

Disruption of Posterior Brain Systems for Reading in Children with Developmental Dyslexia

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Background: *Converging evidence indicates a functional disruption in the neural systems for reading in adults with dyslexia. We examined brain activation patterns in dyslexic and nonimpaired children during pseudoword and real-word reading tasks that required phonologic analysis (i.e., tapped the problems experienced by dyslexic children in sounding out words).*

Methods: *We used functional magnetic resonance imaging (fMRI) to study 144 right-handed children, 70 dyslexic readers, and 74 nonimpaired readers as they read pseudowords and real words.*

Results: *Children with dyslexia demonstrated a disruption in neural systems for reading involving posterior brain regions, including parietotemporal sites and sites in the occipitotemporal area. Reading skill was positively correlated with the magnitude of activation in the left occipitotemporal region. Activation in the left and right inferior frontal gyri was greater in older compared with younger dyslexic children.*

Conclusions: *These findings provide neurobiological evidence of an underlying disruption in the neural systems for reading in children with dyslexia and indicate that it is evident at a young age. The locus of the disruption places childhood dyslexia within the same neurobiological framework as dyslexia, and acquired alexia, occurring in adults. Biol Psychiatry 2002;52:101-110 © 2002 Society of Biological Psychiatry*

Key Words: Dyslexia, reading, fMRI, children, brain

Introduction

Dyslexia is characterized by an unexpected difficulty in reading in children and adults who otherwise possess the intelligence, motivation, and schooling considered necessary for accurate and fluent reading (Shaywitz 1998). It represents one of the most common problems affecting children and adults with prevalence rates ranging from 5 to 17.5% (Shaywitz 1998). Such data have led "the National Institute of Child Health and Human Development (NICHD) within the National Institutes of Health (NIH) [to] consider reading failure to reflect not only an educational problem, but a significant public health problem as well" (Lyon 1998).

There is now a strong consensus that the central difficulty in dyslexia reflects a deficit within the language system and, more particularly, in a lower level component, phonology, which has to do with the ability to access the underlying sound structure of words (Liberman and Shankweiler 1991; Shaywitz 1996, 1998; Wagner and Torgesen 1987). Results from large and well-studied populations with reading disability confirm that in young school-age children, a deficit in phonologic analysis represents the most reliable (Fletcher et al 1994; Stanovich and Siegel 1994) and specific (Morris et al 1998) correlate of dyslexia. Such findings form the basis for the most successful and evidence-based interventions designed to improve reading (Report of the National Reading Panel 2000). A range of neurobiological investigations using postmortem brain specimens (Galaburda et al 1985), brain morphometry (Filipek 1996), and diffusion tensor magnetic resonance imaging (MRI; Klingberg et al 2000) suggests that there are differences in the left temporo-parieto-occipital brain regions between dyslexic and non-impaired readers. Converging evidence using functional brain imaging in adult dyslexic readers also shows a failure of left hemisphere posterior brain systems to function properly during reading (Brunswick et al 1999; Helenius et al 1999; Horwitz et al 1998; Paulesu et al 2001; Pugh et al 2000; Rumsey et al 1992, 1997; Salmelin et al 1996; Shaywitz et al 1998; Simos et al 2000). In

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Table 1. Characteristics of the Subjects

	Group			
	NI (<i>n</i> = 74)		DYS (<i>n</i> = 70)	
	Mean	SD	Mean	SD
Age (years)	10.9	2.4	13.3 ^b	2.7
Sex ^a				
Male	43		49	
Female	31		21	
Race ^a				
Caucasian	74 ^b		66	
African American	0		4	
SES				
High (1 + 2)	70		41	
Average (3)	4		20	
Low (4)	0		6 ^b	
Family history of reading problem ^a				
No	61		34	
Yes	13		36 ^b	
WISC-III Full-Scale IQ	116	12.2	99.5 ^b	15.1
Woodcock–Johnson Psycho-Educational Battery				
Letter-word identification SS	122	13.7	84.2 ^b	10.7
Word Attack SS	120	17.1	85.1 ^b	11.0

NI, nonimpaired readers; DYS, dyslexic readers; SES, social class, based on the Hollingshead index (unpublished data); SS, standard score (mean of 100, SD 15); WISC-III, Wechsler Intelligence Scale for Children.

^aStatistical significance determined by Fisher's exact test.

^b*p* < .001.

addition, some functional brain imaging studies show differences in brain activation in frontal regions in dyslexic compared with nonimpaired readers; in some studies dyslexic readers are more active in frontal regions (Brunswick et al 1999; Rumsey et al 1997; Shaywitz et al 1998), and in others nonimpaired readers are more active in frontal regions (Corina et al 2001; Georgiewa et al 1999; Gross-Glenn et al 1991; Paulesu et al 1996).

These previous functional imaging studies of dyslexia were in adults, and the findings in adults were used to infer what might be found in children with dyslexia, without actually studying them. To determine whether these findings are the result of a lifetime of poor reading or whether they are there during the period of literacy acquisition, we used functional magnetic resonance imaging (fMRI) to compare dyslexic and nonimpaired children during tasks that required phonologic analysis, that is, tapped the problems experienced by dyslexic children in sounding out words.

Methods and Materials

Subjects

We studied 144 right-handed children, 70 dyslexic (DYS) readers (21 girls, 49 boys, aged 7–18 years, mean age 13.3 years) and 74 nonimpaired (NI) readers (31 girls, 43 boys, aged 7–17 years, mean age 10.9 years) after informed consent had been obtained. Subjects for this study were recruited from a number of

sources, including referrals from pediatricians, nurses, psychologists, educators, and family physicians, as well as through notices in parent–teacher association bulletins, public libraries, scouting groups, children's toy stores, and community organizations. Children were first screened with IQ and achievement measures and, if eligible on the basis of these tests, entered the study and were evaluated with fMRI. All children had intelligence in the average range. Criteria for DYS were met if the average of the two decoding subtests (Word Identification and Word Attack) from the Woodcock–Johnson Psycho-Educational Test Battery (Woodcock and Johnson 1989) were below a Standard Score of 90 (below the 25th percentile) or 1.5 standard errors of prediction lower than the expected reading achievement score using the WISC-III (Wechsler 1991) Full-Scale IQ score. Both of these definitions validly identify children as poor readers, with little evidence for differences among subgroups of children formed with these definitions (Fletcher et al 1994; Shaywitz et al 1992a). To ensure good reading skills and that there was no overlap between groups, criteria for NI were reading scores above the 39th percentile. We excluded from the study children with sensory disorders, brain injury, and where the cause of the reading problem was likely attributable to emotional disturbance; clinically apparent neurogenetic disorders; or social, cultural, or economic disadvantage.

This study was approved by the Institutional Review Board and written informed consent was obtained from all subjects.

The subjects' demographic characteristics are shown in Table 1. There were no differences in gender (χ^2 , [1; *n* = 144] = 2.205, *p* = .14) or race (Fisher's exact *p* = .053); the groups did differ on age (*t* [142] = 5.62, *p* < .0001) and family history (first-

degree relative) of reading problems (χ^2 , [1; $n = 144$] = 18.37 $p < .001$). Full-Scale IQ and Woodcock–Johnson reading measures were higher in NI than DYS (all $p < .001$). By history, 20% of the sample had been previously treated for reading difficulties.

Preparation of Subjects

Our general approach to maintaining optimum compliance with the fMRI procedure focused on decreasing anticipatory anxiety and desensitizing the children to the components of the procedure. This was accomplished by first using a coloring book to explain the process and then showing a film illustrating a child going through the entire procedure. Following this introduction the child practiced in a mock-scanner. For this, we used a room that was set up with a table made to mimic the imaging gantry. The sounds of the fMRI were recorded and played on a tape recorder, thus acclimating the child to the sound of the scanner. A mock helmet was used as well. In addition, the child practiced the computer tasks that he or she would be performing during the fMRI. Using this procedure, we were able to obtain a high imaging success rate. We imaged 155 children; in 11 of the children, one or more tasks were not successfully completed, resulting in the 144 subjects reported here.

Imaging

Subjects were imaged in a 1.5 Tesla SignaLX imaging system from General Electric Medical Systems (Waukesha, WI). Children lay supine in the imaging system, looking up through a prism at a screen that was attached to the gantry; stimuli were projected on the screen using a Macintosh laptop computer programmed in Psyscope. The tasks were designed to differentially tap the component processes in reading: identifying letters, sounding out letters, sounding out pseudowords (pseudowords are used so that the child cannot have memorized the word and actually has to sound out the never-before-seen pseudoword), and sounding out and getting to the meaning of a real word. Specifically, the tasks were as follows: identifying letters (i.e., letter case [C] judgment; e.g., Are [t] and [V] both in the same upper/lowercase?); sounding out letters (i.e., single letter rhyme [SLR]; e.g., Do the letters [T] and [V] rhyme?); sounding out pseudowords (i.e., nonword rhyme [NWR]; e.g., Do [LEAT] and [JETE] rhyme?); and getting to the meaning of words (i.e., Semantic Category [CAT] judgment; e.g., Are [CORN] and [RICE] in the same category?). A common baseline, the line orientation (L) judgment task (e.g., Do [VV] and [VV] match?) was used in analysis; each individual task, C, SLR, NWR, and CAT, was contrasted with the (L) baseline condition. The line task was employed as a control because it makes no demands on the major components of reading (orthographic, phonological, or semantic processing) but does engage the same sensory modality (i.e., visual) used in reading. Children responded to the task with a button press, for example, pressing one button for “yes, the two nonwords rhyme” versus pressing another button for “no, the two nonwords do not rhyme.” In-magnet proportion correct responses on the L, C, SLR, NWR, and CAT tasks were, respectively, for NI: .86, .89, .87, .79, .91; for DYS: .83, .82, .75, .59, .75.

Before functional imaging 10 axial-oblique anatomic images

[TE (echo time), 11 msec; TR (repetition time), 500 msec; FOV (field of view), 20×20 cm; 8-mm-thick contiguous slices; $256 \times 192 \times 2$ NEX (number of excitations)] were prescribed parallel to the intercommisural line based on sagittal localizer images (TE, 11; TR, 600 msec; FOV, 24 cm; 5-mm contiguous slices; $256 \times 192 \times 1$ NEX). Ten axial-oblique functional activation images were obtained at the same relative slice location in each subject, extending from the inferior aspect of the temporal lobes to the parietal convexity, effectively covering the entire brain. Activation images were collected using single shot, gradient echo, echo planar acquisitions (flip angle, 60° ; TE, 60 msec; TR, 2000 msec; FOV, 20×40 cm; 8-mm contiguous slices; $64 \times 64 \times 1$ NEX) in the same slice locations used for anatomic images.

In each of the eight total imaging runs, 100 images per slice location were collected while the subject performed one of the four activation tasks (C, SLR, NWR, or CAT) and the line baseline task. The activation tasks and the baseline line task were presented in a block design, with five epochs of line task and four epochs of each activation task within each run. Trials were 4500 msec in duration; on each trial, stimuli were presented simultaneously for 2500 msec followed by a blank screen for 2000 msec.

Blocks of the baseline task of 22.5-sec duration were interleaved with blocks of the activation task; task order was randomized across subjects. Two imaging runs with each activation task were acquired, resulting in a total of 100 images per slice per activation task and 400 images per slice for the line baseline task across the experiment.

Data Analysis

Data analysis was performed using software written in MATLAB (MathWorks, Natick, MA). Motion criteria for rejection of a study were motion exceeding 2 mm translation or 3° rotation. All studies that did not exceed these criteria were included in the final analyses, and all were motion corrected. Before statistical analysis, the images from each run were motion corrected for three translation directions and for the three possible rotations. (Friston et al 1996) Images acquired at the beginning of experimental blocks, corresponding to the period of transient hemodynamic change that occurs initially in response to a task, were discarded, leaving 84 images per activation task for analysis. The remaining images were thresholded (the signal outside of the brain was set to zero) and Gaussian filtered (FWHM 2.6 mm). For generation of single-subject activation maps, activation of pixels was measured by comparing the images for each task to the line task using a split Student's t test with correction for linear drift. This definition of activation provides a conservative criterion for identifying task-related activity in the presence of other sources of signal variation (Skudlarski et al 1999). Anatomic images and activation maps from individual subjects were transformed into a proportional three-dimensional grid (Talairach and Tournoux 1988). This was performed first by in-plane transformation and then by slice interpolation into the 10 most superior slices of Talairach space, centered at $z = +69, +60, +51, +42, +33, +23, +14, +5, -5, -16$, respectively.

The activation maps from individual subjects were used as a

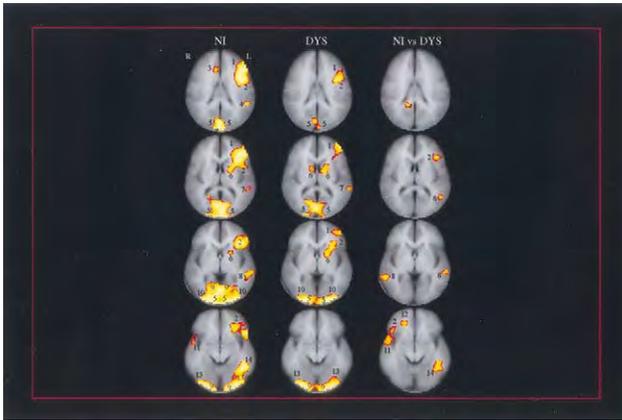


Figure 1. Composite maps (columns 1 and 2) demonstrating brain activation in nonimpaired (NI) and dyslexic (DYS) readers during the nonword rhyme task and composite contrast maps (column 3) comparing directly the brain activation of the two groups. In columns 1 and 2, red-yellow indicates areas that had significantly greater activation ($p = .05$) in the NWR task compared with the line task, and in column 3, red-yellow indicates brain regions that were more active in NI compared with DYS during the NWR task. The four rows of images from top to bottom correspond to $z = +23, +14, +5,$ and -5 in Talairach space (Talairach and Tournoux 1988). The legend for brain activation is as follows: 1) middle frontal gyrus, 2) inferior frontal gyrus, 3) anterior cingulate gyrus, 4) supramarginal gyrus, 5) cuneus, 6) basal ganglia, 7) superior temporal gyrus, 8) superior temporal sulcus and posterior aspect of the superior and middle temporal gyri, 9) lingual gyrus, 10) middle occipital gyrus, 11) anterior aspect of superior temporal gyrus, 12) medial orbital gyrus, 13) inferior occipital gyrus, and 14) posterior aspect of middle temporal gyrus and anterior aspect of middle occipital gyrus. NWR, non-word rhyme.

derived measure of task-related activity and were combined to obtain a group composite activation map comparing, for example, NWR with line (Figure 1 columns 1 and 2) and CAT with line (Figure 2 columns 1 and 2). A randomization procedure was used to generate the distribution of the task-related activation measure to estimate p values (Manly 1997). To randomize, the sign of the mean t value (the activation measure) for each voxel was reversed in half of the subjects. The mean value of the activation measure was then recalculated. This procedure was repeated 1000 times, generating a distribution of the mean activation measure. The observed measure, calculated without sign reversal, was assigned a p value based on its position in this distribution. The proportion of times that the observed measure was more extreme than a randomized value represents a p value, that is, it is the proportion of times we would expect to obtain a mean activation as large or larger than the one obtained if the null hypothesis (no effect) were true. The p value for each voxel exhibiting a positive activation above threshold ($p < .05$) was overlaid on the mean anatomic image for display. To compare directly the NI and DYS readers, the activation measure computed at each voxel comparing NWR and line tasks for the NI readers was compared with the same measure for DYS readers. Significance levels for this contrast were assessed by the randomization procedure as described above. The p value at each

voxel ($p < .05$) was then overlaid on the mean anatomic image for display (Figure 1, column 3).

Skill-Correlation Analysis

To examine the relationship between reading performance and brain activation in posterior brain regions, we correlated the activations observed for NWR and CAT during fMRI and out of magnet performance on the Word Attack (pseudoword) reading test (Woodcock and Johnson 1989). For each subject, we correlated the mean change in t values between NWR and L (and CAT and L) in each voxel with the child's reading score on performance on Woodcock–Johnson pseudoword reading (Woodcock and Johnson 1989). In these analyses, age was included as a covariate, effectively removing the effects of age.

Age-Correlation Analysis

To examine the relationship between age and brain activation, we correlated the activations observed for NWR and CAT during fMRI and age. For each subject, we correlated the mean change in t values between NWR and L (and CAT and L) in each voxel with the child's age in months.

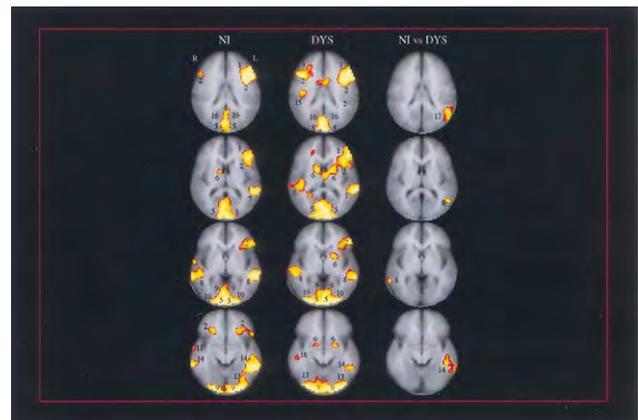


Figure 2. Composite maps (columns 1 and 2) demonstrating brain activation in nonimpaired (NI) and in dyslexic (DYS) readers during the category task and composite contrast maps (column 3) comparing directly the brain activation of the two groups. In columns 1 and 2, red-yellow indicates areas that had significantly greater activation ($p = .05$) in the category task compared with the line task, and in column 3, red-yellow indicates brain regions that were more active in NI compared with DYS during the category task. The four rows of images from top to bottom correspond to $z = +23, +14, +5,$ and -5 in Talairach space. The legend for brain activation is as follows: 1) middle frontal gyrus, 2) inferior frontal gyrus, 3) anterior cingulate gyrus, 4) supramarginal gyrus, 5) cuneus, 6) basal ganglia, 7) superior temporal gyrus, 8) posterior aspect of middle temporal gyrus and anterior aspect middle occipital gyrus, 9) lingual gyrus, 10) middle occipital gyrus, 11) anterior aspect of superior temporal gyrus, 12) medial orbital gyrus, 13) inferior occipital gyrus, 14) posterior aspect of middle temporal gyrus and anterior aspect of middle occipital gyrus, 15) postcentral gyrus, 16) precuneus, 17) angular gyrus, and 18) middle temporal gyrus.

Results

Reading performance in the dyslexic children was significantly impaired: the mean standard score on a measure of pseudoword reading (Woodcock and Johnson 1989; mean \pm SD) was 85.1 ± 11.0 in DYS compared with 120 ± 17.1 in NI ($p < .001$). During fMRI, significant differences between NI and DYS children were observed while the children were engaged in the tasks requiring phonologic analysis (SLR, NWR, and CAT) and not during the case task, which relies on visual perception and not phonology. Because the results for SLR and NWR were very similar and because SLR did not add any additional explanatory power, in the interest of parsimony we have chosen to focus on the results for NWR and CAT. During NWR, the NI readers (Figure 1, column 1) activated primarily left hemisphere regions (including middle frontal gyrus, inferior frontal gyrus, supramarginal gyrus, cuneus, basal ganglia, superior temporal gyrus, superior temporal sulcus and posterior aspect of the superior and middle temporal gyri, lingual gyrus, middle occipital gyrus, inferior occipital gyrus, posterior aspect of the middle temporal gyrus, and anterior aspect of the middle occipital gyrus) and right hemisphere regions in the anterior cingulate gyrus, cuneus, lingual gyrus, middle occipital gyrus, anterior aspect of superior temporal gyrus, and inferior occipital gyrus. The DYS readers (Figure 1, column 2) also activated left hemisphere sites (including middle frontal gyrus, inferior frontal gyrus, cuneus, basal ganglia, superior temporal gyrus, lingual gyrus, middle occipital gyrus, and inferior occipital gyrus) and right hemisphere sites in cuneus, basal ganglia, lingual gyrus, middle occipital gyrus, and inferior occipital gyrus. In Figure 1, column 3, the groups are contrasted directly. The NI readers demonstrated significantly greater activation than DYS children in left hemisphere sites (including inferior frontal gyrus, superior temporal sulcus and posterior aspect of the superior and middle temporal gyri, and posterior aspect of middle temporal gyrus and anterior aspect of middle occipital gyrus) and right hemisphere sites in inferior frontal gyrus, superior temporal sulcus and posterior aspect of the superior and middle temporal gyri, anterior aspect of superior temporal gyrus, and medial orbital gyrus. We did not find differences in the insula, as some investigators have reported (Corina et al 2001; Paulesu et al 1996), although in the NWR task the region of activation in NI readers (Figure 1, column 1) did include the insula. On the contrast image between NI and DYS (Figure 1, column 3) this region is not significantly different between groups, however.

During CAT, the NI readers (Figure 2, column 1) activated primarily left hemisphere regions (including middle frontal gyrus, inferior frontal gyrus, cuneus, supe-

rior temporal gyrus, posterior aspect of the middle temporal gyrus and anterior aspect of the middle occipital gyrus, lingual gyrus, middle occipital gyrus, inferior occipital gyrus and posterior aspect of middle temporal gyrus, and anterior aspect of middle occipital gyrus and precuneus) and right hemisphere sites in inferior frontal gyrus, cuneus, basal ganglia, posterior aspect of middle temporal gyrus and anterior aspect middle occipital gyrus, lingual gyrus, middle occipital gyrus, anterior aspect of superior temporal gyrus, inferior occipital gyrus, posterior aspect of middle temporal gyrus, and anterior aspect of middle occipital gyrus and precuneus. The DYS readers (Figure 2, column 2) also activated left hemisphere sites (including middle frontal gyrus, inferior frontal gyrus, cuneus, basal ganglia, superior temporal gyrus, posterior aspect of middle temporal gyrus and anterior aspect middle occipital gyrus, lingual gyrus, middle occipital gyrus, inferior occipital gyrus, posterior aspect of middle temporal gyrus, and anterior aspect of middle occipital gyrus and precuneus) and right hemisphere sites in middle frontal gyrus, inferior frontal gyrus, cuneus, basal ganglia, superior temporal gyrus, posterior aspect of middle temporal gyrus and anterior aspect middle occipital gyrus, lingual gyrus, middle occipital gyrus, inferior occipital gyrus, postcentral gyrus, precuneus, and middle temporal gyrus. In Figure 2, column 3, the groups are contrasted directly. The NI readers demonstrated significantly greater activation than the DYS children in left hemisphere sites (including the angular gyrus, posterior aspect of middle temporal gyrus and anterior aspect middle occipital gyrus and posterior aspect of middle temporal gyrus, and anterior aspect of middle occipital gyrus) and in right hemisphere sites in the posterior aspect of middle temporal gyrus and anterior aspect of the middle occipital gyrus.

To address the issue of the difference in age between dyslexic and nonimpaired children, we examined a subset that was carefully matched for age: 102 of the 144 children with 53 NI (age [mean \pm SD, range] = 11.8 ± 2.2 , 7.8–17.8) and 49 DYS (age [mean \pm SD, range] = 12.0 ± 2.4 , 7.9–17.4). The group contrasts on NWR and CAT were essentially identical with the results shown for the entire group in Figures 1 and 2.

Skill Correlation

Of interest is the correlation between individual differences in reading performance on standard measures of reading skill out of magnet and individual differences in brain activation patterns in left hemisphere posterior regions. As shown in Figure 3 performance on Woodcock–Johnson Word Attack test of pseudoword reading (Woodcock and Johnson 1989) was positively correlated with activation in posterior regions, particularly in the left

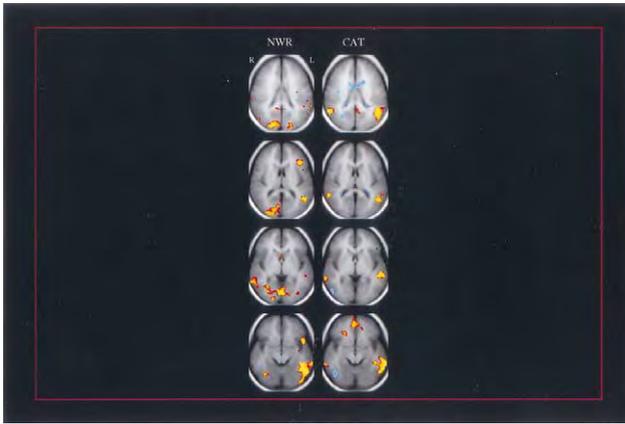


Figure 3. Correlation map between reading skill as measured by the Word Attack reading test (Woodcock and Johnson 1989) performed out of magnet and nonword rhyme (NWR) and semantic category CAT tasks performed during functional magnetic resonance imaging for the group of 144 children. At each voxel, a Pearson correlation coefficient (r) was calculated with age included as a covariate; a normal distribution test was used (Hays 1988). Areas in yellow-red show a positive correlation of in-magnet tasks with the out-of-magnet reading test (threshold, $p < .01$). The four rows of images from top to bottom correspond to $Z = +23, +14, +5$ and -5 of Talairach atlas. Strong correlation was found in the inferior aspect of the temporal occipital region (fourth row), in the more superior aspect of the temporal occipital regions (second and third rows), and in the parietal regions (top row). CAT, semantic category.

occipitotemporal area in both the NWR and CAT and bilateral parietotemporal regions in CAT. The more accurate the performance both on word and on pseudoword reading tasks, the greater the magnitude of the fMRI signal in these left hemisphere regions during in-magnet reading. These findings across the full cohort of children reveal a continuum from very poor to skilled readers (Shaywitz et al 1992b). To explore this brain-behavior relation further, we isolated the average center of mass of activation in the left occipitotemporal area (Talairach coordinates $x: -42; y: -42; z: -5$) and performed multiple regression analyses, adjusting for the effects of age by covariance. The correlation between left occipitotemporal activation during NWR and reading performance on the Woodcock-Johnson Word Attack was $.33$ ($p < .001$). For CAT (Talairach coordinates $x: -53; y: -38; z: -5$), the correlation was $.26$ ($p < .002$).

In addition to these *positive* correlations of CAT activation with reading performance, we also noted a significant *negative* correlation with performance in the *right* occipitotemporal region (shown in blue, $z = -5$). This suggests that as the poorest readers attempted to read the real words in the CAT task, they were engaging an ancillary system in the right hemisphere. Similarly, a negative correlation with performance was evident in the anterior cingulate region (blue, $z = 23$). Anterior cingulate

activation is often equated with attentional demands and effort, and it is reasonable to interpret this finding as indicating that the poorest readers are putting forth a great deal of effort as they attempt to read words.

Age Correlation

We calculated a Pearson correlation coefficient (r) at each voxel between age and activation for each subject group individually for both NWR and CAT tasks (Figure 4). During NWR in the DYS readers, increasing age was *positively* correlated with bilateral activation primarily in the inferior frontal gyri as well as basal ganglia, posterior cingulate gyri, cuneus, and middle occipital gyri and in the posterior aspect of the left superior temporal gyrus (row 1, column 2). In contrast, during NWR in the NI readers, few correlations are apparent with increasing age, and here age was *negatively* correlated with activation in the superior frontal sulcus and middle frontal gyri regions bilaterally (row 1, column 1). To further examine this issue, we

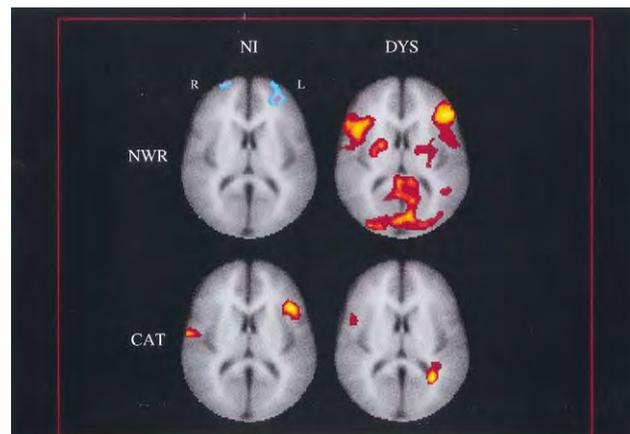


Figure 4. Correlation maps between age and activation for nonimpaired (NI) and dyslexic (DYS) readers. For each group of readers, a Pearson correlation coefficient (r) was calculated at each voxel between age and activation for both nonword rhyme (NWR) and semantic category (CAT) tasks. Areas in yellow-red indicate a positive correlation between age and activation (threshold, $p < .05$). Brain regions in blue-purple indicate a negative correlation between age and activation (threshold, $p < .05$). The slice location is at $z = +12$ in Talairach space. During NWR in DYS readers, increasing age was *positively* correlated with bilateral activation in the inferior frontal gyri, basal ganglia, posterior cingulate gyri, cuneus, and middle occipital gyri, and in the posterior aspect of the left superior temporal gyrus (row 1, column 2). In contrast, during NWR in NI readers, increasing age was *negatively* correlated with activation in the superior frontal sulcus and middle frontal gyri regions bilaterally (row 1, column 1). During the CAT task in DYS readers, increasing age was positively correlated with activation in the *right* inferior frontal gyrus (row 2, column 2). During the CAT task in NI readers, increasing age was positively correlated with activation in the *left* inferior frontal gyrus and the right central sulcus region (row 2, column 1).

isolated the average center of mass of activation in the contrast map (Figure 1, column 3) in the inferior frontal gyrus in the left hemisphere and its homologue in the right hemisphere, regions comprising a radius of 9 mm with coordinates $(x, y, z) \pm 38, +23, \text{ and } +12$. For each subject, we determined the amount of activation in this region of interest (ROI) by averaging the mean change in t values between NWR and L in each voxel of the ROI. The amount of activation in each ROI was then correlated with age. Significant Pearson r values were observed in the DYS children in both the left ($r = .34, p < .01$) and right ($r = .30, p < .05$) inferior frontal gyri; in contrast, in the NI readers, no significant correlations between age and brain activations were observed in these frontal regions.

During CAT, significant positive correlations with age were noted in NI, but not in DYS, in the left inferior frontal gyrus and right precentral sulcus (Figure 4).

Discussion

These results, acquired on an exceptionally large sample representing a broad age range across childhood, indicate significant differences in brain activation patterns during phonologic analysis in nonimpaired compared with dyslexic children. Specifically, nonimpaired children demonstrate significantly greater activation than do dyslexic children in left hemisphere sites including the inferior frontal, superior temporal, parietotemporal, and middle temporal–middle occipital gyri and right hemisphere sites including the inferior frontal, superior temporal, cingulate, and medial orbital gyri. These data converge with reports from many investigators using functional brain imaging that show a failure of left hemisphere posterior brain systems to function properly during reading (Brunswick et al 1999; Helenius et al 1999; Horwitz et al 1998; Paulesu et al 2001; Pugh et al 2000; Rumsey et al 1992, 1997; Salmelin et al 1996; Shaywitz et al 1998; Simos et al 2000) as well as during nonreading visual processing tasks (Demb et al 1998; Eden et al 1996). Our data indicate that dysfunction in left hemisphere posterior reading circuits is already present in dyslexic children and cannot be ascribed simply to a lifetime of poor reading.

In anterior regions the NI children demonstrated greater activation during NWR (Figure 1, column 3) than the DYS children; this finding is consonant with two other reports in children (Corina et al 2001; Georgiewa et al 1999) as well as reports in adults (Gross-Glenn et al 1991; Paulesu et al 1996). At the same time, this finding contrasts with what we (Shaywitz et al 1998) and others (Brunswick et al 1999) have reported in adults, where dyslexic readers showed greater activation in the inferior frontal gyrus. Consideration of the correlation between age and brain activation provided an explanation that could resolve these

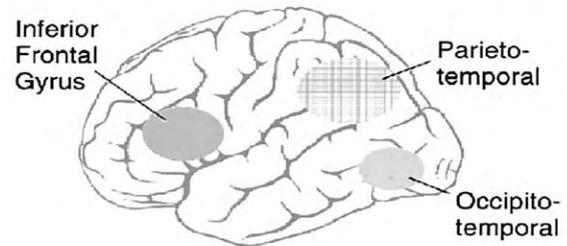


Figure 5. Neural systems for reading. Converging evidence indicates three important systems in reading, all primarily in the left hemisphere. These include an anterior system and two posterior systems: 1) anterior system in the left inferior frontal region; 2) dorsal parietotemporal system involving angular gyrus, supramarginal gyrus and posterior portions of the superior temporal gyrus; 3) ventral occipitotemporal system involving portions of the middle temporal gyrus and middle occipital gyrus. For details, please see text.

differences. Specifically, we found that during the most difficult and specific phonologic task (nonword rhyming) older dyslexic readers engaged the left and right inferior frontal gyrus, a finding consistent with results in adult dyslexic readers which indicate an increase in activation in frontal regions (Brunswick et al 1999; Shaywitz et al 1998). It is reasonable to suggest that older dyslexic readers engage neural systems in frontal regions to compensate for the disruption in posterior regions. During the CAT task, older dyslexic readers engage the right inferior frontal gyrus, whereas older nonimpaired readers engage the left inferior frontal gyrus and right central sulcus region. The category task is considerably more complex than nonword rhyming, engaging not only phonology but lexical and semantic processes as well. The older nonimpaired readers begin to engage the left frontal systems to perform this task; in contrast, older dyslexic readers fail to engage left frontal systems but rather begin using an ancillary system, the right inferior frontal gyrus.

Finally, the significant correlations between performance on a reading measure out of the magnet and brain activations during fMRI tasks suggest that the left occipitotemporal region may be a critical component of a neural system for skilled reading. Accumulating evidence from laboratories around the world indicates that there are a number of interrelated neural systems used in reading, at least two in posterior brain regions, as well as distinct and related systems in anterior regions (Figure 5). As early as 1891, the French neurologist Dejerine (1891) suggested that a portion of the left posterior brain region is critical for reading. Beginning with Dejerine, a large literature on acquired inability to read (alexia) describes neuroanatomic lesions most prominently centered in the parietotemporal area (including the angular gyrus, supramarginal gyrus and

posterior portions of the superior temporal gyrus) as a region pivotal in mapping the visual percept of the print onto the phonologic structures of the language system (Damasio and Damasio 1983; Friedman et al 1993; Geschwind 1965). Another posterior brain region, this more ventral in the occipitotemporal area, was also described by Dejerine (1892) as critical in reading.

More recently, Logan (Logan 1988, 1997) proposed two systems critical in the development of skilled, automatic processing, one involving word analysis (operating on individual units of words such as phonemes, requiring attentional resources and processing relatively slowly) and the second system operating on the whole word (word form; an obligatory system that does not require attention and processes very rapidly, on the order of 150 msec after a word is read; Price et al 1996). Converging evidence from a number of lines of investigation indicate that Logan's word analysis system is localized within the parietotemporal region, whereas the automatic, rapidly responding system is localized within the occipitotemporal area, functioning as a visual word form area (Cohen et al 2000, in press; Dehaene et al 2001; Moore and Price 1999). The visual word form area appears to respond preferentially to rapidly presented stimuli (Price et al 1996) and is engaged even when the word has not been consciously perceived (Dehaene et al 2001). Still another reading-related neural circuit involves an anterior system in the inferior frontal gyrus (Broca's area), a region that has long been associated with articulation and also serves an important function in silent reading and naming (Fiez and Peterson 1998; Frackowiak et al 1997).

Recognition of these systems allows us to suggest an explanation for the brain activation patterns observed in dyslexic children. We suppose that rather than the smoothly functioning and integrated reading systems observed in nonimpaired children, disruption of the posterior reading systems results in dyslexic children attempting to compensate by shifting to other, ancillary systems, for example, anterior sites such as the inferior frontal gyrus and right hemisphere sites. The anterior sites, critical in articulation (Brunswick et al 1999; Fiez and Peterson 1998; Frackowiak et al 1997; Pugh et al 1997), may help the child with dyslexia develop an awareness of the sound structure of the word by forming the word with his lips, tongue, and vocal apparatus and thus allow the child to read, albeit more slowly and less efficiently than if the fast occipitotemporal word identification system were functioning. The right hemisphere sites may represent the engagement of brain regions that allow the poor reader to use other perceptual processes to compensate for his or her poor phonologic skills. A number of studies of young adults with childhood histories of dyslexia indicate that although they may develop some accuracy in reading

words, they remain slow, nonautomatic readers (Bruck 1992; Felton et al 1990). These data now suggest an explanation for these observed clinical findings. In dyslexic readers disruption of both dorsal and ventral left hemisphere posterior reading systems underlies the failure of skilled reading to develop, whereas a shift to ancillary systems in left and right anterior regions and right posterior regions supports accurate, but not automatic, word reading.

This study was designed to minimize some of the problems encountered in previous studies, and thus we examined a large sample, particularly for a functional imaging study; we included a broad age range and studied both boys and girls. We also recognize that there are limitations of our study, notably that inferences about development are based on the cross-sectional features of the study design. A longitudinal study of the development of reading in children with dyslexia would be of particular interest. Knowledge that dyslexic children and adults demonstrate a disruption within the neural systems engaged in accessing the sound structure of words underscores the importance of evaluating phonologic skills in the diagnosis of dyslexia and also of focusing on these skills and their underlying neural systems as targets for informed phonologically based interventions for children and for adults.

Finally, we emphasize that fMRI studies of reading are very much investigational, and the data presented here represent group data. At the present time, fMRI has not progressed to a point where it can be, nor should be, used in the diagnosis of individuals with dyslexia.

The authors thank Carmel Lepore, Hedy Sarofin, and Terry Hickey for their invaluable help in imaging subjects. The authors thank also John Holahan and Cheryl Lacadie for their help with data analysis. This work was supported by grants from the National Institute of Child Health and Human Development (Grant Nos. PO1 HD 21888 and P50 HD25802).

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