

Development of neural mechanisms for reading

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The complexities of pediatric brain imaging have precluded studies that trace the neural development of cognitive skills acquired during childhood. Using a task that isolates reading-related brain activity and minimizes confounding performance effects, we carried out a cross-sectional functional magnetic resonance imaging (fMRI) study using subjects whose ages ranged from 6 to 22 years. We found that learning to read is associated with two patterns of change in brain activity: increased activity in left-hemisphere middle temporal and inferior frontal gyri and decreased activity in right inferotemporal cortical areas. Activity in the left-posterior superior temporal sulcus of the youngest readers was associated with the maturation of their phonological processing abilities. These findings inform current reading models and provide strong support for Orton's 1925 theory of reading development.

Reading is an ability typically learned through explicit training, and many factors, including phonological processing skills, contribute to its successful acquisition^{1–4}. Neurophysiology research has revealed that mature reading is performed by a left-hemisphere network of frontal, temporoparietal and occipitotemporal cortical regions responsible for mapping visual (orthographic) information onto auditory (phonological) and conceptual (semantic) representations^{5–12}. Despite the importance of normative data in understanding developmental learning disorders such as dyslexia, the neural changes underlying normal reading acquisition are not known, and we have yet to uncover the neural mechanisms by which specific phonological skills contribute to reading achievement.

In 1925, Samuel Orton proposed that learning to read requires children to disengage posterior right hemisphere visual representations that interfere with proper word identification¹³. In contrast, a more recent dorsal-ventral neuroanatomical model based on data from dyslexic and control children¹⁴ posits that young readers rely on a left temporoparietal–inferior frontal phonological decoding circuit for reading, and that later acquisition of reading skill is associated with engagement of a left inferotemporal ‘word form area’¹¹. Recent normative studies^{15,16} have demonstrated differences between adults and children in the neural processing of single words, but methodological complexities associated with developmental brain imaging^{17,18} have prevented investigation of reading acquisition as a continuous process from emergence to expertise.

To fully delineate the neural changes associated with reading acquisition, we must incorporate our understanding of the behavioral variables contributing to reading achievement in the design of experiments combining behavioral and neurophysiological measures. The primary question motivating this study was: how do the neural systems responsible for reading change throughout the period of its acquisition? To answer this question, we performed a cross-sectional fMRI study using subjects whose ages spanned the entire period of formal schooling. To avoid confounding performance effects, developmental imaging stud-

ies require that activation tasks be performed equally well regardless of age^{17–19}. Recently, researchers have begun to tackle this problem by manipulating task parameters and restricting the age groups under investigation^{15,16,20}. We approached this issue differently, using an implicit word-processing task⁸ that involves detection of a visual feature (tall letters) within both words and matched false font strings (Fig. 1). Although subjects are not instructed to read the words, reading occurs obligatorily without conscious effort, resulting in comparable brain activity to that associated with explicit reading tasks^{8,21}. Even novice readers can perform the task accurately because subjects are not explicitly required to read the words, minimizing performance differences with age. Studies contrasting dyslexic adults with controls have shown the success of this task in avoiding performance-related confounding factors in comparisons of subjects of different reading abilities^{22,23}. In addition, we contrasted words with visually matched non-lexical stimuli (false font strings) to control for brain processes required for task execution but not specifically for words, such as visual and spatial processing, response selection, motor planning and execution. Studies using fMRI typically measure differences in brain activity between conditions and necessitate use of control tasks based on the assumptions of cognitive insertion²⁴. This closely matched control condition allowed us to isolate those neurodevelopmental changes specifically related to lexical processing from those linked to more general brain development^{25–28}. In addition to fMRI experiments, commonly used behavioral measures of reading and phonological skills were obtained to evaluate the relationship between brain activity and cognitive constructs related to reading ability.

Consistent with the dorsal-ventral model of reading acquisition, we found that young readers primarily engaged the left posterior superior temporal cortex. Furthermore, activity in this region was modulated by children's phonological skills. While this model predicts developmental increases in left inferotemporal activity, however, we found that learning to read was associated with engagement of left inferior frontal and middle temporal cortices as well as disengage-

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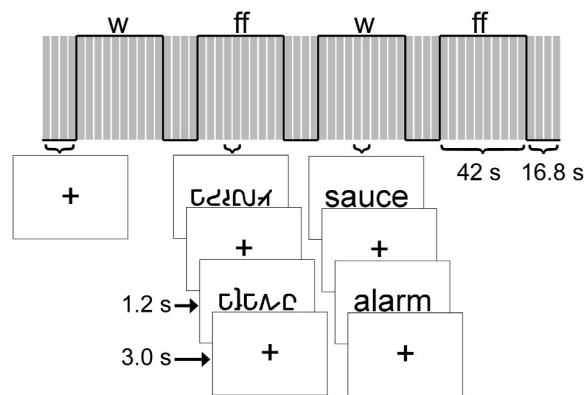


Figure 1 Feature detection and the implicit-reading fMRI task. Alternating epochs of crosshair fixation, words (w) and false font strings (ff) were presented. Fixation epochs consisted of four whole brain volume acquisitions, whereas word and false font string epochs consisted of ten. Subjects were instructed to press a button held in their right hand if the stimulus contained an ascender or 'tall letter' or a button held in their left hand if it did not. In the examples given here, 'sauce' would be given a 'no' response, as would the first false font string shown. The word 'alarm' would be given a 'yes,' as would the second false font string. False font strings matched word stimuli for length, size and location of ascenders and descenders, but correspondences between letters and false font characters were not consistent. To avoid confusion, words containing the letters i and j were excluded. Stimuli were presented for 1.2 s followed by 3 s of crosshair fixation. Two runs were collected in this manner for a total of 40 whole-brain EPI volumes per task condition.

ment of right inferotemporal cortex—a pattern is consistent with Samuel Orton's theory of reading acquisition.

RESULTS

Subjects and task performance

Forty-one subjects were included in the final analysis (age 14.1 ± 5.6 years (mean \pm s.d.); 22 females, 14.6 ± 5.4 years, range 7.0–21.5; 19 males, 13.6 ± 5.9 years, range 6.6–22.1). To ensure that our sample was unbiased across the age span, we confirmed that standardized measures of intelligence and word reading were not significantly related to age (Table 1).

Subjects performed the feature detection tasks with greater than 70% accuracy ($P < 0.001$ compared to chance performance of 50%), and accuracy was equivalent for word and false font string stimuli (words, 93.3%; false font strings, 92.2%, $P = 0.24$, Table 1). Response times for false font strings were 42 ms longer than for words (words, 838 ms; false font strings, 880 ms; $P < 0.001$), a small difference which could slightly increase the chance of false-negative findings. Although task performance was related to age (Table 1 and Fig. 2a), accuracy and response time differences between words and false font strings were not (Table 1 and Fig. 2b). Nor were accuracy and response-time differences related to reading ability or the three phonological measures used as regressors in imaging analyses. Thus, the task and control conditions were equally matched across the age and ability spans of our sample, and developmental effects in brain activity for the word versus false font string contrast cannot be attributed to task performance.

Subjects also completed a forced-choice recognition post-test after imaging sessions to confirm implicit processing of stimuli; subjects were able to accurately discriminate word stimuli presented during scanning from matched distractors (accuracy for words, 64.6%; false font strings, 51.5%). Furthermore, word recognition accuracy correlated significantly with the Woodcock Johnson III Letter/Word Identification Subtest, a measure of single-word reading, even after partialling out relationships with verbal IQ ($r = 0.31$, $P = 0.04$, one-tailed). This demonstrates a strong correspondence between implicit word processing and measures of reading ability.

Implicit reading

To investigate the neural systems engaged during performance of the feature-detection tasks, we contrasted brain activity for each

stimulus type (words and false font strings) with activity during baseline fixation (Fig. 3a,b) in the entire group of 41 subjects. These contrasts showed that the two stimulus types engaged similar cortical and subcortical structures, including striate and extrastriate cortices, motor cortex, supplementary motor area, parietal association cortex, dorsolateral prefrontal cortex, the thalamus and the cerebellum. The contrast of words versus false font strings revealed those structures engaged by the implicit processing of words, including left posterior temporal, left inferior frontal and right inferior parietal cortices (Fig. 3c).

The implicit reading-related brain activity of adults was consistent with previous reports, including posterior temporoparietal cortex, anterior lateral temporal cortex and dorsal and ventral areas of the left inferior frontal gyrus^{8,23} (Fig. 4a). This confirms that adult subjects engaged typical reading networks during implicit word processing^{7,10,29,30}. To examine the neural basis of implicit reading in children, we then restricted our contrast to subjects 9 years old or younger (Fig. 4b). These children engaged mainly a posterior region of the left superior temporal cortex during implicit word processing.

Reading acquisition

To evaluate how the neural basis of reading changes over the course of reading acquisition, we performed a voxel-wise regression between word-versus-false font string difference images and reading ability. As our measure of reading ability, we used a composite score combining measures of single-word reading, novel-word decoding and passage-reading rate and accuracy. This analysis revealed a striking develop-

Table 1 Behavioral profile of subjects and task performance

Behavioral measures	Mean (s.d.)	r^2	P
WASI Full Scale IQ	121.5 (11.0)	0.01	n.s.
Woodcock-Johnson III Letter/Word Identification	113.5 (9.7)	0.02	n.s.
Implicit reading task			
Overall accuracy (% correct)	93.2 (6.3)	0.31	< 0.001
Overall response time (ms)	858.2 (152.3)	0.56	< 0.001
Word/false font accuracy difference (% correct)	1.1 ^a (5.6)	0.00	n.s.
Word/false font response time difference (ms)	-41.5 ^b (57.7)	0.03	n.s.
Head motion (mm/scan)	0.119 (0.071)	0.25	< 0.001
Head motion after correction (mm/scan)	0.050 (0.016)	0.00	n.s.

To exclude the possibility of age-related biases in our sample, we performed linear regression of behavioral measures with age. r^2 is the coefficient of determination for the regression. P -values are two-tailed for the null hypothesis that the slope of the regression line equals zero. WASI Full Scale IQ and Woodcock-Johnson III Letter/Word Identification are standardized scores (population mean, 100; s.d., 15). Chance performance was 50% for the implicit reading task. Head motion was measured as the mean movement of the volume center of intensity between time points.

^a $P = 0.24$, ^b $P < 0.001$ (word vs. false font string paired t -tests).

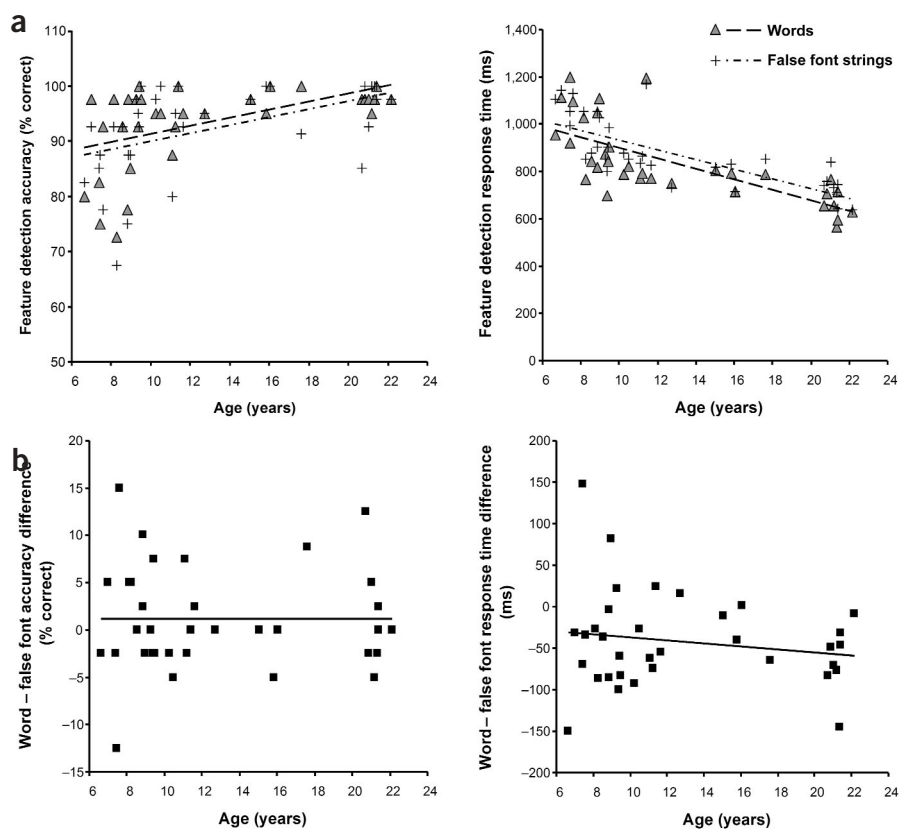


Figure 2 Scatter plots of feature detection performance. **(a)** Accuracies and response times for word and false font stimuli plotted against age. The inclusion threshold was set at 70% for accuracy. Best-fit lines depict similar age effects in word and false font performance. The coefficients of determination (r^2) for the relationships with age were as follows: word accuracy = 0.27, false font accuracy = 0.22, word RT = 0.51, false font RT = 0.58 (all $P < 0.005$). **(b)** Differences between word and false font string accuracy and response time plotted against age. Coefficients of determination (r^2) for the relationships with age were as follows: accuracy = 0.00 ($P = 0.99$), RT = 0.03 ($P = 0.34$). Similar relationships were observed for all measures used as regressors in imaging analyses. Performance matching between task and control conditions was not affected by age, so age-related effects in word versus false font imaging comparisons are free of confounding performance effects.

another in a more posterior region of the fusiform gyrus (Figs. 5 and 6).

Reading and phonological processing

To investigate the specific cognitive processes related to reading acquisition, we examined the relationships between three key phonological skills and word processing³. A rich behavioral literature implicates phonological processing, the use of the sound structure of language to

mental pattern: reading ability correlated positively with activity in left-hemisphere frontal and temporal cortical areas, and negatively with activity in right-hemisphere posterior cortical areas (Fig. 5). To ensure that correlations with reading ability were specific to lexical processing and not related to general maturational changes, we confirmed that false font string-versus-fixation difference images bore none of the same relationships with age or reading ability ($P < 0.05$, uncorrected).

Specifically, implicit reading activity increased with reading ability in two areas of the left ventral inferior frontal gyrus and in the left middle temporal gyrus. Activity in an area of the left inferior frontal sulcus was also positively correlated with reading skill, as suggested in previous reports^{14–16}. We observed no relationship between reading ability and activity in the left inferotemporal cortex, a region housing the putative visual word form area^{31,32}. Whereas this region was robustly activated by both words and false font strings, only the inferior temporal sulcus was active specifically for words ($x, y, z, -56 -40 -8$; $Z = 4.2$; Fig. 3c), as in previous studies⁸. However, this activity bore no relationship with reading ability or age (reading composite $r = -0.09$, $P = 0.57$; age $r = 0.04$, $P = 0.79$; Fig. 6). To ensure that this result was not due to inter-subject variability in location of the visual word form area, we located maxima in single-subject Z-maps within 20 mm of the classic visual word form area ($-43 -54 -12$)^{31,32}. Although peaks of activity were located in this region for 38 of the 41 subjects, no significant relationships with reading ability or age ($P < 0.05$) were observed for the magnitude or location of the nearest maxima to this point, nor the largest maxima within 15 mm or 20 mm. Rather, development of ventral extrastriate pathways toward their mature lateralized state occurred exclusively through developmental decreases in the right hemisphere. Specifically, two right inferotemporal areas were developmentally disengaged, one in the inferior temporal sulcus, the contralateral homolog to the stable left inferior temporal sulcus area, and

process oral or written information, as vital to development of childhood literacy^{1–4}. In young readers, phonological ability accounts for variance in later reading achievement independent of general cognitive ability⁴ and has a causative role in reading failure². Three types of phonological processes are thought to be important for the acquisition of reading skill: phonetic recoding in working memory, phonological awareness and phonological recoding in lexical access (phonological naming)^{3,4}. To determine how these skills are related to brain activity during reading, we regressed functional activity in pediatric subjects ($n = 26$) with scores on three behavioral tests: the Digit Span, a measure of phonetic recoding in working memory; the Lindamood Auditory Conceptualization Test (LAC), a measure of phonological awareness; and the Rapid Automatized Naming Letter Subtest (RAN), a measure of phonological naming. We restricted this analysis to pediatric subjects to coincide with the dynamic period of interaction between reading and phonological skill acquisition⁴. Because the three measures were interrelated ($r_{\text{Digit Span-LAC}} = 0.66$, $r_{\text{Digit Span-RAN}} = -0.44$, $r_{\text{LAC-RAN}} = -0.44$), we confirmed the independence of observed relationships by calculating partial correlations between activated brain regions and each of the three measures, removing the effects of the other two.

The three measures correlated with three distinct patterns of brain activity (Fig. 7). Our measure of phonetic working memory (Digit Span) correlated significantly with activity in the left intraparietal sulcus, an area commonly implicated in working memory in adults^{33,34}. After partialling out relationships with the measures of phonological awareness and phonological naming, the Digit Span was also correlated with the right superior temporal sulcus and the left and right middle frontal gyri. The phonological awareness measure (LAC) correlated with a left hemisphere network of language regions, including the posterior superior temporal sulcus, the primary area recruited by young children during reading (Fig. 4b), and the ventral inferior

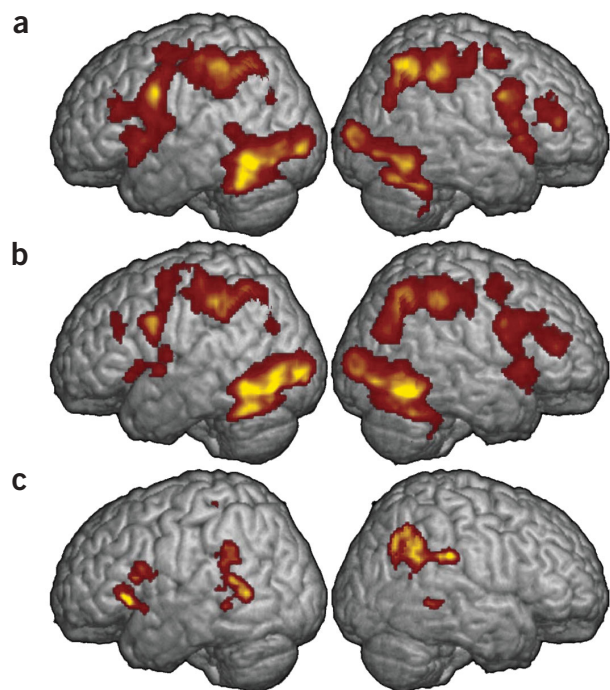


Figure 3 Feature detection and implicit reading task-related activity for the entire sample. Results of *t*-tests for words versus fixation (**a**) and false font strings versus fixation (**b**) show similar patterns of activity for these tasks when compared to fixation. Active for both words and false font strings are the bilateral occipital cortices, fusiform gyri, inferior parietal lobules, precentral gyri, inferior and middle frontal gyri, thalami, cerebellum, right cingulate gyrus, left parahippocampal gyrus and left lentiform nucleus. Active for words only is the left posterior superior temporal gyrus. Active for false font strings only is the right parahippocampal gyrus. Results of *t*-test for words versus false font strings (**c**) reflect the neural correlates of the obligatory implicit processing of visually presented words ('implicit reading'). Active in (**c**) are the bilateral inferior parietal lobules, inferior temporal sulci, left superior temporal sulcus, left inferior frontal gyrus and right cingulate gyrus.

frontal gyrus, an area in which activity increased with reading ability (Fig. 5). In contrast, our phonological naming measure (RAN) correlated with a distinctly different bilateral network, including the right posterior superior temporal gyrus, right middle temporal gyrus and left ventral inferior frontal gyrus. The areas of the ventral inferior frontal gyrus correlating with measures of phonological awareness and phonological naming did not overlap. In fact, virtually no conjunction was observed among areas of brain activity significantly modulated by these three phonological processes, and partial correlations confirmed that each relationship observed was significant independent of the other measures ($P < 0.05$).

DISCUSSION

Understanding the neural bases of normal cognitive skill acquisition is crucial to the investigation of developmental disorders of cognition. Reading serves as an excellent model of childhood learning because this ability is acquired over a protracted period beginning at an age amenable to functional neuroimaging study and continuing throughout formal schooling. Furthermore, the behavioral profile of reading acquisition has been well characterized^{1–4,35–37}, as has its neural signature in adults^{5–12}. Behavioral models^{35–37} consistently describe a pattern of reading acquisition beginning with rote iconographic recognition of words based on visual features or context (for example, the word 'yellow' has two tall lines in the middle; the word 'stop' appears in a red octagonal sign). As children attain alphabetic knowledge, they learn phoneme-to-grapheme correspondences and use phonetic cues to decode words. Mature readers consolidate commonly

occurring letter sequences (such as '-tion-') into clusters and process these clusters as units, allowing them to identify unknown words by analogy to known ones. The endpoint of this developmental process is the mature network of brain regions used by literate adults to read words. In this network, striate and extrastriate cortices transmit visual information along a ventral-stream occipitotemporal pathway to the mid-fusiform gyrus—the putative visual word-form area^{31,32}—which may serve to link abstract orthographic representations with phonological codes. Systems that retrieve and assemble phonological codes, and those that associate meanings with words, are distributed over dorsal stream cortical areas including left inferior parietal, lateral temporal and inferior frontal cortices. The specific role of each of these cortical regions in a given function is still under active investigation.

To date, the complexities of developmental brain imaging have hindered identification of the neural systems responsible for reading acquisition during childhood. Pediatric neuroimaging studies of reading have necessarily excluded children with only rudimentary reading ability because they explicitly required subjects to read words^{15,16,38}. Also, developmental changes specific to lexical processing have not been isolated from those associated with general neural maturation, nor has the relationship between the neural basis of reading and other important reading-related skills been examined. These gaps in knowledge have precluded a complete rendering of a developmental process that is as crucial as it is complex. By using an implicit reading task and a closely matched control condition, we were able to examine reading acquisition as a continuous process occurring over the entire course of schooling. By assessing our subjects' abilities using the same behavioral measures used in psycho-educational studies on reading acquisition, we were able to propose neural mechanisms for some of this field's most important findings. As the field of

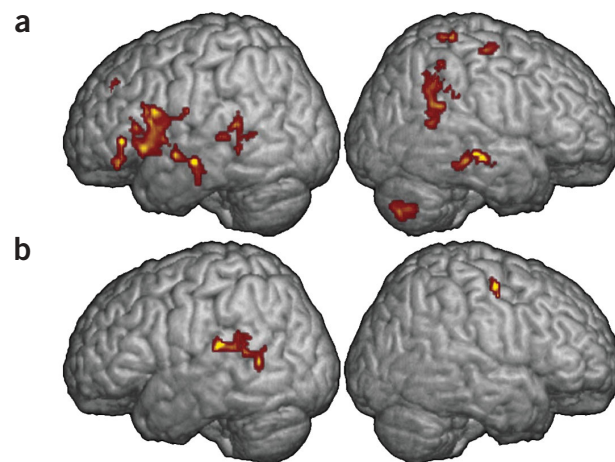
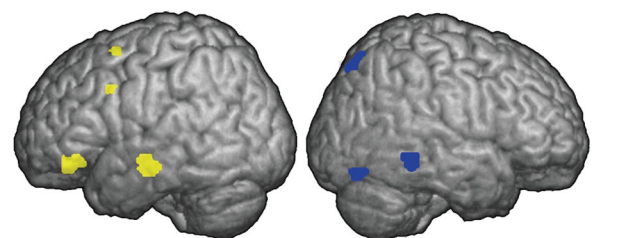


Figure 4 Implicit reading in adults and children. Results of *t*-tests comparing activity during word and false font string processing for (**a**) adults (age ≥ 20 years, $n = 15$) and (**b**) children (age ≤ 9 years, $n = 15$). Active in (**a**) are the right inferior parietal lobule, left superior temporal sulcus, bilateral middle temporal gyri, right pre and postcentral gyri, left inferior frontal gyrus and sulcus, bilateral medial superior frontal gyrus, right cingulate gyrus, left lentiform nucleus and right cerebellum. Active in (**b**) are the left superior temporal gyrus and sulcus, right precentral gyrus and right cingulate gyrus.

Figure 5 Development of the neural basis of word processing.

Developmental changes were assessed by correlation between mean-difference images and a reading composite score (raw Woodcock-Johnson III Letter-Word ID + Word Attack + Gray Oral Reading Test III revised passage score). Positive correlations between activity and reading ability appear in yellow; negative correlations appear in blue. The same pattern, with somewhat lower significance levels, emerged when activity was regressed with age instead of reading ability. Cluster r is the correlation coefficient between the mean BOLD activity in the region and the reading composite score. Peak Z is the maximum Z -score within the region. Coordinates of this maximum Z -score are based on the stereotactic system of Talairach and Tournoux⁴⁹. Coordinates are relative to the anterior commissure in the interaural (x), anterior-posterior (y) and superior-inferior (z) directions.



	Brodmann area	Volume (mm ³)	Cluster r	Peak Z	x	y	z
Positive							
Left							
Middle temporal gyrus	21	1,168	0.72	5.47	-51	-12	-11
Inferior frontal gyrus	47	1,008	0.66	4.31	-51	38	-17
				4.16	-46	32	-12
Superior frontal gyrus	6	240	0.60	4.13	-20	10	51
Cingulate gyrus	31	456	0.58	3.98	-2	-45	28
Inferior frontal sulcus	44/9	264	0.60	3.85	-34	13	27
Negative							
Right							
Inferior temporal sulcus	21/37	416	-0.64	-4.69	65	-39	-10
Precuneus	7	376	-0.59	-4.02	8	-73	48
Fusiform gyrus	19	264	-0.59	-4.00	48	-74	-13

pediatric neuroimaging matures, studies using larger samples, longitudinal designs and multiple cognitive tasks in younger children will allow for more detailed analyses of the developmental changes in the neural organization of reading systems.

Our results indicate that temporoparietal cortex, including the left superior temporal sulcus, matures early in learning and continues to be involved in reading through adulthood. This extends previous evidence that posterior language areas mature earlier than anterior ones^{16,39}. Consistent with electrophysiological evidence in animals, functional imaging studies in humans have implicated the superior temporal sulcus in crossmodal integration, a process needed for mapping print to sound⁴⁰. Indeed, activity in the left superior temporal sulcus correlated with children's phonological awareness skill, the understanding that speech is composed of units of sound (phonemes) that can be represented by visual symbols (letters) in text³. The involvement of cortical regions related to phonological awareness in early reading acquisition is not entirely surprising, as phonological awareness is considered a prerequisite for successful

reading. Measures of this skill in emergent readers predict their later reading achievement⁴. This raises the intriguing possibility that left superior temporal sulcus activity might serve as an early predictor of reading outcome. The distinct patterns observed in relation to different phonological skills supports the hypothesis that these skills contribute differently to the neural basis of reading and provide a neural explanation for the occurrence of discrete deficits in these abilities in subtypes of developmental dyslexia¹. Furthermore, as developmental dyslexia is associated with compensatory recruitment of right temporoparietal cortex¹¹, the hemispheric dissociation in this area

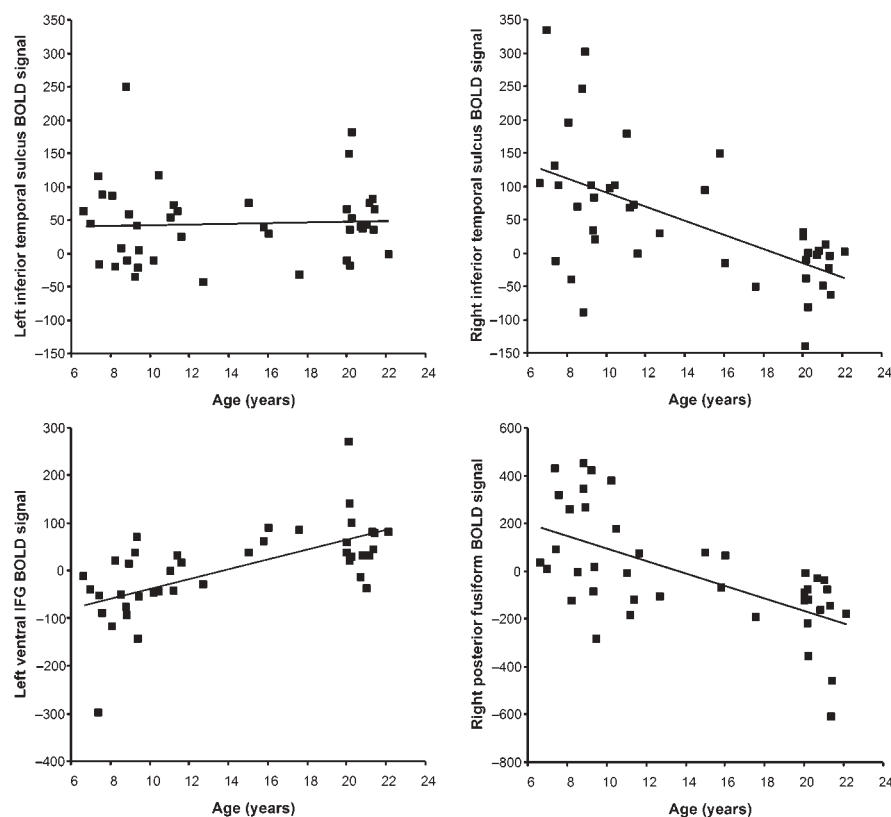
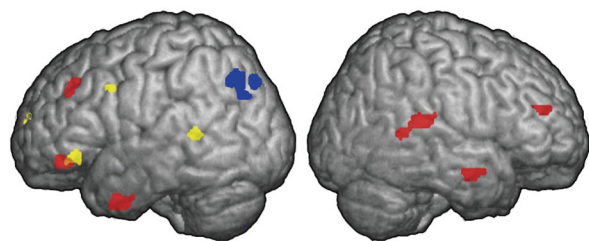


Figure 6 Scatter plots of developmental effects in fMRI BOLD response for representative cortical regions. Points represent subjects' average BOLD signal in the region, given in arbitrary units. The left inferior temporal sulcus region was defined by voxels achieving significance of $P < 0.001$ in the overall ($n = 41$) word-versus-false font string Z -map. This area was engaged by the implicit reading task, but was not modulated by age or reading ability. All other regions were defined by voxels achieving significance of $P < 0.001$ in the reading ability correlation map. The right inferior temporal sulcus region centered around a maximum at ($x y z$, 65 -39 -10). The left inferior frontal gyrus contained two maxima at (-51 38 -17) and (-46 32 -12). When the two apparent outliers were removed from this plot, the slope of the regression line decreased, but the r^2 increased. The right fusiform gyrus maximum occurred at (48 -74 -13). Developmental switching of brain activity from negative to positive or vice versa, as shown here, has been observed in other neuroimaging studies^{15,50}. The longer response times for false font strings than words indicate that the false font task was slightly more difficult. This may have offset the activity negatively across the group, resulting in an apparent polarity switch in brain activity. Age, rather than the reading composite score, is plotted on the abscissa to clearly depict the relationship between brain activity and development.



	Brodmann area	Volume (mm ³)	Cluster <i>r</i>	Peak <i>Z</i>	<i>x</i>	<i>y</i>	<i>z</i>
Phonological awareness							
Left							
Inferior frontal gyrus	47	480	0.74	4.15	-46	31	-10
Frontal pole	10	744	0.70	3.99	-12	57	12
Inferior frontal sulcus	44/9	232	0.67	3.52	-40	11	29
Superior temporal sulcus	22/21	200	0.62	3.50	-51	-42	8
Phonological naming							
Left							
Inferior frontal gyrus	47	352	0.71	4.51	-53	40	-14
Inferior temporal gyrus	20	1,048	0.69	4.22	-40	-2	-34
Middle frontal gyrus	9	536	0.72	4.16	-28	33	32
Right							
Superior temporal gyrus	22	664	0.75	4.39	67	-32	15
Cerebellum		400	0.71	3.99	12	-57	-14
Superior temporal sulcus	21/22	360	0.71	3.97	53	-44	6
Middle temporal gyrus	21	344	0.71	3.68	57	-5	-17
Middle frontal gyrus	46	224	0.67	3.62	32	44	16
Working memory							
Left							
Intraparietal sulcus	39/7/19	3,056	0.72	4.15	-32	-66	38
				3.85	-30	-49	39
Parieto-occipital sulcus	7/19	224	0.65	3.62	-24	-78	37

between measures of phonological awareness and naming may indicate why many reading-impaired children with deficits in both of these abilities are particularly unresponsive to remediation¹.

Activity in the left ventral inferior frontal gyrus increased with reading ability and was related to both phonological awareness and phonological naming ability. Functional imaging studies in adults implicate this area in both semantic^{41,42} and phonological⁴³ processing of words. The phonological relationships observed here localized to discrete areas of ventral inferior frontal cortex, and each of these areas corresponded with an independent focus of reading development. The area related to phonological naming lay just anterior to that related to phonological awareness. These relationships imply a division of ventral inferior frontal cortex into an anterior unit associated with retrieval of phonological codes from long-term storage and a posterior region that manipulates sublexical phonological units. Brain activity in the anterior middle temporal gyrus also increased with reading ability. Previous studies report greater activity in this area during the processing of familiar pictures and words than during that of unfamiliar ones, implying a role in semantic specificity^{10,44,45}.

Although the dorsal-ventral model of reading acquisition predicts progressive development of a left inferotemporal word form area, we observed only progressive disengagement of right ventral stream cortex. This disengagement of right extrastriate cortex over the course of reading acquisition likely indicates that, as they gain exposure to text, children rely less on non-lexical form recognition systems to process words. An fMRI study of orthographic processing in normal adult readers also shows that right fusiform gyrus activity is negatively modulated by the 'lexicality' of stimuli, whereas left fusiform gyrus remains unaffected⁴⁶. These findings do not, however, mitigate the established importance of the left inferotemporal cortex in reading. Most likely, this region develops in very young children for iconographic word recognition strategies³⁸ and remains important over the course of reading acquisition, adapting to its mature role in direct lexical access.

Figure 7 The relationship between word processing and measures of phonology in children. Functional activity in pediatric subjects (age <18, *n* = 26) was correlated with the Lindamood Auditory Conceptualization Test (LAC), a measure of phonological awareness (yellow), the Rapid Automated Naming Letter Subtest (RAN), a measure of phonological naming (red), and the Digit Span, a measure of phonological working memory (blue). Virtually no overlap was observed between the brain regions corresponding with each measure, although Digit Span correlated with activity in the RAN-related middle frontal gyri and right superior temporal sulcus regions when LAC and RAN were partialled out. See **Fig. 5** legend for statistical details.

In summary, we found that left posterior superior temporal cortex is engaged early in the course of reading acquisition and that its activity is modulated by children's phonological skills. These findings confirm and extend the dorsal-ventral model positing early recruitment of left temporoparietal cortical areas for reading. Whereas this model suggests a relationship between reading acquisition and activity in left inferotemporal cortex, however, we found that learning to read was associated with disengagement of right inferotemporal cortex and engagement of left inferior frontal and middle temporal cortices. The developmental decreases in right ventral stream activity were observed without corresponding left extrastriate increases. Remarkably, these findings corroborate Samuel Orton's 1925 theory of reading development that visual "engrams exist in the nondominant hemisphere which may, if not completely elided, cause confusion in recognition and recall" resulting in reading failure¹³. Our finding of progressive disengagement of right ventral extrastriate areas likely indicates a decreasing reliance on non-lexical form recognition systems for word identification, which along with engagement of left frontal and temporal semantic and phonological processing units, constitute the development of a neural basis of reading.

METHODS

Subjects. We studied 57 healthy, monolingual, right-handed native English speakers (31 female) without significant personal or family history of neurological or learning disorders. The Georgetown University Institutional Review Board approved all experimental procedures, and written informed consent was obtained from each participant and a legal guardian. All subjects completed a behavioral battery including commonly used standardized measures of IQ, word identification, decoding, passage reading, reading and oral comprehension, receptive and expressive language, phonological processing, confrontation naming and gross and fine motor coordination⁴⁷. A neuropsychologist (D.L.F.) evaluated behavioral measures for possible learning disorders. Right-handedness was confirmed by the Edinburgh Handedness Inventory (mean 91.4, s.d. 13.0). Sixteen subjects were excluded for possible learning disorder, poor task performance (accuracy <70%), head motion (peak-to-peak motion >0.7 mm) or image artifact (as assessed by two blinded experts), leaving 41 subjects in the final analysis.

fMRI data acquisition. We acquired MRI images on a Siemens Vision Magnetom 1.5-tesla scanner with a circularly polarized head coil equipped with foam padding to restrict head motion. Two three-dimensional T1-weighted images were acquired for each subject. Functional MRI runs consisted of series of whole-brain echo-planar images (EPI) (TR, 4.2 s; TE, 40 ms; 64 × 64 matrix; 230 mm FOV; 46 axial slices; 3.6-mm cubic voxels). To reduce head motion and improve compliance, we trained children extensively on an MRI simulator before scanning. For implicit word processing runs, single five-letter, low frequency (KF 8.1, s.d. 6.1) words were presented, and subjects were instructed to press a button held in the right hand if the word contained letters with ascenders (such as l, f or t; **Fig. 1**), or a button in the left hand if it did not. Half of the stimuli contained ascenders. Epochs of this task alternated with epochs of crosshair fixation and the same task performed using false font strings (**Fig. 1**) matched to words for length and location of ascenders and descenders (such as g, y or p). The mapping from false font characters to letters was inconsistent to prevent subjects from learning to decode false font strings. Words were presented in black Arial font. We generated false fonts by altering

the Arial font to create unfamiliar characters. Subjects showed whether they understood the task first by pointing out words and false font strings with ascenders on a printed list of items. If children had difficulty understanding the instructions, ascenders were described as 'tall letters'. Subjects then completed a 20-item practice run at a computer console. Stimuli were presented for 1.2 s, with a 3-s interstimulus interval. Accuracy and reaction time were measured in all children and eight adults. Each run lasted 4.2 min, and over two runs, 40 whole-head EPI volumes were collected for each condition (words, false font strings and fixation).

fMRI data analysis. Imaging data were analyzed using MEDx (Sensor Systems). Processing steps included head-motion correction, global intensity normalization, Gaussian spatial smoothing (7.2 mm), temporal filtering and spatial normalization to the SPM99 Talairach template (28 parameter affine warp transformation) (see ref. 9 for details). Head motion after correction was not related to the age of the subject (Table 1). All statistical tests were random effects statistical parametric mapping analyses performed using one overall word-minus-false font string mean difference image per subject. Regression with behavioral variables was performed by entering behavioral scores as covariates of interest in 'covariates only' SPM analyses. Statistical parametric mapping comparisons between pediatric and adult fMRI data normalized into the same stereotactic space have been validated for image resolutions greater than 5 mm⁴⁸. The critical threshold for analyses including all subjects was $P < 0.0001$ (uncorrected) with 25 contiguous 2 mm cubic voxels at $P < 0.001$. The critical threshold for analyses including subsets of the group was $P < 0.0005$ (uncorrected) with 25 contiguous 2-mm cubic voxels at $P < 0.005$. The hemispheric renderings in all figures are maximum intensity projections with a penetration distance of 25 mm.

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COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

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