Instructional treatment associated with changes in brain activation in children with dyslexia

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Abstract—*Objective:* To assess the effects of reading instruction on fMRI brain activation in children with dyslexia. *Background:* fMRI differences between dyslexic and control subjects have most often involved phonologic processing tasks. However, a growing body of research documents the role of morphologic awareness in reading and reading disability. *Methods:* The authors developed tasks to probe brain activation during phoneme mapping (assigning sounds to letters) and morpheme mapping (understanding the relationship of suffixed words to their roots). Ten children with dyslexia and 11 normal readers performed these tasks during fMRI scanning. Children with dyslexia then completed 28 hours of comprehensive reading instruction. Scans were repeated on both dyslexic and control subjects using the same tasks. *Results:* Before treatment, children with dyslexia showed less activation than controls in left middle and inferior frontal gyri, right superior frontal gyrus, left middle and inferior temporal gyri, and bilateral superior parietal regions for phoneme mapping. Activation was significantly reduced for children with dyslexia on the initial morpheme mapping scan in left middle frontal gyrus, right superior parietal, and fusiform/occipital region. Treatment was associated with improved reading scores and increased brain activation during both tasks, such that quantity and pattern of activation for children with dyslexia after treatment closely resembled that of controls. The elimination of group differences at follow-up was due to both increased activation for the children with dyslexia and decreased activation for controls, presumably reflecting practice effects. *Conclusion:* These results suggest that behavioral gains from comprehensive reading instruction are associated with changes in brain function during performance of language tasks. Furthermore, these brain changes are specific to different language processes and closely resemble patterns of neural processing characteristic of normal readers.

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Developmental dyslexia is a genetically based[1] language disorder marked by an unusual difficulty, for age and verbal ability, in learning to read and spell words.[2] Estimates of prevalence range from 5 to 10% to 17.5%.[3,4] Children with dyslexia who are undiagnosed or untreated are at high risk for academic underachievement, noncompletion of high school or college, social-emotional problems associated with chronic school failure, and underemployment as adults. Differences between people with dyslexia and good readers include biochemical variations in temporal and parietal lobes,[5] less myelin in these same regions,[6] and structural anomalies in insula,[7] planum temporale, cerebellum, and Heschl's gyrus.[8] Functional studies using fMRI, PET, and magnetoencephalogram while subjects perform reading-related tasks suggest that people with dyslexia may exhibit abnormal activation during sensory visual processing,[9,10] visual speed discrimination thresholds,[11] rapid acoustic processing,[12,13] auditory processing,[14] orthographic processing,[15-17] phonologic processing,[17-25] and automatized phases of motor skill acquisition.[26] Evidence therefore suggests that dyslexia is best understood as the consequence of failures in multiple brain regions in a complex, functional reading system[27] and in functional disconnections among these regions.[23,24,28]

A large body of research suggests that a core deficit underlying dyslexia is in phonologic processing (i.e., difficulty in processing language sounds).[29,30] However, a growing body of research documents the role of morphologic awareness in reading and reading disability.[31-36] Morphologic awareness refers to the understanding of how word parts contribute to word meaning; for example, the same spelling "er" is a morpheme in the word "builder" (i.e., connoting someone who builds) but not in the word "corner." One purpose of this study was to determine whether a task involving morphologic processing might differentially activate the brains of good and poor readers, compared to a phonologic task. The current study was also designed to determine whether intensive

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instructional treatment is associated with changes in fMRI activation patterns during both phonologic and morphologic processing in children with dyslexia. By exploring effects of treatment on two different language processes, we can determine whether activation changes that result from comprehensive reading instruction, if they exist, are nonspecific or are differentially associated with specific reading-related language skills. We hypothesize that, despite relying on different neuronal circuitry, both language processes will show changes in activation patterns in children with dyslexia after an intensive treatment program.

Methods. *Subjects.* Subjects included 10 children with dyslexia (4 girls, 6 boys) and 11 normal readers (5 girls, 6 boys) who were group-matched for age. The University of Washington Human Subjects Institutional Review Board approved this study, and each subject (as well as parent/guardian) gave written informed consent. The dyslexic subjects were selected from probands in a family genetics study of dyslexia, as described previously.[2] These subjects were recruited through contacts with schools, other professionals, and widely advertised announcements in newspapers throughout the Seattle area. Entry criteria included a Verbal IQ of ≥90 on the Wechsler Intelligence Scale for Children–third edition[37] and evidence of underachievement by at least one SD in standardized measures of real word or pseudoword reading accuracy or rate or oral reading accuracy or rate.[2] All probands in the family genetics study were contacted, and those who were right-handed, had not yet received any intervention through the program, and did not have nonremovable foreign metal (such as oral braces) were invited to participate in the fMRI study. (It was subsequently determined, however, that one of these subjects was predominately left-handed, based on the Edinburgh Handedness Survey.[38]) Of the 14 who agreed to be in the study, 10 had imaging data of sufficient quality (i.e., minimal motion artifact, as described below) on both initial and follow-up scans.

Control subjects were recruited via word of mouth and advertisements in the hospital and in community newspapers. Control subjects qualified if they were reading at or above grade level on the Woodcock Reading Mastery Test[39] (see below), had no reported history of reading difficulty or of neurologic disorder, were right-handed (confirmed by the Edinburgh Handedness Survey[38]), and had no contraindication for MRI scanning. A total of 20 control subjects were scanned twice, and 11 of them had imaging data of sufficient quality within each scan.

The dyslexic and control groups did not differ significantly on sex, age, or Verbal IQ (table). At the initial scan, the children with dyslexia were reading on average about one SD below the population mean for age on the Word Identification (reading real words) and Word Attack (reading pseudowords) subtests of the Woodcock Reading Mastery Test.[39] Scores on these tests were significantly below this group's mean Verbal IQ. All control subjects were reading at or above the population mean on these same tests. The controls and children with dyslexia differed significantly in age-corrected standard scores for both of these tests. Scores on the Wide Range Achievement Test (third edition) Spelling test[40] were also significantly lower for the dyslexic subjects than for the control subjects. Dyslexic subjects were also impaired (below the population mean and significantly different from controls) in the three language markers for dyslexia: 1) phonologic coding (elision subtest),[41] 2) rapid automatic naming (RAN)[42]/rapid automatic switching (RAS),[43] and 3) orthographic coding[44] (see the table).

Instructional treatment. The children with dyslexia were imaged before and after a 28-hour (2 hours per day over 14 days) instructional treatment program.[45] The content of this instructional treatment met the requirements of a national panel of reading experts in the United States that reviewed the research literature to identify the components of reading instruction that are scientifically supported[46]: linguistic awareness, alphabetic principle, fluency, and reading comprehension. None of the subjects received any concurrent treatment other than that provided by the current study.

The control group was also imaged twice but did not receive treatment. The interval between scans was longer for the control subjects (mean = 3.6 months; SD = 1.5) than for the children with dyslexia (mean = 1.9 months; SD = 1.8) (t = 2.1, df = 19, p = 0.03). The scan protocol, tasks, and order of tasks were identical across repeated scans for each subject.

Table *Demographic and test performance data for the control (n = 11) and dyslexic subjects (n = 10) before instructional treatment*

Demographic and test data	Dyslexic, mean ± SD	Control, mean ± SD	p Value
Age, mo	139.1 ± 9.8	137.5 ± 7.9	0.69
Verbal IQ*	112.0 ± 10.7	116.8 ± 8.3	0.26
Word Identification*	86.1 ± 10.5	107.6 ± 8.1	<0.001
Word Attack*	87.0 ± 7.4	108.4 ± 6.5	<0.001
WRAT3 Spelling*	82.7 ± 5.0	114.6 ± 6.9	<0.001
Phonological Coding†	8.7 ± 1.5	11.3 ± 1.0	<0.001
RAN (Letters)‡	2.4 ± 1.9	−1.0 ± 0.5	<0.001
RAS (Letters and Numbers)‡	3.2 ± 2.5	−0.8 ± 0.5	<0.001
Orthographic Coding§	31.1 ± 21.5	68.2 ± 23.2	0.002

* Mean = 100, SD = 15; † mean = 10, SD = 3; ‡ z-score, for time where + is below the mean; § decile scores.

Functional MRI tasks. Two fMRI scans were performed with two sets of tasks to assess brain activation during phoneme mapping (the ability to make correct associations between letters or letter combinations and sounds) and morpheme mapping (the ability to make correct associations between word parts that signal grammatic information, such as suffixes, and their meaning when affixed to root words). The pair of alternating tasks developed for phoneme mapping were Letters-Phoneme Matching and Letters Only Matching (figure 1). For the Letters-Phoneme Matching task, only pseudowords were used so that children could not perform the task solely on the basis of word-specific knowledge. In each trial two pseudowords (three- to five-letter pronounceable monosyllables) were presented visually, one above the other. Each word had one or two pink letters and the other letters were black. During the Letters-Phoneme Matching task, the child was asked to indicate with a button press whether the pink letters in the top and bottom pseudowords could stand for the same sound (e.g., Could *oa* in *ploat* stand for the same sound as *ow* in *drow*? Could *kn* in *knop* stand for the same sound as *k* in *kack*?). The Letters Only Matching task required the child to decide whether two letter strings (e.g., *szpy* and *sxpy*) matched exactly. Length of the letter strings was comparable to the length of the pseudowords in the Letters-Phoneme Matching task. This control task required attention to all letter positions, but did not involve any phonologic processing. Thus, comparison of activation during these two tasks isolated the areas of activation specifically related to the construct of phoneme mapping.

The pair of alternating tasks developed for morpheme mapping consisted of Comes From and Synonym Judgment (see figure 1). During the Comes From task, the child saw and heard two words, one presented above the other. In half of the Comes From trials, the top word contained a derivational suffix that rendered it semantically related to the bottom word (e.g., *builder* and *build*). For the other half of the Comes From trials, the top word contained a spelling pattern sometimes used as a derivational suffix (e.g., *er*), but which did not convey meaning in this particular case. Thus in these trials the top word was semantically unrelated to the bottom word (e.g., *corner* and *corn*, in which the *er* in *corner* was not a suffix indicating that *corner* is semantically related to *corn*). For the Comes From task, the child indicated with a button press whether the top word on the screen was semantically related to ("comes from") the bottom word. This task was paired with a control task, Synonym Judgment, in which the child determined whether the top word means the same as the bottom word (e.g., *small* and *little*). In these two tasks, correct judgments did

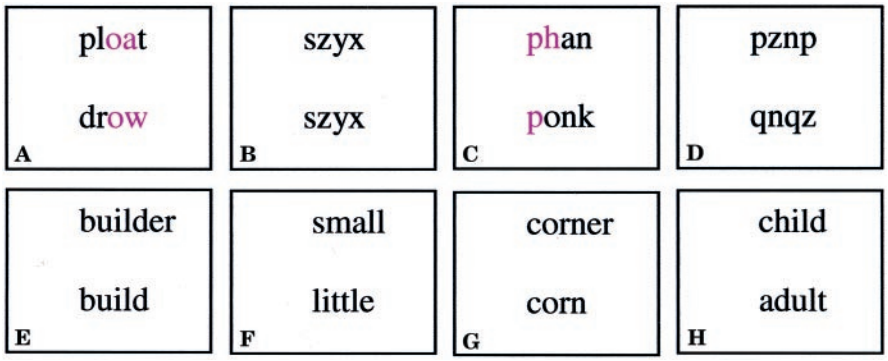

Figure 1. Stimuli for phoneme mapping and morpheme mapping. Activation during Letters-Phoneme Matching (A and C) was contrasted with activation during Letters Only Matching (B and D). For the Letters-Phoneme Matching task, subjects were asked to indicate whether the pink letters in the top word could represent the same sound as the pink letters in the bottom word. For the Letters Only Matching task, subjects were asked to indicate whether the letter strings matched exactly. In this example, the response would be "Yes" (button press) for Letters-Phoneme Matching item (A), as oa *in* ploat *can make the same sound as* ow *in* drow*, and "Yes" (button press) for Letters Only Matching item (B). The response would be "No" (no button press) for Letters-Phoneme Matching item (C), as the* ph *in* phan *cannot make the same sound as the* p *in* ponk*, and "No"(no button press) for Letters Only Matching item (D). Activation during Comes From (E and G) was contrasted with activation during Synonym Judgment (F and H). For the Comes From task, subjects were asked to indicate whether the top word "comes from" the bottom word. For the Synonym Judgment task, subjects were asked to indicate whether the top word means the same as the bottom word. In this example, the response would be "Yes" (button press) for Comes From item (E), as* builder *"comes from"* build *and "Yes" (button press) for Synonym Judgment item (F). The response would be "No" (no button press) for Comes From item (G), as* corner *does not "come from"* corn*, and "No" (no button press) for Synonym Judgment item (H).*

not depend on ability to read the words because stimuli were presented both visually and auditorally. Average word length was the same across conditions. [In addition, with one exception, none of the yes items in the Comes From task involved the phonologic shift in the pronunciation of the affixed word in relation to the unaffixed word (e.g., *a* in first syllable of national vs *a* in nation). Phonologic shifts are known to be difficult for dyslexic children.[32,33] Thus, morpheme mapping should not share phonologic processing requirements with phoneme mapping.] Like the Comes From task, the Synonym Judgment task required the child to read and listen to words and to make semantic judgments, but did not involve any processing of derivational suffixes. Thus, comparison of activation during these two tasks isolated the areas of activation specifically related to the construct of morpheme mapping.

Each of the functional MRI scans lasted 5 minutes and 42 seconds. For each scan, the two contrasting tasks were alternated, with four repetitions of each task lasting 30 seconds each. In addition, a fixation condition (cross-hair), lasting 18 seconds, was presented at the beginning, in the middle, and at the end of the series in order to provide a standard baseline. A slide with instructions appeared for 6 seconds before each condition. Visual word pairs were presented for 6 seconds, with no interstimulus interval. For all tasks, children indicated a "yes" response by pressing a button held in the dominant hand. The button press had to occur during the 6-second stimulus presentation to be counted as correct. For each task condition half of the items had "yes" as the correct answer.

Stimuli were presented and responses were recorded using Eprime software (Psychology Software Tools, Pittsburgh, PA). The subject viewed the visual stimuli through a pair of goggles that were connected via high-resolution fiber optic cables to two Infocus projectors, which were, in turn, connected to the Eprime computer.

Scan acquisition. Structural and functional MR imaging were performed on a 1.5 Tesla MR imaging system (General Electric, Waukesha, WI). Scanning included a 21-slice axial set of anatomic images in plane with functional data (repetition time [TR]/echo time [TE] 200/2.2 msec, fast spoiled gradient echo pulse sequence, 6 mm thick with 1 mm gap, 256 × 256 matrix). These anatomic series were followed by two fMRI series using two-dimensional gradient echo echoplanar pulse sequence (TR/TE 3,000/50 msec, 21 slices, 6 mm thick with 1 mm gap, 64 × 64 matrix, 114 volumes total, time = 5 minutes 42 seconds). Half of the subjects in each group had the phoneme mapping set of tasks during the first scan and half had morpheme mapping set of tasks first. A high-resolution three-dimensional series was then acquired in the sagittal plane using a fast spoiled gradient echo pulse sequence (1.2 mm, no gap, TR/TE = 11.1/2.2 msec, flip angle = 25 degrees, field of view = 24 cm).

Image processing. fMRI scans were analyzed using MEDx (version 3.4.1) (Sensor Systems, Sterling, VA). Scans were considered acceptable for analysis if at least two of the four alternating cycles within the scan had less than 3 mm of movement. There were no differences between groups on the number of acceptable volumes. The data were motion corrected in three dimensions using the Automated Image Registration protocol imbedded in MEDx. Data were then linear detrended, and a *t*-test was performed contrasting the two conditions within each scan, expressed as a z-score. Each subject's activation z-map was spatially smoothed with a 4 mm Gaussian filter and converted to standard stereotaxic space of Talairach[47] using FLIRT (www.fmrib.ox.ac.uk/fsl/). Maps showing significant activation for each group and session were generated[48] and coregistered with images from a high-resolution three-dimensional brain, supplied in the MEDx package, that had also been converted to standard Talairach space. Significantly activated clusters were identified on these group maps using a threshold of $z > 2$ and $p < 0.05$.[49] This approach considers the significance of activation in the voxel of interest as well as in adjacent voxels to identify a voxel as significantly activated, and also corrects for multiple comparisons. In order to compare z-maps across two groups, we computed standardized mean differences by calculating a z-map contrasting respective values using the two-sample test statistic for comparison of means, $z = (\text{mean } z_1) - (\text{mean } z_2)/\text{square root}(1/n_1+1/n_2)$, where mean z_1 = mean z map for control subjects, mean z_2 = mean z map for dyslexic subjects, n_1 = N of control group (11), and n_2 = N of dyslexic group (10).[50] Similarly, for comparisons across time, z_1 = mean z map for subjects at initial scan, mean z_2 = mean z map for subjects at follow-up scan. This standardized mean difference z-map can be used to determine regions where two groups of unequal size significantly differ in their activation. Significant ($z > 2$) clusters were identified on these difference maps.

Results. *Performance on the reading tests.* The 10 dyslexic children improved significantly from the beginning to the end of the 3-week intervention on three measures related to the tasks they performed during scanning. On the Word Attack subtest of the Woodcock Reading Mastery Test Revised,[39] which relies on phoneme mapping, the mean standard score for dyslexic subjects increased from 87.0 (SD = 7.4) to 93.7 (SD = 10.8), $t = 2.7$, $df = 9$, $p =$

0.03. Because standardized measures of morphologic processing are not available, we used two experimenter-designed tasks, which our cross-sectional and longitudinal studies are showing to be reliable and valid for assessing literacy skills. These tasks assess morpheme mapping and oral reading accuracy for words with and without suffixes. On a Comes From task using word pairs different from the ones used during scanning, the mean score for the dyslexic subjects increased from 70.2 (SD = 4.6) to 74.0 (SD = 2.9) out of 80 items ($t = 2.4$, $df = 9$, $p = 0.04$). On a decoding task that included words with and without suffixes, mean accuracy increased from 30.7 (SD = 7.3) to 34.5 (SD = 4.0) out of 58 ($t = 2.9$, $df = 9$, $p = 0.02$).

Imaging results. For the results that follow, phoneme mapping refers to the comparison of the Letters-Phoneme Matching and Letters Only Matching tasks in the first set, and morpheme mapping refers to the comparison of the Comes From and Synonym Judgment tasks in the second set.

Control subjects. The two sets of tasks used during imaging activated different parts of the brain. For the control subjects, regions of activation for phoneme mapping included bilateral (left > right) superior, middle, and inferior frontal gyrus, left middle temporal gyrus, bilateral (left > right) angular gyrus/inferior/superior parietal lobe, and bilateral inferior temporal/fusiform gyrus. Activation for control subjects on the initial scan for morpheme mapping was observed bilaterally in striate cortex and other parts of occipital lobe, fusiform gyrus, bilateral parietal lobe, left middle and inferior frontal cortex, and a very small region in right superior frontal cortex. Activation was generally greater at the follow-up scan than at the initial scan for morpheme mapping, whereas the reverse was the case for phoneme mapping. However, the location of activation for both functions was generally consistent across time. In addition to the regions activated at the initial scan for morpheme mapping, control subjects also demonstrated activation in bilateral orbital frontal cortex and bilateral inferior temporal/fusiform gyrus at the follow-up scan.

Dyslexic subjects. For the dyslexic group, very small regions of activation were observed before treatment for phoneme mapping in right cerebellum, right inferior temporal gyrus, bilateral (left > right) orbital, inferior, and middle frontal gyri, bilateral (right > left) superior frontal gyrus, and left superior parietal gyrus. After treatment, most of these same regions were activated to a larger extent; additional regions of activation included left cerebellum, left inferior temporal, bilateral fusiform gyrus, and right superior parietal gyrus. Before-treatment activation for morpheme mapping was observed in bilateral (right > left) precuneus/striate regions and right superior parietal lobe. After treatment, these same regions were activated to a larger extent, and additional areas of activation included fusiform gyrus, left parietal lobe, and bilateral (left > right) orbital, inferior, middle, and superior frontal gyrus.

Dyslexic vs control group comparisons. Figures 2 through 5 show the brain areas where activation was greater for the control subjects than for the children with dyslexia at the initial scan and where children with dyslexia demonstrated changes between pre- and post-treatment scans. Images for phoneme mapping are shown in the sagittal and axial planes, whereas images for morpheme mapping are shown in the coronal plane, as these views best represent the data showing group differences and changes over time.

Phoneme mapping. At the initial scan, the control subjects had greater activation than children with dyslexia on phoneme mapping in left inferior and middle frontal gyri (see figure 2A). Figure 2B shows regions where control subjects had significantly more activation than children with dyslexia at follow-up scan. The substantial reduction of group differences in inferior and middle frontal gyral activation following treatment of the dyslexic subjects was due both to an increase in the level of activation of inferior and middle frontal gyri for the dyslexic subjects (see figure 2C) and to a decrease in the level of activation for the control subjects (see figure 2D). (The control subjects showed no significant increases over time in activation in any of the regions of interest in figures 2 through 5.)

At the initial scan, control subjects also showed greater activation than children with dyslexia on phoneme mapping in bilateral (left > right) superior parietal region (see figure 3A). Figure 3B shows that these group differences no longer existed after treatment of the dyslexic subjects. The elimination of group differences following treatment of the dyslexic subjects was due to both an increase in the level of activation of superior parietal region for the dyslexic subjects (see figure 3C), with changes on the right being greater than changes on the left, and to a decrease in the level of activation for the control subjects (see figure 3D), with significant changes on the right only.

Differences between the dyslexic and control groups on phoneme mapping at the initial scan were also observed in bilateral angular gyrus, bilateral superior frontal gyrus, bilateral (left > right) fusiform, left middle, and inferior temporal gyri, and bilateral (left > right) inferior parietal lobe. These regions did not show significant change before and after treatment for the dyslexic subjects. Group differences were, however, eliminated at the follow-up scan, owing to nonsignificant decreases in activation in the control group and nonsignificant increases in activation in the dyslexic subjects. The only regions that continued to show group differences at the follow-up scan were the left middle and inferior frontal gyri areas, shown in figure 2B, and a very small region of left superior parietal lobe, shown in figures 2B and 3B.

Morpheme mapping. At the initial scan, the control subjects had greater activation than children with dyslexia on morpheme mapping in right fusiform gyrus (figure 4A). Figure 4B shows that these group differences no longer existed after treatment of the dyslexic subjects. The elimination of group differences following treatment of the dyslexic subjects was due to a significant increase in the level of activation of the fusiform gyrus for the dyslexic subjects (figure 4C). There was no significant decrease in activation among the control subjects (figure 4D).

At the initial scan, control subjects also showed greater activation than children with dyslexia during morpheme mapping in right superior parietal region (figure 5A). Figure 5B shows that these group differences no longer existed after treatment of the dyslexic subjects. The elimination of group differences following treatment of the dyslexic subjects was due primarily to a decrease in activation among the control subjects (figure 5D), although there was a significant increase in activation among the dyslexic subjects in an area more superior (figure 5C) to

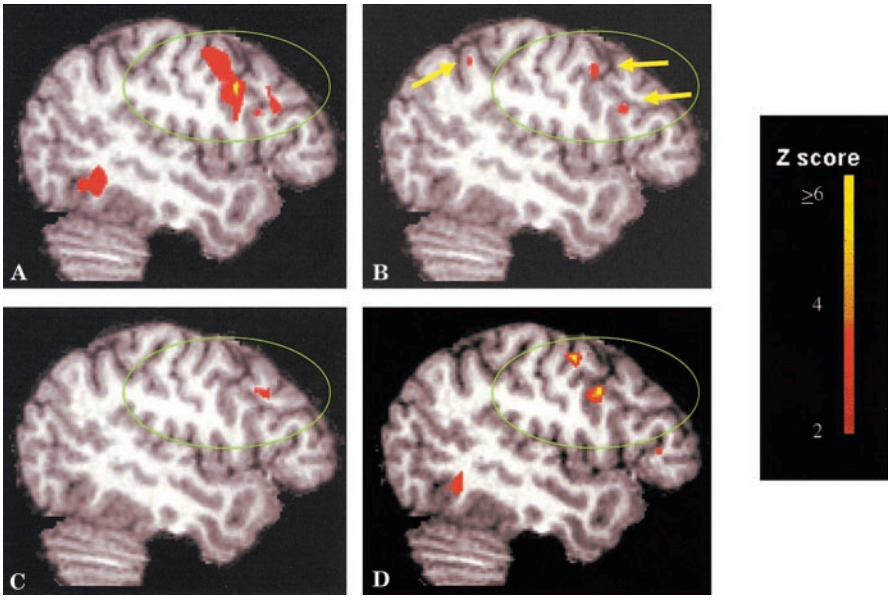

Figure 2. Left middle and inferior frontal gyrus during phoneme mapping (Talairach level: x = −40). (A) Areas of greater activation for controls than children with dyslexia at the initial scan. (B) Areas of greater activation for controls than children with dyslexia at the follow-up scan. (C) For dyslexic subjects only: areas of greater activation at follow-up scan as compared with initial scan. (D) For control subjects only: areas of less activation at follow-up scan as compared with initial scan. (The control subjects showed no significant increases in activation in any regions.) Regions of interest are circled in green. Arrows indicate the only regions that were more activated for control than for dyslexic subjects at follow-up scans. (The small posterior region of activation is the same area of superior parietal lobe that is identified in figure 3B.) Right and left superior parietal region during phoneme mapping (Talairach level: z = 43).

the area in which the original group differences were observed (figure 5A).

In addition to the right fusiform gyrus and right superior parietal region, the control subjects showed significantly more activation than the dyslexic subjects on morpheme mapping at the initial scan in bilateral occipital-parietal junction and left middle frontal gyrus. These regions did not show significant change before and after treatment for the dyslexic subjects. Group differences were, however, eliminated at the follow-up scan, owing to nonsignificant decrease in activation in the control group and nonsignificant increase in activation in the dyslexic subjects. The only region for which group differences were observed at the follow-up scan on morpheme mapping was a small region of right striate cortex (identified in figure 5B). This region did not show group differences at the initial scan.

Discussion. Results of this study demonstrate that after 3 weeks of comprehensive treatment, brain activation patterns in children with dyslexia

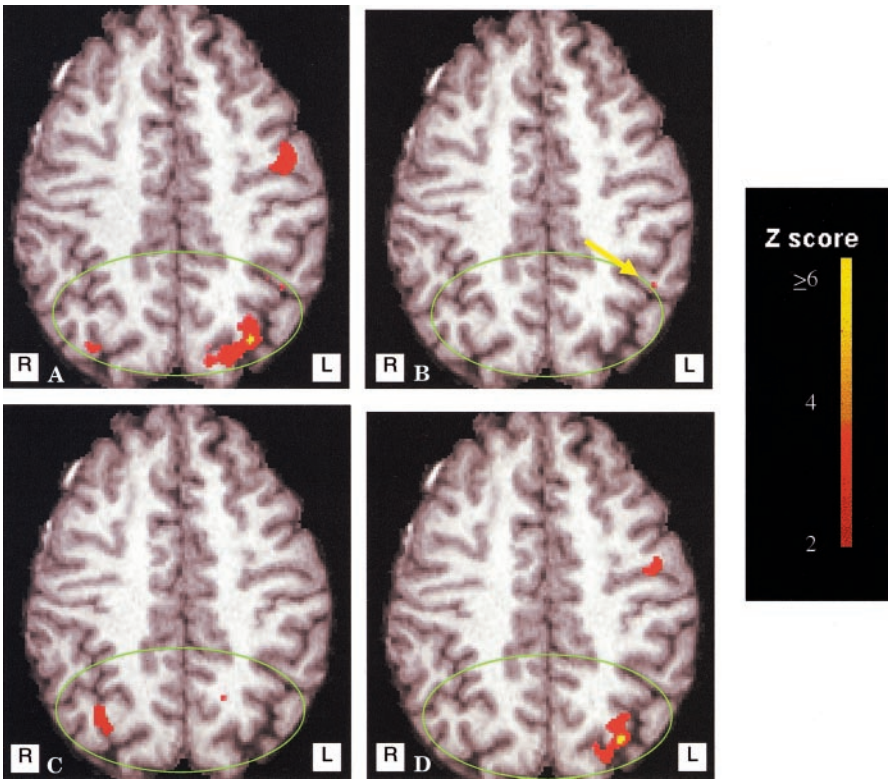

Figure 3. Right and left superior parietal region during phenome mapping (Talairach level: z = 43): (A) Areas of greater activation for controls than children with dyslexia at the initial scan. (B) Areas of greater activation for controls than children with dyslexia at the follow-up scan. (C) For dyslexic subjects only: areas of greater activation at follow-up scan as compared with initial scan. (D) For control subjects only: areas of less activation at follow-up scan as compared with initial scan. (The control subjects showed no significant increases in activation in any of the regions of interest in figures 2 through 5.) Regions of interest are circled in green. Arrows indicate the only regions that were more activated for control than for dyslexic subjects at follow-up scans.

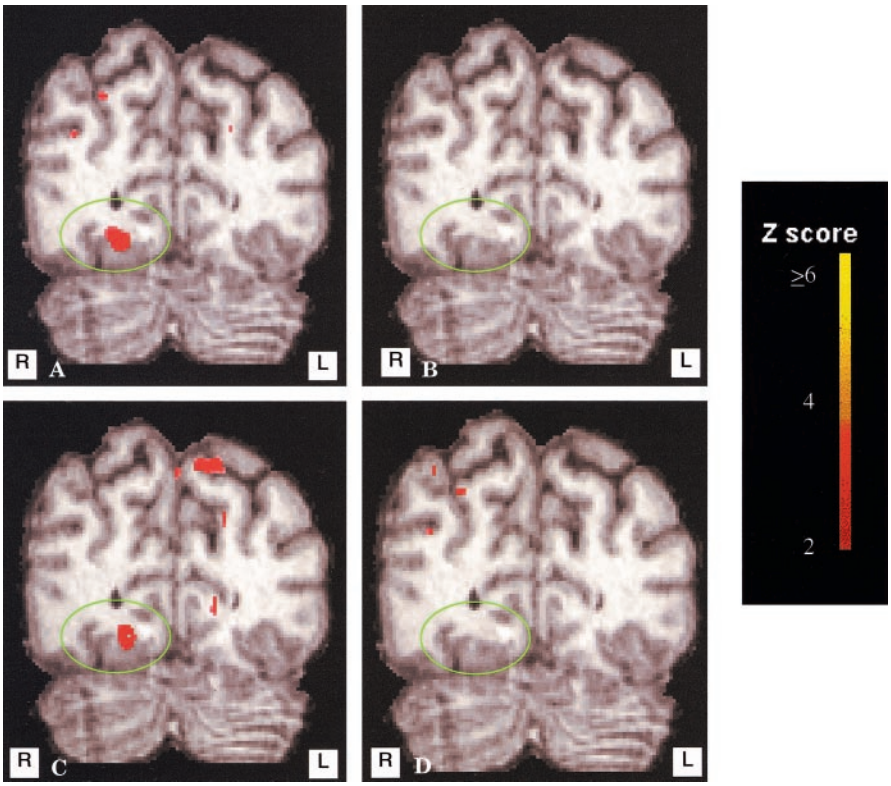

Figure 4. Right fusiform gyrus during morpheme mapping (Talairach level: y = −71): (A) Areas of greater activation for controls than children with dyslexia at the initial scan. (B) Areas of greater activation for controls than children with dyslexia at the follow-up scan. (C) For dyslexic subjects only: areas of greater activation at follow-up scan as compared with initial scan. (D) For control subjects only: areas of less activation at follow-up scan as compared with initial scan. (The control subjects showed no significant increases in activation in any of the regions of interest in figures 2 through 5.) Regions of interest are circled in green. There were no regions that were more activated for control than for dyslexic subjects at follow-up scans.

changed to resemble the patterns of normal control subjects during two specific language processes, phoneme and morpheme mapping. This study provides an additional demonstration that changes in brain activation during phonological tasks are detectable in response to instructional intervention (as previously demonstrated with MRS[51] and magnetic source imaging [MSI][52]). The current study extends the finding of a treatment effect to morpheme mapping processes and demonstrates that brain activation patterns are different for the two specific language processes. Even in control children, phoneme mapping and morpheme mapping activated different regions, which is not surprising given the growing

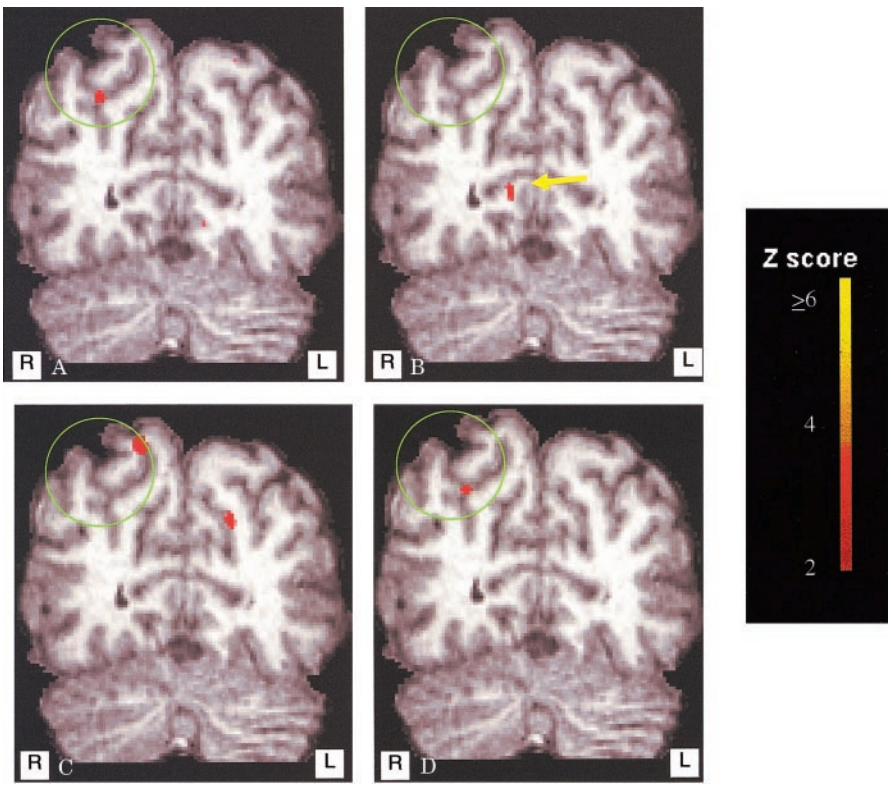

Figure 5. Right superior parietal region during morpheme mapping (Talairach level: y = −67): (A) Areas of greater activation for controls than children with dyslexia at the initial scan. (B) Areas of greater activation for controls than children with dyslexia at the follow-up scan. (C) For dyslexic subjects only: areas of greater activation at follow-up scan as compared with initial scan. (D) For control subjects only: areas of less activation at follow-up scan as compared with initial scan. (The control subjects showed no significant increases in activation in any of the regions of interest in figures 2 through 5.) Regions of interest are circled in green. Arrows indicate the only regions that were more activated for control than for dyslexic subjects at follow-up scans.

literature showing that different patterns of brain activation are associated with different levels of normal language processing; for example, lexical meaning and sentence syntax.[53]

Figures 2C through 5C show regions in which the dyslexic children demonstrated more activation following treatment than before treatment. At the same time that they were showing increases in activation, control subjects were showing decreases in activation (figures 2D through 5D), presumably due to practice effects that were not being experienced by the dyslexic subjects. Thus, the lack of group differences at the follow-up scan must be attributed to both increases in activation among the dyslexic subjects and decreases in activation among the control subjects. Although it is not possible to definitively link the increases in activation among the dyslexic subjects to treatment, it is reasonable to assume that observed improvements in reading skills would be accompanied by changes in the brain, and the observed activation changes suggest a brain-behavior relationship. Furthermore, the regions where activation was increased for phoneme mapping and morpheme mapping in dyslexic children are consistent with the regions that were found to be activated in control subjects at the initial scan. Changes for the dyslexic subjects for phoneme mapping are also consistent with previous studies demonstrating an association between phonologic decoding and left middle and inferior frontal gyrus in both dyslexic[17,20,25] and control subjects.[17,20,22] Previous studies identifying regions associated with morpheme mapping have not been reported.

Our findings suggest that instructional treatment does not result in novel functional reorganization that creates neural pathways different from those used by normal readers for these specific language tasks. Instead, the results suggest that treatment amplifies activation in circuits normally employed to process these language functions. Results further suggest that improvements in reading are not the result of more global cognitive changes (e.g., improved attention) that 1) would be represented by activation changes different from those observed in normal readers and 2) would not be differentiated for the two specific language processing tasks. Instead, our results suggest that treatment was associated with brain activation changes that were specific to the two different language mapping tasks, and that the modified brain activation patterns in children with dyslexia were very similar to those observed in normal readers. Dyslexia is a pervasive disorder with genetic and structural correlates. The results do not suggest that treatment made dyslexic brains into normal brains, rather that treatment was associated with a change in brain function toward a more normal pattern in the two language tasks administered.

The phonologic core deficit theory[29] hypothesizes that dyslexia is caused by an inability to make correspondences between letters or letter combinations and the sounds they represent. Consistent with this theory, we found that brain activation in dyslexic children was significantly less than in control children during phoneme mapping. Although some areas of activation for controls on phoneme mapping were also activated in the children with dyslexia (inferior, middle, and superior frontal gyrus, left superior parietal, right inferior temporal) at the initial scan, the level of activation was significantly less in the children with dyslexia. Other regions of activation for controls on this task (left middle temporal, bilateral angular/inferior parietal, right superior parietal, and bilateral fusiform) were not activated for children with dyslexia at the initial scan. Regions of primary treatment-related activation changes (inferior and middle frontal gyrus and superior parietal lobe) for phoneme mapping are not consistent with a recent MSI study[52] that found activation changes primarily in the posterior portion of the superior temporal gyrus. Inconsistency in the regions of activation is probably the result of different methods (fMRI vs MSI) and different phonologic processing tasks (phoneme mapping in our study vs visual pseudoword rhyme matching in the MSI study).

In addition, we demonstrated that children with dyslexia initially differed from controls in brain activation during morpheme mapping. This finding is consistent with previous research suggesting that a single language processing abnormality in developmental dyslexia is unlikely.[27] Treatment-related changes in morpheme mapping were found primarily in right fusiform gyrus and superior parietal lobe.

One limitation of this study is the absence of a group of nontreated dyslexic children who were scanned at the same interval as the treated dyslexic children. Because the lack of differences between dyslexic and control subjects after treatment is somewhat the result of practice effects in the control subjects that are absent in the treated dyslexic subjects, it would be helpful to know what the effects of practice would be in a nontreated dyslexic group. Another limitation is the small sample size. Results from this study should, therefore, be considered preliminary and in need of confirmation in future studies. Additional studies are now underway in our laboratory with larger samples.

The findings of the current study are important because they suggest that children with genetically constrained developmental dyslexia are not only teachable, as evidenced by improvements in scores on reading tests, but that fairly brief, intensive intervention can be associated with observable changes in the brain's response to language tasks. Presumably, this is because the dyslexic children are performing the task differently than they did before treatment. Furthermore, these brain changes 1) are specific to different language processes and 2) qualitatively resemble the pattern of neural processing characteristic of normal readers. Our results suggest that the brain events underlying specific language processes in children with dyslexia can be modified to closely resemble activation patterns of normal children

when instructional components are carefully orchestrated in environments that teach multiple facets of language. As previously suggested,[51] the brain is both an independent variable that constrains response to intervention and a dependent variable that responds in some way to environmental input.

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