Age-Related Changes in Reading Systems of Dyslexic Children

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Objective: To examine age-related changes in the neural systems for reading in nonimpaired and dyslexic children and adolescents.

Methods: Functional magnetic resonance imaging was used to study age-related changes in the neural systems for reading in a cross-sectional sample of 232 right-handed children 7 to 18 years of age (113 dyslexic readers and 119 nonimpaired readers) as they read pseudowords.

Results: In nonimpaired readers, systems in the left anterior lateral occipitotemporal area developed with age, whereas systems in the right superior and middle frontal regions decreased. In contrast, in dyslexic readers, systems in the left posterior medial occipitotemporal regions developed with age. Older nonimpaired readers were left lateralized in the anterior lateral occipitotemporal area; there was no difference in asymmetry between younger and older dyslexic readers.

Interpretation: These findings offer a possible neurobiological explanation for the differences in reading acquisition between dyslexic and nonimpaired readers and provide further evidence of the critical role of the left occipitotemporal region in the development of reading.

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Converging evidence from a number of lines of investigation points to three important neural systems for reading in children and adults: one anterior system around the inferior frontal gyrus involved in word analysis (decoding); and two posterior systems, one in the parietotemporal region also involved in word analysis, and the other more inferior in the occipitotemporal region responsible for skilled, fluent (automatic) reading. Much of this information has come from functional brain imaging studies that compare nonimpaired readers with dyslexic readers. These investigations have consistently demonstrated a failure of left-hemisphere posterior brain systems to function properly in dyslexic readers.[1–12]

Despite the consistency of data in posterior reading systems, relatively little is known about the *development* of these systems in typical readers, and even less is known of the development of these systems in dyslexic children. The approach used in this study builds on the accumulating evidence 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.[13]

Although previous studies[14,15] have reported age-related changes in activation patterns, each study has come to different conclusions as to which specific brain regions are involved in the development of reading. We hypothesized that the development of a specific neural system located within the left occipitotemporal region accounts for the development of fluent reading in nonimpaired readers. We also hypothesized that this system does not develop with age in dyslexic readers, and that dyslexic readers rely on an alternative neural pathway for reading. This study was motivated by the belief that elucidation of the specific systems developing with age in nonimpaired and dyslexic readers would provide insights into potentially differing mechanisms used for reading in each group.

In this study, we examined the development of neu-

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ral systems for reading in a sample of 232 dyslexic and nonimpaired children and adolescents while they were engaged in a reading task that required phonological analysis. Strengths of this current study include the unusually large sample size for an imaging study, the data analysis using a general linear model (GLM) approach, and the comprehensive reading assessment used. In addition, in contrast with previous studies that were limited to nonimpaired readers, this study examined both nonimpaired and dyslexic children and adolescents representing a broad age range.

Subjects and Methods

Subjects

We studied 232 right-handed children: 113 dyslexic (DYS) readers (35 girls, 78 boys; ages, 7–18 years; mean age, 12.7 years) and 119 nonimpaired (NI) readers (52 girls, 67 boys; ages, 7–17 years; mean age, 11.3 years) after informed consent had been obtained (Table). 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[16] was less than a standard score of 90 (<25th percentile) or 1.5 standard errors of prediction less than the expected reading achievement score using the Wechsler Intelligence Scale for Children—Third Edition[17] Full Scale Intelligence Quotient score.

Tasks

Two types of tasks were used: line orientation and rhyme judgment. For each task, the subject viewed two simultaneously presented stimulus displays, one above the other, and was asked to make a same/different judgment by pressing a response button if the displays matched on a given cognitive dimension: either line orientation (Line: eg, "Do [\\\/] and [\\\/] match?") or rhyme (Nonword Rhyme [NWR]: "Do [LEAT] and [KETE] rhyme?")

Imaging and Data Analysis

Subjects were imaged in a 1.5-Tesla Signa LX imaging system from General Electric Medical Systems (Waukesha, WI). Data analysis was performed using software written in MATLAB (MathWorks, Natick, MA). Single-subject activation maps were generated by comparing the images for the NWR task to the Line task using a split *t* test. The activation maps from individual subjects were used as a derived measure of task-related activity and were combined to obtain a group composite activation map comparing NWR with Line. The effect of age on activation was assessed within groups (DYS and NI groups separately) using GLM. The within-group

Table. **Subject Characteristics**

	NI (n = 119)		RD (n = 113)		Fisher's Exact	
Male sex, n	67		78		p = 0.057	
Measure	**Mean**	**SD**	**Mean**	**SD**	t	p
Age (yr)	11.3	2.5	12.7	2.8	4.23	<0.001
WISC-III						
VIQ	118.8	12.9	96.53	13.3	11.2	<0.001
PIQ	107.3	12.6	98.40	14.0	4.5	<0.001
FSIQ	114.4	11.8	97.04	13.5	9.1	<0.001
Woodcock–Johnson						
Letter Word Identification	120.1	13.7	84.25	11.2	20.2	<0.001
Word Attack	119.3	17.2	84.98	12.0	16.5	<0.001
Passage Comprehension	122.9	11.7	92.84	12.7	17.0	<0.001
In-Magnet Tasks						
Line Accuracy	0.91	0.10	0.87	0.1	2.4	0.017
Nonword Rhyme Accuracy	0.84	0.12	0.66	0.2	9.0	<0.001
(Raw Scores)						
Woodcock–Johnson						
Letter Word	46.4	5.3	33.9	8.8	14.5	<0.001
Word Attack	23.2	4.8	10.4	7.1	11.7	<0.001
Gray Oral Reading Test						
Rate	33.5	16.4	10.5	12.6	11.3	<0.001
Accuracy	26.0	14.1	8.0	9.4	10.3	<0.001
Comprehension	34.9	13.5	24.8	13.0	5.5	<0.001

NI = nonimpaired; RD = dyslexic readers; SD = standard deviation; WISC-III = Wechsler Intelligence Scale for Children—3rd Ed; FSIQ = Full Scale Intelligence Quotient; VIQ = Verbal Intelligence Quotient; PIQ = Performance (non-verbal) Intelligence Quotient.

models included age and in-magnet performance on NWR (to remove within-group variation in reading skill).

Asymmetry Index

An asymmetry index was determined for each subject by calculating the difference of intensity of activation in left and right regions of interest (ROIs) and normalizing by the square root of sum of squares of those activations. The resulting asymmetry index was then analyzed using the GLM model to establish the significance of the difference of asymmetry between NI and DYS readers.

Results

Behavioral Findings

Sex, age, cognitive ability, and reading performance measures are presented in the Table. Reading performance in the DYS children was significantly impaired. As shown in Figure 1, raw scores on a measure of phonological awareness and three indices of reading (word identification, fluency, and reading comprehension) were greater in older children compared with younger children in both NI and DYS groups. Similarly, performance on the line orientation and NWR tasks was higher in older children compared with younger children in both groups (see Supplementary Fig 1).

Brain Imaging Findings

AGE-RELATED CHANGES IN READING SYSTEMS. In NI readers (Fig 2, column 1), systems in the left anterior lateral occipitotemporal region were more active in older compared with younger readers, whereas systems in both right and left superior and middle frontal regions were more active in younger compared with older readers. For DYS children (see Fig 2, column 2), the left inferior frontal gyrus and right and left posterior medial occipitotemporal regions were more active in older compared with younger readers; bilateral superior frontal and anterior cingulate regions were more active in younger compared with older readers.

The thresholded voxel based correlation maps in Figure 2 are presented to display the spatial distribution of these differences. To further validate the significance of the effect, we defined ROIs that previous studies have indicated are critical for reading[8]: inferior frontal, parietotemporal and occipitotemporal, the latter parsed into lateral and medial systems. In addition, we examined superior frontal and middle frontal regions, which others have shown to decrease over time. Correlations of activation with age, with in-magnet NWR accuracy included as a covariate, were calculated for the NI and DYS groups separately (Fig 3). For NI readers, an age-related *increase* in activation was observed in the left anterior lateral occipitotemporal region ($p = 0.0003$), and an age-related *decrease* in activation was noted in the right middle frontal/superior frontal region ($p = 0.001$). For DYS readers, an age-related *increase* was noted in the left posterior medial

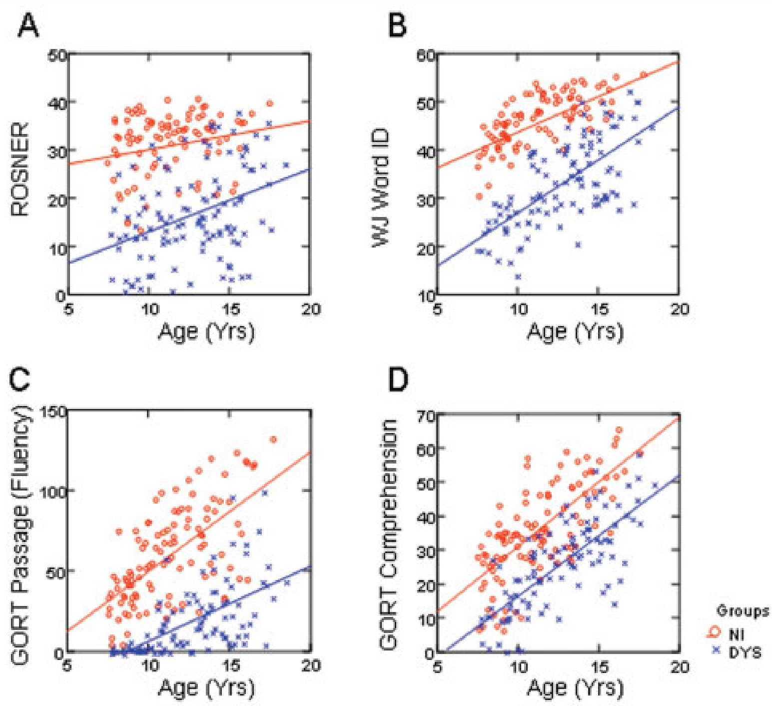

Fig 1. Performance in four reading related domains in nonimpaired (NI; red circles*) and dyslexic (DYS;* blue X's*) readers related to the age of the children. Scores are shown for the measure of (A) phonological awareness[30] and three measures of reading: (B) word identification,[16] (C) fluency, and (D) comprehension.[31] Raw scores are plotted.*

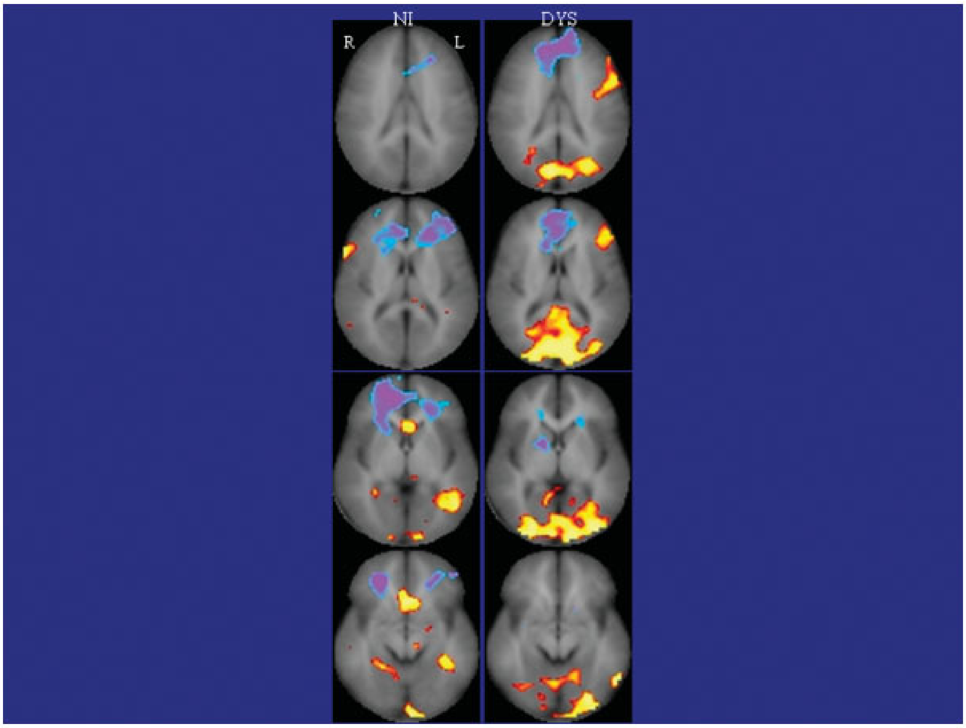

Fig 2. Correlation maps between age and activation for nonimpaired (NI) and dyslexic (DYS) readers during a nonword rhyming (NWR) task. For each group of readers, a correlation with age was calculated using general linear model (GLM) with skill (in-magnet accuracy) included as a covariate. Areas in yellow and red indicate a positive correlation between age and activation (threshold, $p < 0.05$*). Brain regions in blue and purple indicate a negative correlation between age and activation (threshold,* $p < 0.05$*). The four rows of images from top to bottom correspond to* z = +23, +14, +5, *and* −5 *in Talairach space.*[32] *Age-related* increases *in NI readers are seen primarily in the left anterior lateral occipitotemporal region, and in DYS readers in the left inferior frontal gyrus and left and right posterior medial occipitotemporal regions. Age-related* decreases *in NI readers are seen mainly in the left and right superior and middle frontal gyri, and in DYS readers in the bilateral superior frontal gyri and anterior cingulate gyrus.*

occipitotemporal region ($p = 0.002$), and an age-related *decrease* was observed in right superior frontal region ($p = 0.003$). The four scatter plots in Figure 3 include all data points. Because some of the data points can be considered outliers or to exert undue influence on the observed correlations, the four scatter plots were redrawn with the suspect data points removed (see Supplementary Fig 2). Only the correlation of the right superior frontal gyrus with age in the DYS group failed to attain statistical significance after removing those data points.

ASYMMETRY OF DEVELOPING SYSTEMS. To identify potential changes in the degree of asymmetry with age, we examined the relation between the asymmetry index and age in each reading-related ROI, comparing left with right. A significant correlation of asymmetry with age was observed only in the anterior lateral occipitotemporal region. Here there was a significant correlation of asymmetry with age in NI readers ($p < 0.0003$), whereas there was no significant correlation of asymmetry with age in DYS readers ($p < 0.9$). Furthermore, the difference between the correlation of asymmetry and age in NI and DYS readers was significant ($p < 0.009$): older NI readers were more left lateralized; there was no difference in asymmetry between younger and older DYS readers (Fig 4).

Discussion

Our findings indicate that the neural systems for reading that develop with age in nonimpaired readers differ from those that develop in dyslexic readers. The most significant contrasts focus on those systems within the left occipitotemporal area. Here, older compared with younger nonimpaired readers demonstrate an increased engagement of the left anterior lateral occipitotemporal region. In contrast, older compared with younger dyslexic readers demonstrate an increase in activation in the left posterior medial occipitotemporal region. Support for the importance of the left anterior lateral occipitotemporal region for the development of skilled reading also comes from our data for nonimpaired readers indicating this as

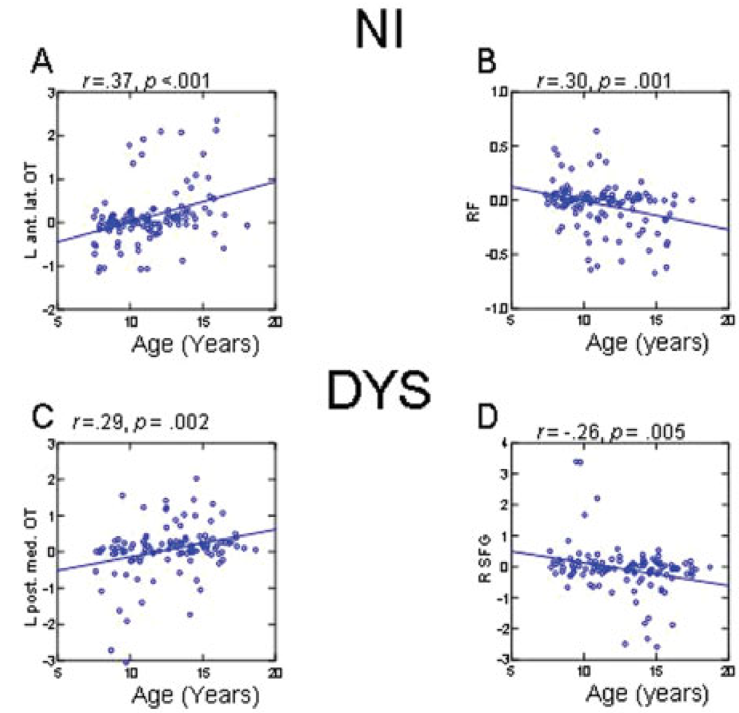

Fig 3. Regressions for activations and age for those regions of interest (ROIs) where age was significantly related to either increases or decreases in activation. These ROIs include: (A) for nonimpaired (NI) readers, increases in the left anterior lateral occipitotemporal (L ant. lat. OT) region (Talairach coordinates: x = *39,* y = *−50,* z = *2), and (B) decreases in the right frontal (RF) region (Talairach coordinates:* x = *−22,* y = *41,* z = *0); and (C) for dyslexic (DYS) readers, increases in the left posterior medial occipitotemporal (L post. med. OT) region (Talairach coordinates:* x = *29,* y = *−79,* z = *4), and (D) decreases in the right superior frontal (RSFG) region (Talairach coordinates:* x = *−13,* y = *44,* z = *23).*

the only area demonstrating a significant difference in asymmetry with age (see Fig 4).

These findings indicate that systems for reading that develop with age in dyslexic readers differ from those in nonimpaired readers, primarily in being localized to a more posterior and medial region, rather than a more

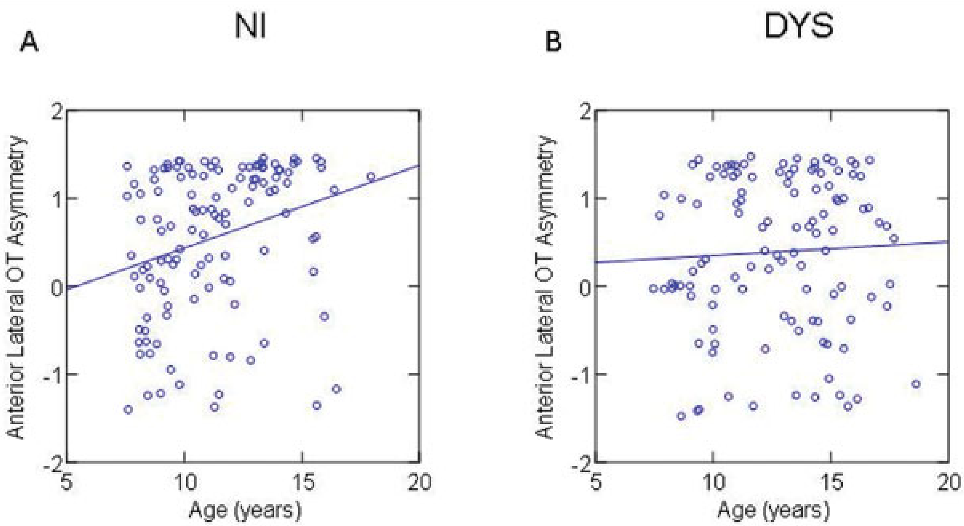

Fig 4. Asymmetry in the anterior lateral occipitotemporal (OT) region in (A) nonimpaired (NI) and (B) dyslexic (DYS) readers. Higher scores represent more lateralized (positive = left lateralized, negative = right lateralized), whereas lower scores represent less lateralization. Older NI readers are more left lateralized than are younger NI readers. There is no difference in lateralization in older and younger DYS readers. Asymmetry index is calculated as described in the text.

anterior and lateral occipitotemporal region. Interestingly, this difference in activation patterns between the two groups of readers has parallels to reported brain activation differences observed during reading of two Japanese writing systems: Kana and Kanji. For example, left anterior lateral occipitotemporal activation, similar to that seen in nonimpaired readers, occurred during reading Kana.[18] Kana script uses symbols that are linked to the sound or phoneme (comparable with English and other alphabetic scripts). In Kana and in alphabetic scripts, children initially learn to read words by learning how letters and sounds are linked; then, over time, these linkages are integrated and permanently instantiated as a word form. Knowledge of how letters and sounds are linked allows a reader to sound out and read new words. Recent research supports the notion that the anterior lateral occipitotemporal system (a region that Cohen and Dehaene have termed the visual word-form area[19–22]) is associated with the ability to read words fluently, the hallmark of a skilled reader. Just how this area functions to integrate phonology (sounds) and orthography (print) is as yet unknown. Current studies are now focusing on whether visual word recognition takes place serially, in a progressive, step-by-step approach,[20] or conversely, if the left anterior lateral occipitotemporal system functions as an interface between bottom-up visual form information and top-down semantic and phonological properties in a more dynamic integrative process.[3,23] Studies using functional imaging combined with sophisticated task presentations may help to resolve this question.[24] Comparisons of the location of the system for skilled reading found in this study and those regions described in previous reports are shown in Supplementary Figure 3.

In contrast, posterior medial occipitotemporal activation, comparable with that observed in dyslexic readers, was noted during reading of Kanji script.[18] Consideration of the mechanisms used for reading Kanji compared with Kana provide insights into potentially different mechanisms that develop with age in dyslexic contrasted with nonimpaired readers. Kanji script uses ideographs where each character must be memorized, suggesting that the posterior medial occipitotemporal region functions as part of a memory-based system. We suppose that as dyslexic children mature, this posterior medial system supports memorization rather than the progressive sound–symbol linkages observed in nonimpaired readers. And evidence exists that dyslexic readers are not able to make good use of sound–symbol linkages as they mature; instead, they come to rely on memorized words. For example, phonological deficits continue to characterize struggling readers even as they enter adolescence and adult life,[25,26] and persistently poor adult readers read words by memorization so that they are able to read familiar words but have difficulty reading unfamiliar words.[9]

Thus, our findings support and now extend previous findings to indicate that the system responsible for the integration of letters and sounds, the anterior lateral occipitotemporal system, is the neural circuit that develops with age in nonimpaired readers; conversely, dyslexic readers, who struggle to read new or unfamiliar words, come to rely on an alternate system, the posterior medial occipitotemporal system, which functions via memory networks. Our findings also indicate that it is a single reading system that develops with age: for nonimpaired readers it is the anterior lateral, and for dyslexic readers it is the posterior medial occipitotemporal region. Such findings are in agreement with a report[27] indicating that, over time, literacy can best be modeled as a single unitary construct rather than as multiple, separate, components of reading (eg, phonological awareness, word reading, passage comprehension).

A number of similarities exist between the findings in this report and previous studies in unimpaired children. For example, Schapiro and colleagues[28] report significant correlations with age in left occipitotemporal regions during a word–picture matching task using functional magnetic resonance imaging in 332 healthy (unimpaired) children aged 4.9 to 18.9 years. Schlaggar and coworkers[14] and Turkeltaub and colleagues[15] have noted increases in activation with age in left inferior frontal regions. We also implicated the inferior frontal region in reading development, however, with important differences. In our large sample of children, the increase in activation with age in the left inferior frontal region was observed only in dyslexic readers and was restricted to the voxel-wise analysis (see Fig 2). The correlation with age in the inferior frontal region using ROI analyses was not robust, and the usual level of significance did not survive in the ROI analysis when corrected for multiple comparisons. In addition to the regions that increased in activation with age, Turkeltaub and colleagues[15] note regions that decreased in activation with age, particularly right posterior cortical regions. In this report, decreases in activation with age were also noted, particularly in right superior frontal regions in both nonimpaired and dyslexic readers, but not in posterior regions.

Some of our findings contrast with previous reports. Thus, Schlaggar and coworkers[14] note decreases in activation in left extrastriate regions, and as discussed earlier, we (as well as Schapiro and colleagues[28]) found this area to increase in activation with age. We did not observe the age-related increase in activation of the left parietotemporal region that Turkeltaub and colleagues[15] reported. It is possible that maturation of the parietotemporal region occurred earlier than maturation of the occipitotemporal systems; thus, little change can be observed over the age range of the children participating in this study. However, a recent study[29] using a different functional imaging modality (magnetoencephalography) in children followed longitudinally from kindergarten to second grade also failed to find significant increases in activation of the left parietotemporal region, regardless of the level of eventual reading ability. As in this study, the major changes associated with development of reading ability involved the left occipitotemporal region. These findings suggest that the results of this study possibly can be extended down to 5.5 years of age.

Methodologies in this study differ from previous reports and could explain some of the differences observed. This study focused on phonological processing using a task that required children to try to rhyme two pseudowords and used a block design. Schlaggar and coworkers[14] used single real-word reading in an event-related design, and Turkeltaub and colleagues[15] used implicit real-word reading in an event-related design. In addition, both Schlaggar and coworkers[14] and Turkeltaub and colleagues[15] examined smaller populations that were dichotomous, consisting of a group of children and a group of adults, and included only nonimpaired subjects. In contrast, our study is based on a much larger sample size of school-age children and adolescents, and included both nonimpaired and dyslexic readers with good representation across an age range extending from 7 to 18 years. This allowed dimensional approaches to data analysis (GLM methodology). The age-related effects found here, particularly for dyslexic readers, await the availability of prospective longitudinal data that can specify the developmental course of these brain systems more fully. For now, our findings emerging from a large cross-sectional sample of both nonimpaired and dyslexic readers across a broad age range provide a plausible and useful account of the development of the neural systems for reading and suggest a possible neurobiological explanation of the different mechanisms for reading relied on by each group.

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