Dyslexia-specific Brain Activation Profile Becomes Normal Following Successful Remedial Training

Article *in* Neurology · May 2002

DOI: 10.1212/WNL.58.8.1203 · Source: PubMed

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Dyslexia-specific brain activation profile becomes normal following successful remedial training

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Abstract—*Objectives:* To examine changes in the spatiotemporal brain activation profiles associated with successful completion of an intensive intervention program in individual dyslexic children. *Methods:* The authors obtained magnetic source imaging scans during a pseudoword reading task from eight children (7 to 17 years old) before and after 80 hours of intensive remedial instruction. All children were initially diagnosed with dyslexia, marked by severe difficulties in word recognition and phonologic processing. Eight children who never experienced reading problems were also tested on two occasions separated by a 2-month interval. *Results:* Before intervention, all children with dyslexia showed distinctly aberrant activation profiles featuring little or no activation of the posterior portion of the superior temporal gyrus (STGp), an area normally involved in phonologic processing, and increased activation of the corresponding right hemisphere area. After intervention that produced significant improvement in reading skills, activity in the left STGp increased by several orders of magnitude in every participant. No systematic changes were obtained in the activation profiles of the children without dyslexia as a function of time. *Conclusions:* These findings suggest that the deficit in functional brain organization underlying dyslexia can be reversed after sufficiently intense intervention lasting as little as 2 months, and are consistent with current proposals that reading difficulties in many children represent a variation of normal development that can be altered by intensive intervention.

NEUROLOGY 2002;58:1203–1213

Dyslexia, a persistent difficulty in acquiring word reading skills, affects a significant proportion of school-aged children and is a serious contributor to academic failure. Dyslexia seems to have a neurologic basis, but the precise nature of this impairment is not fully understood. There is agreement among researchers that the core problem in dyslexia is related to a functional impairment within the brain mechanism specialized for language, specifically in the component responsible for phonologic analysis. Reading acquisition in children requires the development of an appreciation for the segmental nature of speech, a skill known as phonemic awareness. Once the child realizes that spoken words are composed of smaller segments (the phonemes), he or she can learn to treat written words as multisegment units and grasp the correspondence between letters (or letter complexes) and phonemes. This concept is known as the alphabetic principle and lies at the heart of teaching programs that focus primarily on the development of phonemic decoding skills. Many studies have shown that children with dyslexia have poor phonemic awareness skills.[1-3] These deficiencies lead to the poor development of word recognition skills.[4] Thus, measures of phonemic processing predict later reading achievement[5-7] and can be reliably used to identify children with dyslexia.[2,3]

With the emergence of functional imaging methods that allow for the detection, localization, and quantification of brain activity associated with cognitive function, it is possible to assess systematically the putative brain mechanisms underlying dyslexia. Functional brain imaging is well suited for the study of activation profiles peculiar to dyslexia.

Functional brain imaging is noninvasive and can be used repeatedly with both dyslexic children and normal control participants in the context of exploratory studies. Two functional imaging methods have been used with children: fMRI and, most recently, magnetic source imaging (MSI). Like PET, which is used only with adults because it involves injection of radioactive isotopes, fMRI captures blood flow and

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Supported in part by grants from NSF (REC-9979968), National Institute of Neurological Disorders and Stroke (NS37941–01), and NICHD (DA10715) to A.C.P.

Received July 27, 2001. Accepted in final form January 27, 2002.

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local metabolic changes contingent on the differential degree of activation of various brain structures during the performance of specific tasks. MSI, conversely, provides a real-time, spatiotemporal map of brain activity by directly measuring electrical currents in neuronal aggregates during task performance.

Because dyslexia is not typically associated with structural brain lesions,[8] its mechanism could be a deviant form of functional organization of the brain structures that subserve reading-related functions. Such functional aberrations would be expected to appear as brain activation profiles specific to dyslexic individuals, and therefore different from those of nondyslexic individuals engaged in the same language-processing tasks. Previous research using all three imaging modalities suggest that engagement in tasks that require phonologic decoding (such as reading of pseudowords) is associated with increased activation in some areas. These include the posterior portion of the superior temporal, the angular, and supramarginal gyri (henceforth collectively referred to as the temporoparietal region), and also the inferior frontal lobe, primarily in the left hemisphere.[9-11] In addition, word and pseudoword reading tasks engage areas on the basal surface of the temporal lobe in the vicinity of the lingual and the fusiform gyri[12-14] to a greater extent than when nonlinguistic visual stimuli are used. Despite several inconsistencies among studies with respect to the engagement of a particular area in reading,[15] the overall consensus is that a network of areas are involved in word recognition, each of which may be differentially activated depending on specific task demands.[9]

PET studies comparing activation profiles of adults with dyslexia to those of nonimpaired readers have found reduced blood flow in the left temporoparietal area during performance of reading and phonologic processing tasks[16-18] but normal activation in the left inferior frontal areas.[18,19] In addition, the asymmetry of activity favoring the left hemisphere, usually observed in normal readers during reading tasks, has been found to be significantly attenuated in adults with dyslexia.[20] These results are consistent with data from fMRI studies, in which nonimpaired readers as a group demonstrated an incremental activation in temporoparietal areas with increasing demands for phonologic analysis. In contrast, impaired readers did not demonstrate this pattern.[21,22] In addition, the latter group showed reversed (right $>$ left) hemispheric asymmetries of activation in posterior temporal regions when compared with the group of nonimpaired readers.

Two main conclusions emerge from these studies. First, left hemisphere temporoparietal areas in children and adults with dyslexia fail to show the activation seen in nonimpaired readers during engagement in tasks that pose substantial demands for phonologic analysis. Second, dyslexic readers may rely on the engagement of both inferior frontal (in adult dyslexics) and right hemisphere temporoparietal areas to a greater extent than nonimpaired readers.

Recently, we used MSI to demonstrate the existence of a distinct spatiotemporal profile of brain activation associated with word and pseudoword reading that reliably differentiated between individual children with and without dyslexia. The validity of this procedure for obtaining spatiotemporal profiles of activation during complex cognitive tasks has been established in clinical studies in which MSI-derived maps demonstrated excellent concordance when compared with invasive brain maps, including electrocortical stimulation mapping and the Wada procedure.[23-27]

The aberrant profile in children with dyslexia features predominant activation of the *right* posterior superior temporal gyrus (STGp), and the *right* inferior parietal region (angular and supramarginal gyri). In contrast, most normal readers display predominant activation of the *left* STGp and the *left* inferior parietal region. This activity typically occurs between 300 and 800 ms after stimulus onset (sometimes persisting up to approximately 1200 ms), and is preceded by activation of the left lingual and fusiform gyri, predominantly in the left hemisphere. When the stimuli to be read are meaningful, late activity (300 to 800 ms) is also found in the middle temporal gyrus and mesial temporal cortex in both groups. Although these differences between good and poor readers are found in the context of both word[28] and pseudoword[29] reading tasks, they are more likely related to the engagement of neurophysiologic processes involved in phonologic decoding. We have shown previously that decoding is severely disrupted by direct electrical stimulation of the left STGp[30] and that facility in phonologic decoding is a major predictor of success in reading acquisition.[5-7] This region displays normal levels of activity during performance on simple word recognition tasks presented in the auditory modality.[28] The discrepancy in the activation profiles between the auditory and the printed word processing tasks points to a functional disruption in the brain circuit that supports reading rather than a functional deficit restricted to the temporoparietal region. However, performance of more complex phonologic processing tasks may reveal differences between dyslexic and nonimpaired children with respect to the degree of activation of this area.[31]

Although dyslexia is a chronic reading disorder that may persist into adulthood,[32] recent studies have demonstrated that it can be remediated with relatively short periods of intensive remedial instruction.[33,34] In agreement with the notion that phonologic processing difficulties form the core characteristic of the most common type of dyslexia, instructional programs that focus primarily on the development of phonemic awareness and decoding skills produce the best outcomes. The apparent contradiction between the neurologic hypothesis of dyslexia and the "malleability" of the phenotypic profile of the disorder introduce the following possibilities: 1) intervention may be associ-

Table *Demographic information*

Subject no./ group	Sex/age, y (mo)	WJ-III score, %		IQ	ADD?	Medication
		Pre	Post*			
1/D	M/15 (1)	13	55	103	Yes	Adderal
2/D	M/10 (7)	2	59	95	Yes	Ritalin
3/D	M/10 (11)	2	38	110	No	Ritalin
4/D	F/8 (8)	3	55	105	Yes	Ritalin
5/D	F/7 (4)	2	50	110	Yes	Ritalin
6/D	M/7 (10)	18	60	101	No	—
7/D	M/11 (1)	1	38	98	Yes	Ritalin
8/D	M/17 (1)	1	45	102	No	—
9/NI	M/10 (2)	38	39	99	No	—
10/NI	F/8 (1)	50	48	107	No	—
11/NI	M/9 (7)	85	83	122	No	—
12/NI	M/14 (1)	82	85	101	No	—
13/NI	M/10 (1)	60	60	113	No	—
14/NI	M/9 (8)	52	50	95	No	—
15/NI	M/10 (2)	49	53	99	Yes	Ritalin
16/NI	M/12 (4)	75	74	121	No	—

* Follow-up testing was performed using alternate forms.

D = dyslexic; NI = nonimpaired; WJ-III = Woodcock–Johnson PsychoEducational Test III; ADD = attention deficit disorder.

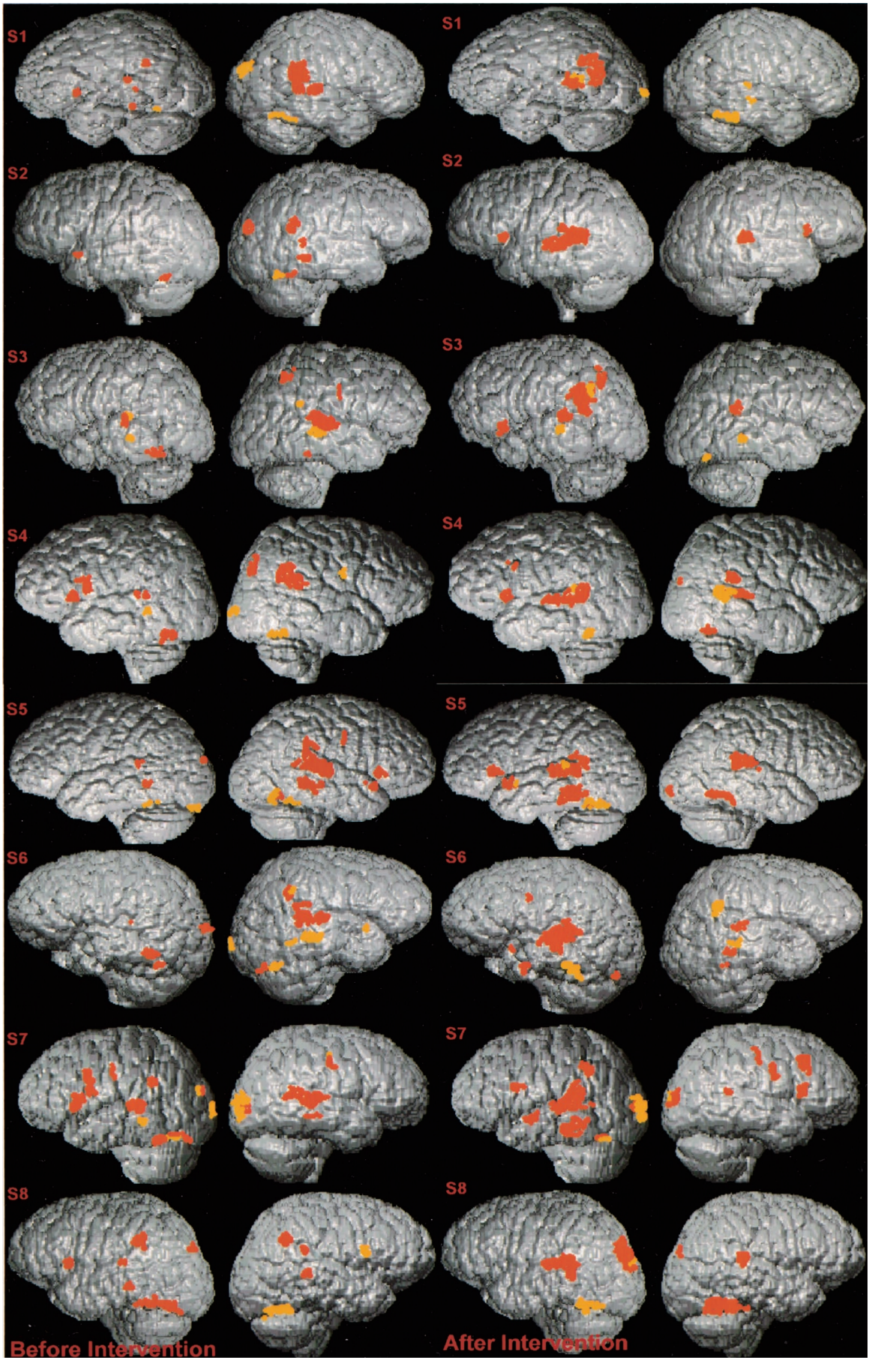
ated with the establishment of a new brain circuit for reading, one that is not present in normal readers ("compensatory" hypothesis); and 2) intervention may help "repair" the functionally aberrant brain circuit for reading, establishing a circuit that is virtually identical to the one typically established in the brain during reading acquisition ("normalization" hypothesis).

To examine these hypotheses, we identified eight children, aged 7 to 17 years, who presented with severe reading difficulties. MSI scans were obtained from these children during performance of a phonologic decoding task before and after they received approximately 80 hours of one-to-one instruction for 1 to 2 hours/day for 8 weeks. This instruction focused primarily on the development of phonologic processing and decoding skills. To assess the temporal stability of MSI-derived brain activation maps, a second group of eight age-matched children who had never experienced reading problems were tested on two separate occasions, with a 2-month interval, during which they received regular reading instruction at school.

Subjects and methods. *Subjects.* The group of eight children with dyslexia (six boys) had a mean age of 11.4 years (range 7 to 17 years) and presented with severe reading and phonologic decoding problems, as indicated by a score below the 18th percentile on the Basic Reading Skills cluster from the Woodcock–Johnson III Tests of Achievement (W-J III).[35] Six of the eight children (three boys) were diagnosed with attention deficit disorder without hyperactivity (ADD) and placed on stimulant medication throughout the 2-month study period (including the days of the pre- and postintervention MSI scans). Diagnosis of ADD was based on the *Diagnostic and Statistical Manual, 4th ed.* criteria using the Conner rating scale.[36] These children were not excluded from the study because ADD commonly co-occurs with dyslexia, and all five responded well to pharmacologic intervention. The group of eight nonimpaired children (five boys, three girls, solicited through advertisements placed in the University of Texas–Houston campus) had a mean age of 10.3 years (range, 8.0 to 14.2 years), with scores above the 50th percentile on the Basic Reading Skills cluster. One of the control subjects met diagnostic criteria for ADD, responded positively to pharmacologic intervention, and was retained in the study.

All 16 children were native English speakers with average or above-average intelligence (score >85 on the Wechsler Intelligence Scale for Children–III[37]). Mean full-scale IQ was 102 (±4.5) for the group of dyslexic children and 107 (±10.5) for the group of nonimpaired children ($p > 0.22$). The group had no history of a hearing deficit, neurologic injury, or disease, emotional disorder, or visual impairment. In addition, all children were right-handed as indicated by a score of +0.40 or greater on the Edinburgh Handedness Inventory,[38] and there were no significant differences between groups in the degree of left-hand preference ($p > 0.1$). Table 1 presents demographic and psychoeducational data on all subjects.

Procedures. Stimuli and tasks. MSI scans were obtained during performance of a visual pseudoword rhyme-matching task.[29] Children viewed four blocks of 25 pairs of pseudowords and attempted to determine whether the stimuli in each pair rhymed or not. Each pseudoword was shown for 1500 ms to prevent potential contamination of the data by visual offset evoked responses. The interstimulus interval (offset to onset) was fixed at 1000 ms but the intertrial interval varied randomly (between 1500 and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Before Intervention
After Intervention

2300 ms) to prevent habituation. Stimuli were 4 to 5 letters long and orthographically dissimilar (within a given pair) to discourage performing comparisons on the basis of orthographic information (e.g., "yoat" and "wote"). The children were instructed to raise their index finger each time two pseudowords rhymed, but not to respond if they did not rhyme. The responding hand was counterbalanced across children. Stimuli were projected through a liquid crystal display (LCD) projector (Sharp Model XG-E690U; Mahwah, NJ) onto a white screen located approximately 1.5 meters in front of the child. Stimuli subtended 1.0 to 2.0 degrees of horizontal, and 0.5 degrees of vertical visual angles. Event-related magnetic fields (ERF) were recorded to the first stimulus of each pair to ensure that the brain activity recorded corresponded to phonologic decoding operations and not to the additional cognitive operations that matching of the stimuli entailed.

MSI recording and analyses. MSI scans were obtained with a whole-head, 148-channel neuromagnetometer array (4-D Neuroimaging, Magnes WH2500; San Diego, CA) that consisted of 148 magnetometer 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 MRI scans are described in detail elsewhere.[23,39] Briefly, the magnetic flux measurements were filtered with a bandpass filter between 0.1 and 20 Hz and digitized at 250 Hz. Then the single-trial ERF segments in response to 50 to 70 stimulus presentations were averaged separately for each sensor, after excluding those containing eye movement or other myogenic or mechanical artifacts. As previously mentioned, only ERF evoked by the first stimulus in each pair of pseudowords were analyzed. To identify the intracranial sources of the ERF, a mathematical model was used that considered the intracranial activity sources (sets of active neurons) as equivalent to physical current dipoles[40] and provided an estimate of the location and strength of these sources at successive 4-ms intervals during the temporal evolution of a given ERF. Activity sources were considered acceptable if they were associated with a correlation coefficient of 0.9 or greater between observed and predicted magnetic flux distributions. There is currently considerable data supporting the validity of the single-moving dipole model for reliably localizing and lateralizing neurophysiologic activity associated with language function.[23-27] At our center, MSI-derived activation maps correspond very closely with the results of invasive functional brain mapping techniques in patients with brain insult who were candidates for neurosurgical intervention, including the intracarotid Amytal procedure and electrocortical stimulation mapping.

The location estimates of each "dipolar" activity 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 anatomic location of activity sources was determined after coregistering MSI coordinates onto the subject's structural MRI scan. This was achieved by marking the same MSI fiducial points with vitamin pills during the MRI scans. In this way, activity sources that account for a particular ERF component indicate the location of brain areas activated at each consecutive 4-ms time frame in response to the pseudoword stimuli. A standard MRI atlas of the human brain[41] served as a reference for the identification of the cerebral structures where sources were localized. Activity sources were consistently found across subjects in the following seven regions: posterior portion of the superior (STGp), middle temporal (MTGp), supramarginal (SMG), angular (ANG), and inferior frontal gyri (IFG); and basal temporal and mesial temporal cortices (MTL). Two sets of activity sources were identified and localized: those that accounted for early ERF (up to 150 ms post–stimulus onset) and those that accounted for the late components (after 150 ms post–stimulus onset). Early activity sources are typically localized in modality-specific cortices (in this case, occipital cortex in the vicinity of the calcarine fissure) and are presumably related to primary sensory processing of the stimulus. Previous research has shown that systematic task and hemisphere-specific effects are found only for "late" activity sources, i.e., those computed after 150 ms post–stimulus onset.[23,28,29] The number of reliably localized activity sources in each of these areas in each hemisphere served as the dependent measure in the statistical analyses. This measure is the most reliable and valid index of the degree of regional cerebral activation, specific to various language operations in several studies involving neurologically intact volunteers and patients.[23-27,42]

Intervention. The Phono-Graphix program (Read America, Orlando, FL) was used in six children and the Lindamood Phonemic Sequencing program (Lindamood-Bell, San Luis Obispo, CA) in two children. These programs were chosen because their effectiveness in addressing the core reading difficulties in children with dyslexia is well documented in implementation studies.[33,34] Their value was clearly evident in the current study. Before the intervention, all children had extremely poor scores on measures of phonologic decoding: table 1 shows that six children scored below the 3rd percentile on the W-J-III, and two children at the 13th and 18th percentiles (mean, 5.25 ± 6.5). Postintervention scores (see table 1) were in the average range (i.e., 38th to 60th percentile; mean, 50 ± 8.8). No apparent differences were found in the

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Figure 1. Brain activation profiles from each of the eight dyslexic children, obtained on a pseudoword rhyme-matching task before (left-hand columns) and after (right-hand columns) intensive remedial instruction. Subjects 1 through 6 received training using the Phono-Graphix program, whereas the Lindamood Phonemic Sequencing program was used for Subjects (S) 7 and 8. After the intervention, a dramatic increase in the activation of left temporoparietal regions (predominantly the posterior portion of the superior temporal gyrus) was noted in every child, rendering activation profiles very similar to those observed in each of the eight children without reading problems presented in figure 3. Earlier activity (150 to 250 ms) that is observed primarily in basal temporal areas immediately after the initial activation of the primary visual cortex is shown in yellow, whereas later activity (mostly in temporoparietal areas, between 250 and 1200 ms) that consistently varied as a function of group is shown in orange.

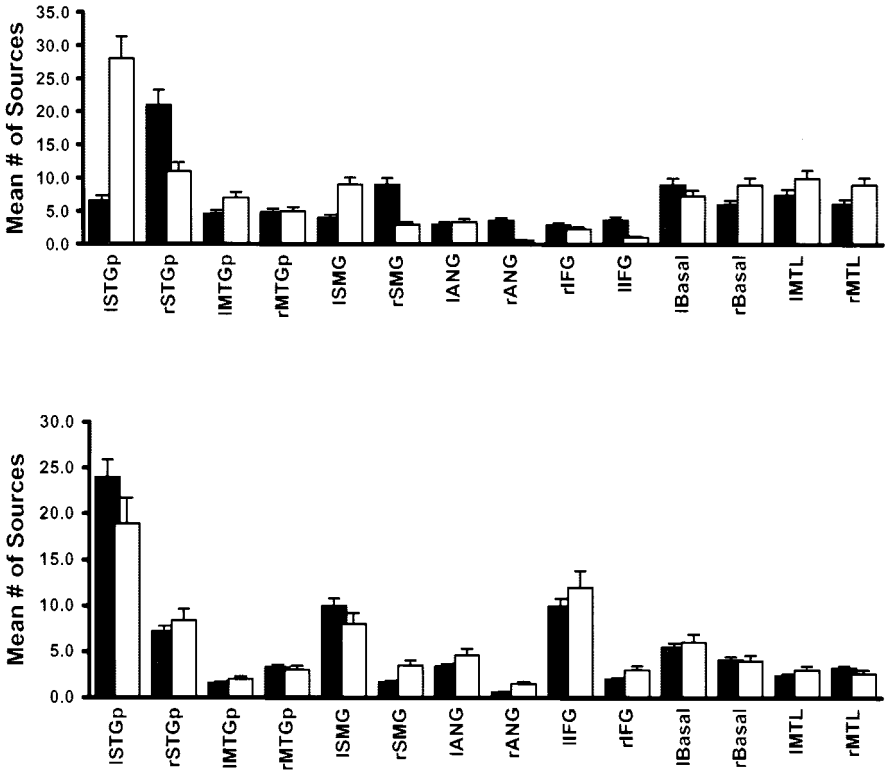


Figure 2. (Upper panel) Mean number (and SEM) of activity sources in seven brain regions derived from the brain activation profiles before (black bars) and after intervention (white bars) in the group of dyslexic children (n = 8). (Lower panel) Initial (black bars) and follow-up data (white bars) from the group of nonimpaired children (n = 8). l = left; r = right; STGp = posterior portion of the superior temporal gyrus; MTGp = posterior portion of the middle temporal gyrus; SMG = supramarginal gyrus; ANG = angular gyrus; IFG = inferior frontal gyrus; Basal = basal temporal cortex; MTL = mesial temporal lobe.

efficacy of the reading intervention or in the degree of change in activation profiles between the two programs in the current sample.

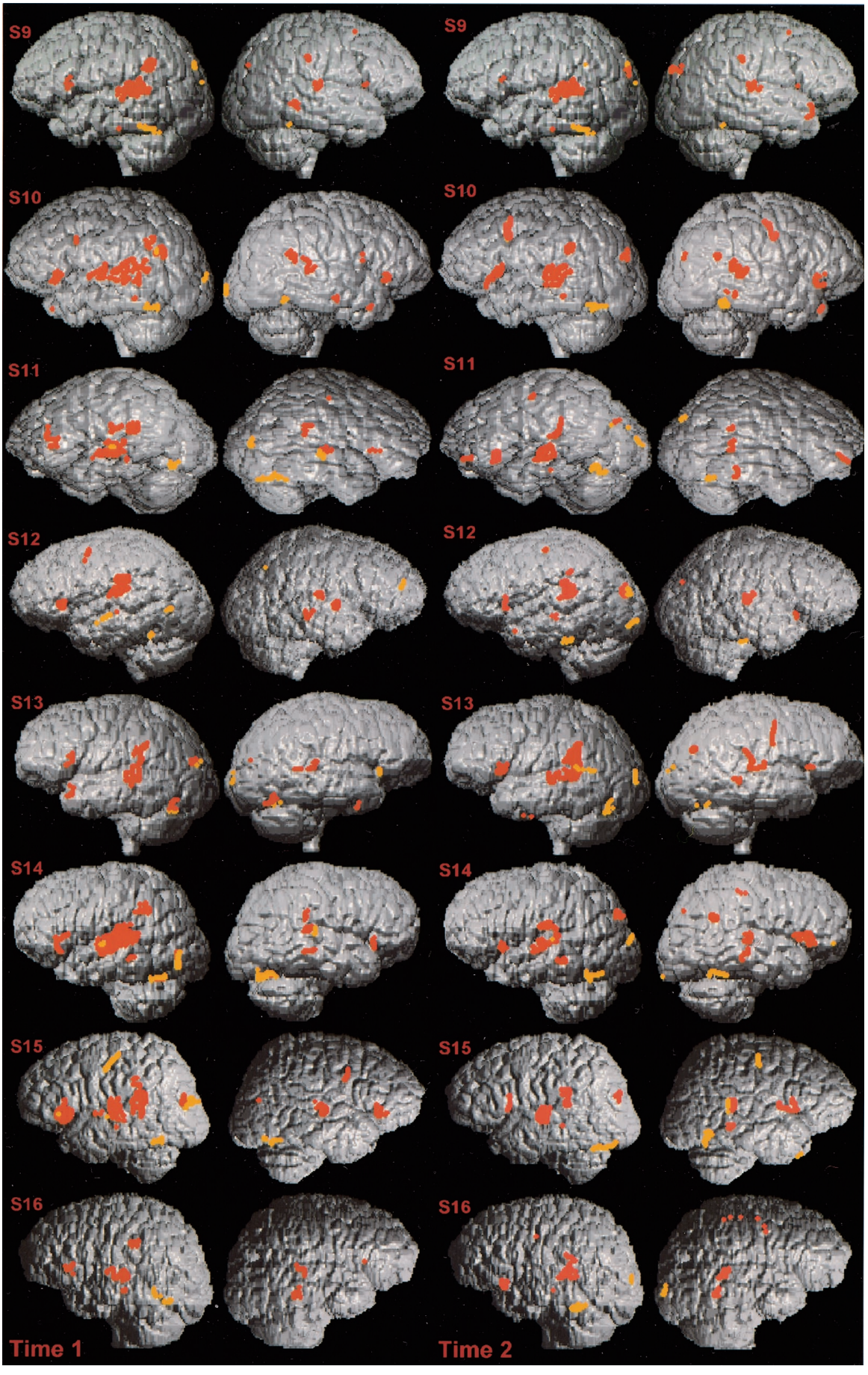
Results. The individual activation profiles obtained before the intervention from each of the children are shown in the left-hand column of figure 1. Before intervention, all children with dyslexia showed the expected dyslexia-specific profiles marked by little or no activation of temporoparietal areas in the left hemisphere. In contrast, children with no reading impairments activated these areas in the left hemisphere. After intervention, all children with dyslexia showed significant gains in reading skills, such that their scores on basic word reading tests increased into the average range. The MSI activation profiles obtained immediately after completion of the program showed corresponding dramatic changes in regional brain activation. In contrast, no systematic changes in the activation profiles of children in the nonimpaired group were found.

These observations were supported by a statistical analysis using a multivariate approach to analysis of variance (ANOVA) with Group as a between-subject variable and three within-subject variables (Time: Preintervention/Time 1, Postintervention/Time 2; Area: STGp, SMG, ANG, MTGp, MTL, IFG, basal temporal; and Hemisphere: Left, Right). All subsequent pairwise comparisons were evaluated using the Bonferroni method. Given the presence of a four-way interaction ($F[6,84] = 5.51$, $p < 0.0001$), analyses were performed separately for pre- and postintervention data in each group.

In the group of children with dyslexia the three-way interaction term was significant ($F[6,42] = 7.96$, $p < 0.0001$). Before intervention, there was an Area × Hemisphere interaction ($F[6,42] = 3.97$, $p < 0.005$) that was mainly due to greater activation in the *right* than in the left STGp ($t[7] = 3.34$, $p < 0.012$). A similar but nonsignificant trend was also noted for SMG and ANG (figure 2). After intervention there was again an Area × Hemisphere interaction ($F[6,42] = 2.7$, $p < 0.026$), as the number of sources in the *left* STGp was greater than the number of sources in the right STGp ($t[7] = 6.87$, $p < 0.0001$). Nonsignificant trends in the same direction were found for SMG and ANG (see figure 2).

Nonimpaired children showed the expected activation profiles during both scans, featuring greater left than right hemisphere activation in temporoparietal areas (see figures 2 and 3). As expected, the profiles of activation of nonimpaired children did not change systematically across the two testing sessions, as indicated by the lack of significant main effects or interactions involving the Time of Test factor. The Area × Hemisphere interaction was present ($F[6,42] = 36.29$, $p < 0.0001$). Greater left than right hemisphere activity was consistently found for activity sources in STGp ($t[7] = 8.48$, $p = 0.0001$), SMG ($t[7] = 9.74$, $p = 0.0001$), and IFG ($t[7] = 8.96$, $p = 0.0001$). Hemi-

Figure 3. Individual brain activation profiles from eight children who had never experienced reading difficulties obtained in the context of the pseudoword rhyme-matching task at Time 1 (left-hand columns) and 2 months later (Time 2, right-hand columns). Early activity (150 to 250 ms after stimulus onset) is shown in yellow and later activity (250 to 1200 ms) is shown in orange.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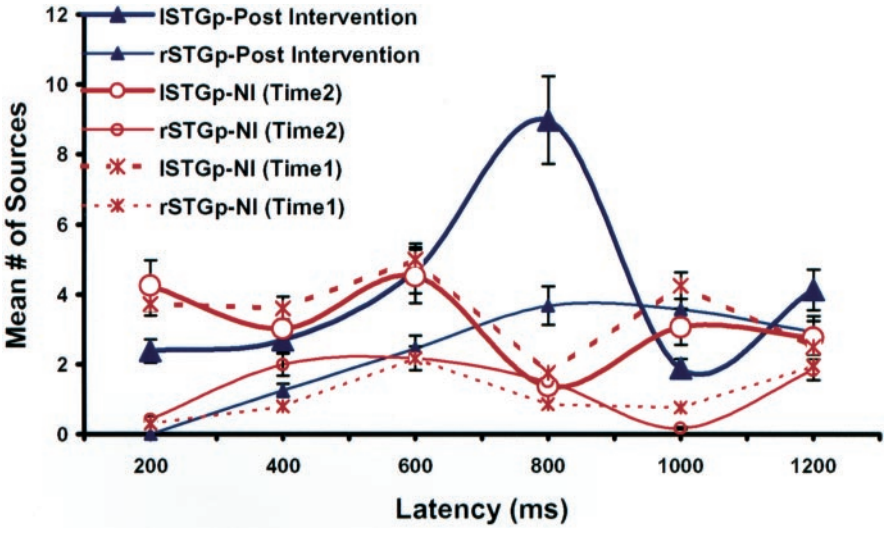

Figure 4. Mean number (and SEM) of activity sources in the left (l) and right STGp (r) as a function of time after the onset of the pseudoword stimuli. Data from the group of nonimpaired children (NI) are presented for each testing session to demonstrate the stability of the spatiotemporal profiles over time.

sphere asymmetries for ANG activity were in the expected direction (left > right) but were not significant at the adapted critical level of 0.05/7 = 0.007 ($p > 0.016$).

A direct comparison between the two groups at Time 1 revealed a Group × Area × Hemisphere interaction ($F[6,84] = 9.57$, $p < 0.0001$). Group differences in regional activation were restricted to the left ($t[14] = 4.77$, $p = 0.0001$) and right STGp ($t[14] = 4.40$, $p = 0.004$). At Time 2, however, no significant ANOVA terms involving the Group factor were found ($p > 0.1$).

Performance on the pseudoword-rhyming task was higher for the nondyslexic group (51.1% vs 73.5% correct, $p < 0.0001$, two-tailed t-test). Consistent with our previous findings,[2] there was a significant association between the degree of activity in STGp and response accuracy. Positive correlations (computed across groups) were found between the percentage of correctly detected rhyming pairs and both left STGp activation ($r = 0.58$, $p < 0.016$) and hemispheric asymmetry indices for STGp activity sources ($r = 0.61$, $p < 0.004$). Although the children with dyslexia performed better after intervention than before (mean correct: 60.28%, $p < 0.003$, two-tailed t-test), nonimpaired children again outperformed them (mean correct: 71.63, $p < 0.0007$, two-tailed t-test). As score variance across groups was reduced at the follow-up test, correlations between performance and activation measures attenuated, and none were significant. There was a strong positive association between the changes in the degree of left STGp activation and the improvement in response accuracy as a function of intervention ($r = 0.683$, p <. 004), whereas no such relation was found between right STGp activity and performance ($p > 0.1$).

The postintervention temporal course of STGp activation is presented graphically in figure 4 for the group of children with dyslexia and for the nonimpaired children. Notice the consistency in the overall shape of the time plot in both hemispheres across the two testing sessions in the nonimpaired children. Even after the intensive remedial instruction, the peak in left STGp activity (mean, 837 ± 285 ms) occurred noticeably later than the corresponding peak obtained from the group of children who never experienced reading problems (mean, 600 ± 368 ms).

Inspection of individual activation profiles (figure 1) reveals some interesting trends. Across all children with dyslexia, the most pronounced and consistent changes were found in the left STGp, ranging in degree between +115% and +2100% (mean, +643%). On average, a moderate reduction in the degree of activity in the right STGp was also found that ranged between −100% and −40% in six children, whereas a small increase (+50% for Subject 2 and +78% for Subject 8) was noted in the other two children (mean, −34%). Subject 8 is particularly noteworthy because he was 17 years old. He showed changes in the degree of STGp activation that were similar to the younger children (+130% in the left and +50% in the right hemisphere). Furthermore, the amount of change in reading skills accounted for by changes in both left and right STGp activity was 70.6%, with 63.4% attributable to the left STGp but only 7.2% attributable to the right STGp. Therefore, it appears that an increase in left STGp and inferior parietal activity, rather than a reduction in right hemisphere activity, underlies the improvement in basic reading skills induced by reading intervention in children with dyslexia, a finding consistent with the previous results implicating the left STGp in phonologic processing.[10,29,30,43,44]

Discussion. Our findings show that successful completion of an intensive remediation program in reading is associated with dramatic changes in brain activation profiles in children with very severe reading difficulties. All children were characterized by pronounced word recognition and phonologic processing difficulties, which represent the core problem in dyslexia.[5-7,45] As expected, before enrolling in the intervention program, all eight children showed the typical dyslexia-specific profile featuring little or no activity in the left STGp and inferior parietal areas, and strong activation of homologous regions in the right hemisphere. Completion of an intense, phonologically based reading program resulted in marked improvement in phonologic decoding abilities and normalization of the brain activation profiles in all children.

The most pronounced intervention-related change in activation was found in the posterior portion of the left superior temporal gyrus in all eight children. Increased activity was also noted in adjacent inferior

parietal areas (supramarginal and angular gyrus), but the amount of change did not reach significance, probably owing to the small sample used in the study. In most children in the current study, these changes in the degree of regional activation rendered the brain activation profile associated with word reading virtually indistinguishable from that found in age-matched children who never experienced reading problems.[28,29] In two other children, right STGp activity persisted after the intervention, coupled with a pronounced increase in activation of the left STGp. The small number of children displaying this particular profile of change cannot be used to draw any conclusions regarding the potential significance of individual differences in psychoeducational profiles in determining the specific features of the postintervention activation profile. This finding is, nonetheless, consistent with the claim that the functional reorganization associated with intervention resulted in a brain circuit that is very similar to the one that normally develops in children who do not experience difficulties in learning to read ("normalization" hypothesis).

Despite this evidence, visual inspection of the temporal features of the activation profiles indicated that the initial engagement of the left STGp in phonologic decoding may not occur as fast as in children who never experienced difficulties in learning to read. Given the relation between onset of left STGp activation and reading speed that has been found in another MSI study,[43] this preliminary finding may suggest that the posterior temporal circuit established by training in dyslexic children may not be as efficient as that in children with normal developmental histories. This observation is consistent with reports that although reading accuracy measures may improve dramatically following intensive but brief remediation programs, measures of reading fluency show that these children are slow to achieve the requisite automaticity and speed that characterizes proficient readers.[34] Conversely, data from a proton MRS and an fMRI study suggest that compensatory strategies involving articulatory recoding of print may also be at work following training that focuses on the development of phonologic processing skills. These strategies appear to be associated with increased metabolic demands placed on left prefrontal areas,[46] including the inferior frontal regions,[47] and operate in parallel with the increased neurophysiologic activity in posterior temporal regions.

An issue that has important repercussions in interpreting functional brain imaging data are whether it is possible to ascertain whether an increase in the recorded signal in a particular area (in the current case, STGp) indicates that the subject is performing the task under investigation with increased efficiency. Increased task-related electromagnetic signal recorded from a particular area, using any functional imaging method, may indicate increased neuronal activity in that area. This may not indicate that the area in question has a greater contribution to the experimental task used in the study. It could merely reflect the engagement of one or more neurophysiologic processes that do not constitute the most efficient way of processing the stimuli. Nonetheless, there is converging evidence from several lines of research indicating that increased magnetic signal localized in STGp *during* the act of reading pseudowords is associated with increased levels of neuronal signaling which, in turn, reflects the engagement of a neurophysiologic process that is indispensable to the conversion of print to sound. This evidence can be summarized as follows: 1) electrical stimulation of cortical patches within the border of STGp, which shows activity during reading, interferes with the ability to read pseudowords like "yote," (a task that requires phonologic decoding but does not disrupt the ability to pronounce letter strings that can be read as whole units, like "yacht")[30]; 2) the onset of STGp activation after presentation of printed pseudowords correlates strongly with the speed with which subjects read these stimuli aloud[44]; 3) initial results from an ongoing kindergarten through second-grade longitudinal study show that an increase in left STGp activity over time is a strong correlate of improvement in reading skill, especially in children who had not mastered important prereading skills in kindergarten[43]; and 4) data reported here indicate that the amount of increase in the degree of left STGp activity is a significant predictor of improvement in response accuracy in the pseudoword-rhyming task as a result of intervention.

The mechanism that prevents normal engagement of the left STGp in tasks that require phonologic analysis of print in dyslexic children before receiving adequate instruction is not currently clear. One possibility is that this region does not participate in any tasks that involve complex phonologic analysis in this group. This explanation appears unlikely in view of findings that on auditory word recognition tasks children with dyslexia can display strong activation in this region, and may not differ significantly from the group of nonimpaired readers.[28] A second possibility is that activity in this region is normally coupled with activation in the left angular gyrus, which was also dramatically reduced in the children with dyslexia compared with nondyslexic children. Failure to engage the left angular gyrus in tasks that require phonologic decoding has recently been reported in imaging studies using fMRI[48] and PET,[49] supporting earlier proposals that this area plays a crucial role in the conversion of print to sound.[50,51] The latter possibility is consistent with our observation that in nonimpaired readers, the left angular gyrus typically becomes engaged immediately after left basal temporal areas and before the onset of activation in the supramarginal and superior temporal gyri.[12] This tight temporal coupling of activation between ventral visual association cortex and the angular gyrus is in close agreement with evidence from lesion data, suggesting the crucial role of functional connections between the two areas in reading.[52]

Two nonmutually exclusive proposals can be made regarding the nature of the compensatory changes observed in older dyslexic children or adults with persistent reading difficulties. Our data provide an empirical basis for choosing among these alternatives. One proposal points to an increased tendency to engage the inferior frontal gyrus,[21,46,47] while a second implicates increased reliance on the right STGp (and nearby temporoparietal areas). Intensive intervention that addresses the core processing difficulty in these children seems to be associated primarily with increased engagement of the left STGp and, to a lesser extent, to decreased engagement of the right STGp. These findings indicate that phonologic decoding of print depends more on engagement of the neurophysiologic processes performed by the left STGp that failed to engage before the intervention.

The small size of the sample warrants some caution in interpreting these results and we would like to evaluate a much larger sample to establish relationships of the imaging findings with subject characteristics (e.g., dyslexia subtypes, IQ, presence of attention deficit disorder). However, it is also important to recognize that despite differences among the children in the study with respect to these variables, the changes in brain activation profiles were observed in every child. The robustness of this effect is also a good indicator of the potential clinical utility of the MSI protocol used in this and previous studies involving children with dyslexia.[28,29] Such results were not surprising, however, given that evidence of the validity of individual MSI-derived maps of regional activation has been obtained by comparison with standard invasive techniques in large series of consecutive neurosurgical patients.[23-27]

The current study examined a nonrandom sample of children with dyslexia who were selected based on two main criteria: 1) the predominance of phonologic awareness and decoding problems in the children's psychoeducational profile; and 2) the severity of these problems, as all eight children scored in the lower 18th percentile on related measures (most children actually scored below the 3rd percentile). As is usually the case, these problems were associated with severe difficulties in word recognition leading to essentially nonfunctional reading ability for each child's (academic) grade level. In addition, the study did not attempt to vary program content or intensity. A variety of other programs exist that offer options such as instruction in small groups and greater relative emphasis on the building of word recognition and comprehension skills. There is clear evidence from large-scale implementation studies that one-to-one instruction in reading may not be very successful in addressing phonologic decoding problems in the most seriously impaired children unless it contains explicit and intensive instruction in phonologic awareness and the alphabetic principle. However, the ability to recognize a large corpus of printed words and understand their meaning is the ultimate goal of reading instruction. A long-term follow-up assessment is also desirable in efficacy studies, given reports that brief, intensive programs must be supplemented by less intensive "maintenance treatment" for several months or even years to ensure a relatively stable positive outcome. In addition, continuing instruction is necessary to foster efficient word recognition skills and to improve reading speed (fluency).

The results presented above have important implications for current notions regarding the nature of dyslexia, and also for views of neural development and plasticity. First and foremost, it appears that although dyslexia has a demonstrable neurologic basis, it is not a neurologic disease. Rather, word reading difficulties most likely represent variations in normal development that can be reversed by means of reading intervention targeting phonologic processing and decoding skills. The implications of these findings for education are clear: instruction seems to play a significant role in the development of neural systems that are specialized for reading. When provided with appropriate and sufficiently intense instruction, reading difficulties can be overcome in many children. Such a view is entirely consistent with current theories regarding reading development, which indicate that reading proficiency is scaffolded on oral language proficiency as a secondary consequence of the development of oral language capacity in the human species.[4] When successful intervention occurs, our study suggests that neural systems are altered and that these neural systems are much more plastic than previously believed. Similar instruction-related changes may occur at earlier ages in the normative course of reading development. It remains to be determined if there is an optimal time window to effect such changes through proper instruction. However, the current study involved a broad age range and the changes were apparent in each child. The issue may not be when the intervention is delivered, but whether the intervention targets the appropriate skills and is sufficiently intense to impact the brain. Because very young children who are at risk for reading difficulties show patterns similar to those found in older children and adults with dyslexia,[43] it may be that many at-risk children end up developing the full phenotypic profile of dyslexia because 1) they fail to be identified early on, or 2) they never receive appropriate intervention that would entrain the brain mechanisms that mediate word recognition. Such a view provides a more optimistic outlook for the prognosis of dyslexia, which various studies show is a chronic, persistent disorder.

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