. These findings support the notion that following visual processing of printed stimuli (which takes place in complex visual processing areas), poor readers do not use their left temporoparietal region for phonological processing of the visual symbols, but ineffectively employ their inferior frontal and right posterior temporal cortices (Simos et al., 2005; Simos, Breier, Fletcher, Foorman, et al., 2000; Simos, Breier, Fletcher, Bergman, & Papanicolaou, 2000). There is also evidence that the aberrant activation profiles of children with RD can be reversed, at least with respect to the degree and duration of neurophysiological activity, following intensive remedial instruction (Aylward et al., 2003; B. A. Shaywitz et al., 2004; Simos, Fletcher, et al., 2002; Temple et al., 2003). Although these studies have reported "normalizing" changes in brain activity for tasks that place serious demands on the network of brain areas that support phonological decoding, little is known about the prior instructional history of the participants. Moreover, no research has focused specifically on students who have not responded to quality classroom or supplemental instruction. These children are of particular interest, as they demonstrate persistence in their reading problems and may require highly intense intervention to learn to read. There is also little research on the potential of the system that supports whole-word reading to demonstrate instruction-related functional plasticity, especially in inadequate responders. Accordingly, the goal of the present study was to investigate changes in

the spatiotemporal activation profile associated with an oral word reading task resulting from an intensive reading intervention in children who had responded inadequately to prior instruction.

Method

Participants

This study involved a group of students identified as at risk for RD at the end of kindergarten and beginning of first grade from six non–Title 1 schools in a large urban school district in Texas (Mathes et al., 2005). These schools were selected because of evidence indicating that they had strong core reading programs. The risk status of all children in kindergarten in these schools was evaluated using the teacher-administered *Texas Primary Reading Inventory* (TPRI; Fletcher et al., 2002). Those children who were identified as at risk based on the screening section of the TPRI received additional 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) and then to an intensive intervention after Grade 1, depending on their response to the Grade 1 intervention ($n = 27$; Denton, Fletcher, Anthony, & Francis, in press). The Grade 1 interventions represented (a) enhanced classroom reading instruction, in which classroom teachers were receiving extensive professional development in reading 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 than students who were at risk of RD 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 responded inadequately to reading instruction that was effective for most students, were the focus of another intervention in Grades 2 and 3 (Denton et al., in press). Twenty-seven students who had demonstrated an inadequate response to prior reading instruction, most of whom had participated in Mathes et al.'s (2005) study, received a 16-week intervention package involving decoding and fluency skills. The decoding intervention was provided for 2 hours per day for 8 weeks and was based on the *Phono-Graphix* program (McGuiness, McGuiness, & McGuiness, 1996). The fluency intervention followed the decoding intervention and involved one hour of daily instruction for 8 weeks based on the *Read Naturally* program (Ihnot, Mastoff, Gavin, & Hendrickson, 2001). The 16-week intervention resulted in significant improvement in reading decoding, fluency, and comprehension.

A subset of students from Denton et al. (in press) volunteered for a MEG imaging study before the 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 their participation, and one student did not return for all the recording sessions. Baseline scores on standardized reading tests presented in Table 1 indicated that group mean performance was at least 1 *SD* below the average on untimed measures of word and pseudoword reading accuracy, with particularly low performance on word fluency based on the Sight Word Efficiency subtest of the *Test of Word Reading Efficiency* (TOWRE; Torgesen, Wag-

ner, & Rashotte, 1999), Form A. The participants averaged 8 years 9 months in age (range = 7 years 9 months–9 years 8 months). There were 9 girls and 6 boys, with 10 children of African American descent, 2 Hispanics, and 3 European Americans. Most were in Grade 3 ($n = 8$), with 5 in Grade 2, and 2 were retainees in Grade 1. Twelve participants had previously received enhanced classroom instruction, whereas 3 had received both enhanced classroom instruction and a supplemental intervention.

Stimuli and Task

Magnetic source imaging (MSI) scans were acquired while children performed a timed word reading task composed by combining stimuli from the TOWRE Forms A and B. As this test consists of words of increasing length and reading difficulty, the horizontal visual angle subtended by the stimuli varied from 0.6 to 4 degrees. Stimuli were projected centrally for 1500 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 words as quickly as possible as soon as they disappeared from the screen to avoid contamination of the MEG data segments by movement-related magnetic artifacts. Stimuli were arranged into four blocks of 25 items in order of increasing difficulty as they appear on the TOWRE forms. The recording was discontinued after eight successive reading errors.

MEG Procedures

MEG 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 coregistration with the patient's structural magnetic resonance imaging (MRI) scans have been 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. For each participant, an equal number of ERF epochs was used to create averaged magnetic responses across the three visits to avoid introducing bias regarding the signal–noise ratio of the data in favor of later visits (where there was a general tendency for a greater number of correct responses). The resulting averaged ERFs, in all cases, consisted of an early portion (typically between 70 and 150 ms post–stimulus onset) and a late portion (typically between 150 and 1000 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 using data from a subset of magnetic sensors covering both extremes of each dipolar distribution. To avoid localization errors produced by smearing of the magnetic flux from one source by

the flux induced by the other source, two simultaneous source solutions were retained 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 point. Therefore, a maximum number of (930 ms/4 ms) × 2 sources = 464 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 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 (19/30 hemispheres, binomial test $p <$ .05) in the following areas: posterior portion of the superior temporal gyrus (Brodmann's Area [BA] 22), supramarginal gyrus (BA 40), angular gyrus (BA 39), inferior frontal gyrus (BA 44/45), premotor cortex (BA 6), ventral occipito-temporal cortex (BA 37), lateral occipito-temporal cortex (BA 19), middle temporal gyrus (BA 21), and mesial temporal cortex (hippocampus and parahippocampal gyrus).

Spatiotemporal profiles of brain magnetic activity were quantified by two complementary variables. 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 earlier. This measure directly reflects the total duration of neurophysiological activity that takes place during stimulus processing and prior to the initiation of an overt behavioral response (i.e., 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, based on 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–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.

Given that differences in the degree of activity *among* brain regions are largely uninterpretable in functional imaging studies, data on the number of activity sources (or total duration of regional activity) were submitted to a MANOVA, with visit (first, second, and third) and hemisphere (left and right) as the within-subjects variables. 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 that supports the cognitive function exemplified by the experimental task. To preserve this information in the analyses, onset latency data were submitted to an ANOVA that included area (with nine levels), visit (first, second, and third), and hemisphere (left, right) as the within-subjects factors.

Results

Standardized Reading Tests

Table 1 displays group scores on the Sight Word Efficiency subtest of the TOWRE (Form A; Torgesen et al., 1999), the Word Attack subtest of the *Woodcock-Johnson Psychoeducational*

Battery, third edition (WJ-III; Woodcock, McGrew, & Mather, 2001), and the WJ-III Basic Reading Composite (combining the Word Attack and Letter–Word Identification subtests), collected independently of the intervention study. On a group basis, scores improved significantly on each of these three measures, as indicated by main effects of visit, $F(1, 14) = 39.57$, $p < .0001$, for the Basic Reading Composite; $F(1, 14) = 36.65, p < .0001$, for the Word Attack subtest; and $F(1, 14) = 52.48$, $p < .0001$, for TOWRE scores. Note that although this subgroup tended to show more impairment in decoding skills at baseline compared to the overall intervention group, the outcomes after the intervention were similar to those of the overall group in Denton et al. (in press).

In-Scanner Task Performance

On average, children showed significant gains in naming accuracy during the performance of the fluency task across the three visits, as indicated by a linear trend for the number of words read correctly, $F(1, 14) = 65.86, p < .0001$ (see Figure 1).

Degree of Magnetic Activity

A change over time was noted only for the number of activity sources found in the posterior part of the middle temporal gyrus in both hemispheres (BA 21). This main effect of visit, $F(2, 28) = 3.70, p < .04$, indicated a linear, bilateral increase across the three testing sessions (linear trend, $p < .02$). This trend is displayed graphically in Figure 2. There were no other significant effects of visit or hemisphere, suggesting bilaterally symmetric activity across visits for all nine areas where activity sources were consistently found.

Onset Latency of Regional Activity

The aim of these analyses was twofold: first, to examine changes in onset latency in each of the nine consistently active brain regions during the course

of the 16-week intervention program; and second, to identify potential changes in the relative onset of activity across brain regions. On the basis of a previous report regarding an aberrant pattern of relative timing of activation in at-risk children (Simos et al., 2005), we sought to verify this finding in the context of an oral word reading task and to examine if this aberrant pattern was amenable to instructional interventions.

The first set of analyses revealed both decreasing (for the middle temporal gyrus and the occipitotemporal

region) and increasing (for premotor and inferior frontal cortices) trends for onset latency (see Figure 3). A Visit × Hemisphere effect was found for the middle temporal gyrus, $F(2, 28) = 37.57, p < .0001$, and the lateral occipitotemporal region, $F(2, 28) = 6.30, p < .006$. Follow-up tests indicated decreasing trends that were restricted to the left hemisphere activity for the middle temporal gyrus, $F(2, 28) = 27.92, p < .0001$, and to the right hemisphere for the lateral occipitotemporal region, $F(2, 28) = 4.84, p < .02$. Follow-up pairwise comparisons between con-

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TABLE 1
Standardized Measures of Reading Skills at First and
Last MEG Recording Sessions

Measure	1st Visit			3rd Visit		
	M	**SD**	**range**	**M**	**SD**	**range**
WJ-III						
Basic Reading Composite	77	8.0	58–87	87	6.3	78–98
Word Attack	79	8.3	57–88	93	7.3	86–107
TOWRE	75	8.7	59–87	80	8.3	66–92

Note. MEG = magnetoencephalography; WJ-III = *Woodcock-Johnson Psychoeducational Battery*, 3rd ed. (Woodcock, McGrew, & Mather, 2001); TOWRE = *Test of Word Reading Efficiency* (Torgesen, Wagner, & Rashotte, 1999), Sight Word Reading Efficiency subtest.
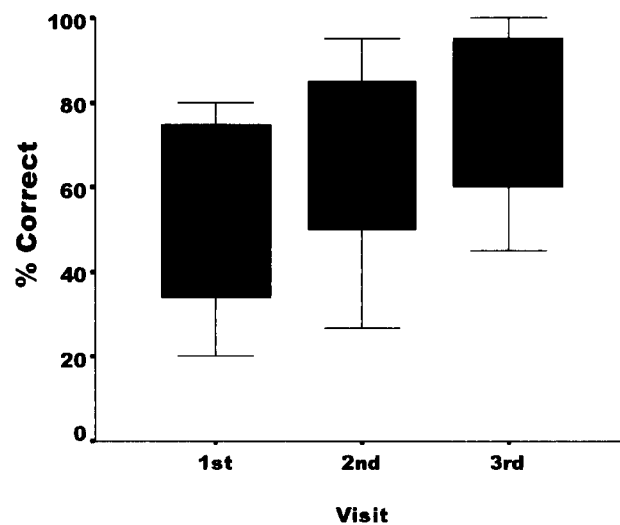

FIGURE 1. Naming accuracy (percentage of words read correctly) during the MEG scan at each visit. Bold horizontal lines indicate the group mean. Shaded blocks represent 95% confidence intervals, whereas vertical bars mark the entire range of individual scores at each visit
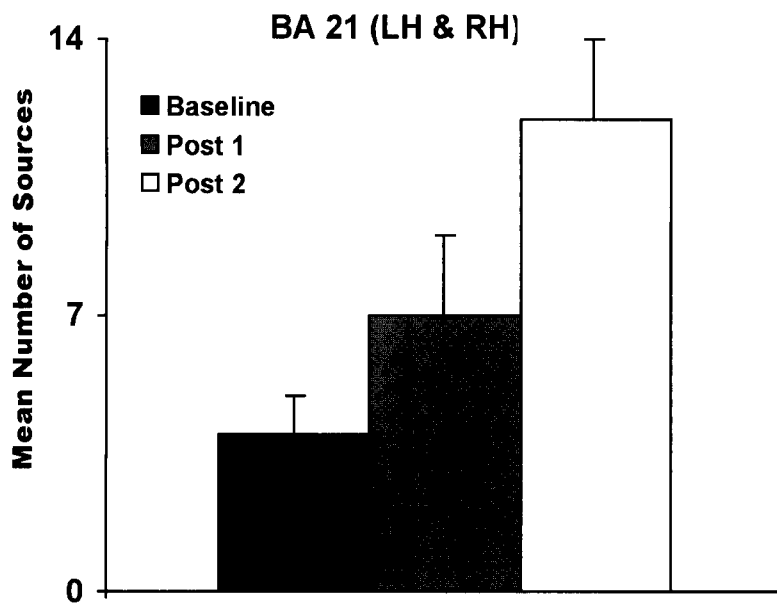
FIGURE 2. Mean number of activity sources in the posterior portion of the middle temporal gyrus (collapsed across hemispheres) that corresponds to Brodmann's Area (BA) 21. These consecutive activity sources were computed at 4-ms intervals and reflect the total duration of dipolar magnetic activity that took place between 200 and 700 ms after the onset of the word stimuli. The data for this figure were normalized separately for each participant based on the total number of activity sources found anywhere in the brain for a given recording session. Vertical bars indicate standard error of the mean. LH = left hemisphere; RH = right hemisphere; Post 1 = data acquired at the first postintervention visit; Post 2 = data obtained at the end of the study period.
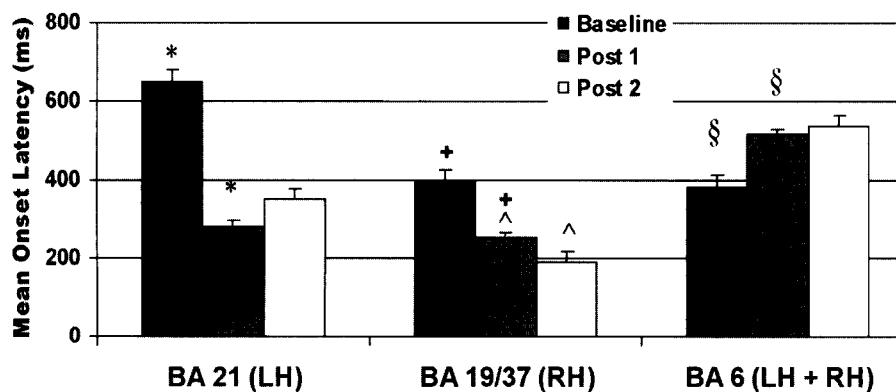
FIGURE 3. Changes in mean onset latency of activity (in ms after the onset of the word stimuli) in three brain areas across visits. Brodmann's Area (BA) 21 corresponds roughly to the posterior portion of the middle temporal gyrus, BA 19/37 indicates the lateral aspect of the occipitotemporal region, and BA 6 corresponds to the premotor area. Symbols * + ^ § indicate means that were significantly different at the .01 level. LH = left hemisphere; RH = right hemisphere; Post 1 = data acquired at the first postintervention visit; Post 2 = data obtained at the end of the study period.

secutive visits revealed a significant reduction between baseline and the first postintervention visit for onset of activity in the left middle temporal gyrus, $F(1, 14) = 13.63$, $p < .002$. No further reduction was noted between the second and third visits. In contrast, onset latency in the right occipitotemporal region decreased in a quasi-linear manner across the three visits (linear trend), $F(1, 14) = 63.78$, $p < .0001$. Moreover, onset latency increased bilaterally in premotor cortex across all three visits (main effect of visit), $F(2, 28) = 15.64$, $p < .0001$ (linear trend, $p < .0001$), although the change reached statistical significance between baseline and the first postintervention session, $F(1, 14) = 18.78$, $p < .001$. It should be noted that a decreasing trend was also noted for onset latency in activity in the superior temporal gyrus, along with a trend in the opposite direction for activity in the inferior frontal region. Both trends were found between baseline and the first postintervention session, but they did not meet the critical level of alpha ($p < .01$) set for post hoc tests.

To determine if changes in MEG-derived parameters of neurophysiological activity mapped onto the observed improvement in oral word reading efficiency across visits, on an individual basis, we performed a series of hierarchical multiple regression analyses. First, individual standardized values for the number of activity sources were used as predictors of in-scanner reading accuracy. In these analyses, data for areas that are presumed to play a compensatory role for reading (frontal, premotor, right hemisphere temporoparietal) were entered as one group, whereas data for areas that are key components of the typical mechanism for reading (left temporoparietal, left and right middle temporal, and temporo-occipital areas) were entered as a separate group. The model that included the former group of predictor variables was significant, adjusted $R^2 = .20$, $F(3, 44) = 4.74$, $p < .006$, and adding the second group of predictor variables did not warrant in-

clusion in the model ($p > .19$). The only significant contributor to individual variability in performance was the duration of activity in the left BA 21, $\beta = .39$, $t = 2.81$, $p < .008$, partial $r = .38$. The same procedure was followed for onset latency data and the model that included BA 19/37, BA 21, and BA 22 (in the left hemisphere) was significant, adjusted $R^2 = .38$, $F(4, 40) = 8.40$, $p < .0001$. Adding variables that reflected the onset of activity in prefrontal and premotor cortices bilaterally, and also activity in the right BA 22, made an additional significant contribution, $F(5, 35) = 2.55$, $p < .01$. The adjusted R^2 for the complete model was .53, $F(9, 44) = 6.36$, $p < .0001$. Only two significant predictors of individual reading accuracy scores emerged: onset of activity in the right BA 19/37, $\beta = -.49$, $t = -4.23$, $p < .0001$, partial $r = -.45$, and in the left premotor region, $\beta = .30$, $t = 2.30$, $p < .03$, partial $r = .24$. Taken together, these data indicate that oral word reading accuracy may be positively affected by the onset of activity in right extrastriate regions and by the duration of activity in BA 21 in the left hemisphere. The earlier the onset of activity in the former region, and the greater the duration of activity in the latter, the greater the accuracy. Conversely, early onset of activity in prefrontal regions (in the left hemisphere) was negatively correlated with reading accuracy.

In the second set of analyses, the temporal progression of regional activity at each visit was examined first by ranking the 18 anatomical locations (9 regions × 2 hemispheres) where activity sources were found consistently according to the mean *onset* latency of activity in each region. Then, 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. To control for Type I error for multiple comparisons, all tests were evaluated at $p = .001$. In Figure 4, brain areas that did not differ from one another on onset latency are

coded with similar shades of gray. Areas that showed significantly different onset latency are coded with contiguous shades of gray on the scale that accompanies each template.

Discussion

To our knowledge, this is the first imaging study to demonstrate changes in spatiotemporal activity patterns associated with an oral word reading task in children who participated in intensive remediation programs targeting both sublexical word reading and fluency skills. This intervention approach included intensive training on phonological processing and decoding skills, followed by a second intervention designed to improve fluency and automaticity. At the end of the intervention, children showed significant improvement on both phonological decoding skills and sight-word reading efficiency (Denton et al., in press). Performance improvements were paralleled by two types of significant changes (duration and onset latency) in regional brain activity as follows:

1. increased degree (or total duration) of neurophysiological activity in the posterior portion of the middle temporal gyrus (BA 21) bilaterally;
2. decreased onset latency of activity in BA 21 (left hemisphere) and in the lateral occipitotemporal region (BA 19/37, right hemisphere); and
3. increased onset latency of activity in the premotor region.

With the exception of onset latency in BA 21, these parameters of neurophysiological activity accounted for a significant proportion of variance in oral word reading accuracy. It should be noted that this activity was measured in real time *before* the phenomenon of interest (i.e., pronouncing the word stimuli) actually took place. This feature of MEG-derived activation profiles makes it more likely that changes in the profile of activity in middle temporal and occipitotemporal
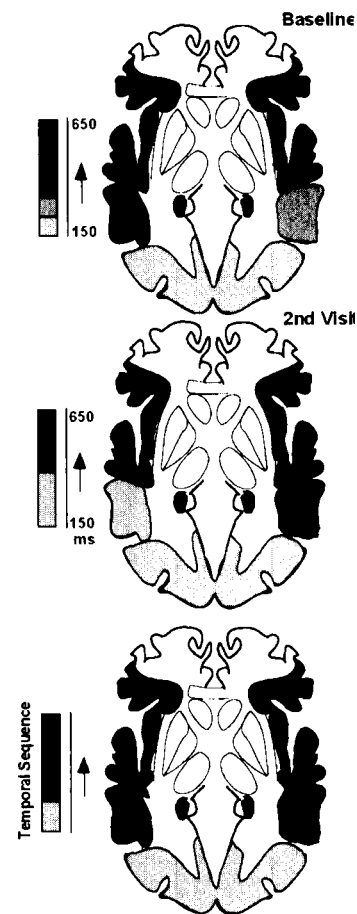

FIGURE 4. Schematic layout of regional differences in onset latency of neuromagnetic activity. At each visit, areas drawn in the same shading showed activity at about the same latency after the onset of the word stimuli. Notice the progression of activity from occipitotemporal to left frontal and right middle temporal cortices at baseline (top panel) as indicated by statistically significant differences ($p < .001$) in the onset latency of regions marked with contiguous colors on the scale displayed on the left of the brain template. During the second visit (middle panel) occipitotemporal activity was followed by near simultaneous onset of activation in temporal and frontal cortices. Finally, at the end of the 16-week intervention (lower panel), early occipitotemporal activity was again followed by temporal and left frontal activation, although right frontal activity occurred significantly later, shortly before the stimuli disappeared from the screen, which cued participants to start pronouncing the word names.

regions were at least partly responsible for the postintervention changes in reading ability.

There is growing evidence that the neurophysiological processes that take place in these regions, which encompass ventral and lateral extrastriate visual areas (BA 19/37) as well as the posterior portion of BA 21, are involved in graphemic and lexical–semantic operations associated with the recognition of printed stimuli (Booth et al., 2002; Fiebach et al., 2002; McCandliss et al., 2003; Simos, Breier, et al., 2002). Hemodynamic activation peaks in these regions are typically found with left-hemisphere predominance in unimpaired readers (Fiebach et al., 2002; Gaillard, Balsamo, Ibrahim, Sachs, & Xu, 2003; Hagoort et al., 1999; Herbster, Mintum, Nebes, & Becker, 1997). In MEG studies, a clear left-hemisphere predominance in the degree of activity in BA 19 and BA 37 is found in adult poor readers (Simos, Breier, et al., 2002) but not in younger unimpaired readers (Simos et al., 2001; Simos et al., 2005). With respect to activity in BA 21, MEG studies reveal only slight left-sided asymmetries during word reading (Simos, Breier, et al., 2002). It is therefore not clear if left-hemisphere predominance in the degree of activity in BA 19, BA 21, and BA 37 should be expected during word reading in unimpaired readers, or whether the lack of a hemispheric asymmetry represents an aberrant feature of the activation profile associated with RD. Our results indicated a bilateral increase in the duration of neurophysiological engagement of BA 21 with intervention, although only activity in the left hemisphere predicted reading accuracy in the scanner. Moreover, a reduction in onset latency of activity in BA 21, which may reflect enhanced efficiency of neurophysiological operations involved in word recognition, was notable only in the left hemisphere. These findings are therefore in agreement with earlier reports highlighting the role of the left hemisphere in the performance im-

provement associated with intervention (Simos, Fletcher, et al., 2002; Temple et al., 2003).

An unexpected finding, however, was the strong linear relationship between reading accuracy and the onset of activity that takes place during the early stages of stimulus processing in the right extrastriate cortex. However, previous studies did not assess regional activity in real time and, thus, did not allow researchers to look into this aspect of brain activity. Although the role of the left occipitotemporal region in complex visual–graphemic processing is now supported by several studies, mostly with experienced readers, there are some indications that the right occipitotemporal region may play a greater role in beginning reading. This is supported by findings of bilaterally symmetric duration of activity in this region in children as opposed to adult skilled readers (Simos et al., 2001) and, of course, by the present findings. One possible explanation is that this region operates as a complex visual processing area in beginning readers, supporting an early strategy of visual letter/word recognition (see, e.g., Ehri, 1996; Gough, 1993).

The increase in the onset latency of premotor activity (accompanied by a similar trend for onset latency in the inferior frontal gyrus) was in the opposite direction of changes in reading fluency. The amount of change in latency in this region (especially in the left hemisphere) was a significant predictor of improvement in reading accuracy. This may reflect a shift in the compensatory role of premotor and inferior frontal cortices to a role that is typical of the brain circuit for reading in average readers.

The present findings contrast with the results of previous MEG (Simos, Fletcher, et al., 2002) and fMRI studies (Temple et al., 2003) that showed increased activity in the temporoparietal cortex in the left hemisphere during pseudoword reading tasks. This region is presumably involved primarily in the phonological

processing of both spoken and written language (Simos, Breier, Wheless, et al., 2000). Although students in the present study were not explicitly taught the stimuli they were asked to read under the rapid stimulus exposure and presentation rate of the MEG task, the stimuli were real words to which most students are regularly exposed as sight words. On the other hand, both earlier studies used tasks that placed fewer demands on phonological decoding than the task used in the present study. The finding that activation of the temporoparietal cortex was not the most prominent feature of the activation profiles associated with a naming task even after intervention corroborates previous fMRI (Pugh et al., 2000) and electrocortical stimulation studies with nondisabled readers (Simos, Breier, Fletcher, et al., 2002). These findings are particularly relevant in showing that engagement of the posterior portion of the left superior temporal gyrus may not be necessary for reading sight words aloud. According to a popular theory of word recognition (e.g., Logan, 1997), access to word-like representations of printed stimuli relies heavily on a ventral–posterior circuit, consisting primarily of ventral temporo-occipital regions and the middle temporal gyrus, when the stimulus is familiar and task demands are appropriate (Pugh et al., 2000). Conversely, the mechanism that supports reading novel (e.g., pseudowords) or low-frequency stimuli relies more heavily on a dorsal system (consisting of Wernicke's area and the angular gyrus) with an anterior (frontal) component (Broca's area; Pugh et al., 2000; Simos, Breier, et al., 2002). This functional differentiation within the brain mechanism for reading corresponds to some extent to the two routes of the classical dual-route theory (Coltheart, Curtis, Atkins, & Haller, 1993).

Another notable finding of the present study was that in addition to the expected improvement in decoding accuracy, participants showed

more significant gains in reading fluency and comprehension after the first stage of the intervention, which focused primarily on phonological decoding skills (Denton et al., in press). This was paralleled by evidence of improved engagement of two components of the brain mechanism for reading (viz., the middle temporal and occipitotemporal regions) believed to be closely involved in orthographic and word-level analysis of print. A similar finding of increased inferior temporal lobe activity following intervention that did not entail training at the word-level has been reported in an fMRI study (Temple et al., 2003). It could be argued that children employed a decoding ("sounding out") strategy to pronounce the word stimuli in the MEG task. With that strategy, however, one would expect to see significant increases in temporoparietal activity, which was not the case in the present study. It is also possible that children with persistent reading problems require initially intensive training (or retraining) on phonological processing and decoding skills. This training—particular at the level of intensity in the first phase of the present study—may trigger a cascade of neurophysiological events that affect the capacity of the brain mechanism for reading to respond to print regardless of specific task requirements for subword-level processing.

Our finding of enhanced engagement of the middle temporal gyrus during reading is consistent with a similar finding in older children who had participated in a year-long intervention that focused on the development of phonological decoding skills (B. A. Shaywitz et al., 2004). To fully understand the impact of the order of the interventions, students would have to be assigned to different sequences that were comparable in intensity, which would be difficult to justify given the impairment in word recognition that characterized most nonresponders. The finding that the neurophysiological changes were more significant

for the first phase of the intervention is consistent with the results for the larger cohort in Denton et al. (in press), in which changes were apparent in both phases but larger effects were found for the first (decoding) phase than for the second (fluency) phase. However, as in the larger study, the trend for improvement in onset latency in the lateral occipitotemporal region persisted to the end of the study period. Given that behavioral performance on word reading accuracy and speed continued to improve during the same period, the change in the timing of the neurophysiological response of an area that appears to be involved in orthographic processing may be associated with the training and reading practice that children received during the second, fluency component of the 16-week intervention.

One limitation of the present study was that it did not include a group of average readers or an untreated group of students with persistent RD to assess group differences in regional activation over time. Previous studies that included a typically achieving group that was tested over time in MEG (Simos, Fletcher, et al., 2002) and fMRI imaging–intervention studies (B. A. Shaywitz et al., 2004) did not demonstrate major changes in brain activation patterns over time. However, average readers did show strong activation of occipitotemporal regions (including the posterior portion of the middle temporal gyrus). Changes observed for both the degree/duration and onset latency of activity in this region are consistent with at least one previous study reporting a similar degree of activation between unimpaired readers and adults with persistent developmental RD (S. E. Shaywitz et al., 2003). Nonetheless, including an average group of readers imaged over time would rule out maturational and developmental effects. Such effects could also be addressed with an untreated group of inadequate responders. In Denton et al. (in press), one cohort received a no-treatment baseline and did

not show behavioral effects. Obtaining samples of inadequate responders that are large enough to justify a no-treatment group may be difficult, however, given the low number of inadequate responders apparent in Mathes et al. (2005), suggesting a need for very large intervention studies.

To conclude, our findings extend previous results using hemodynamic and neuromagnetic imaging methods in demonstrating significant changes in the spatiotemporal profile of activation associated with word reading in response to reading remediation. These changes indicated improved engagement of neurophysiological processes involved in graphemic analysis and in word-level processing of print. Decreased latency and increased duration of engagement were found in brain areas that are strongly suspected to be necessary for these processes and could therefore be considered as largely normalizing. Indices of neurophysiological activity in these regions were significant predictors of performance. Results from MEG (Simos et al., 2005; Simos, Fletcher, et al., 2002) and fMRI studies (Aylward et al., 2003; B. A. Shaywitz et al., 2004) converge in demonstrating patterns of change toward the patterns seen in average readers, as opposed to the development of predominantly compensatory patterns of brain activation. In particular, intensive instruction on word-level skills is capable of inducing significant neurophysiological changes, even in children with RD who have received adequate classroom or supplemental instruction.

Future investigations should examine additional factors that may influence response to intervention. These studies should involve larger samples of children that better represent the skill profiles and possible etiologies suspected in the population of children with reading problems. More variability in both response to instruction and the corresponding neurophysiological profiles might be apparent, particularly if the reading skills of the sample

of inadequate responders are more variable. Nonetheless, the MEG data were closely related to performance data at the individual level, making the reported effects of intervention credible despite the small sample.

Another issue that deserves closer scrutiny concerns the type of intervention (in terms of intensity, duration, and content) associated with permanent changes in brain activation profiles that are capable of sustaining a lasting and clinically significant improvement in reading performance. The value of these types of studies in identifying factors related to inadequate response warrants the cost and difficulties of conducting multitiered intervention studies that will yield samples of inadequate responders for further study.

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