Dyslexia (Specific Reading Disability)

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Converging evidence from a number of lines of investigation indicates that dyslexia represents a disorder within the language system and more specifically within a particular subcomponent of that system, phonological processing. Recent advances in imaging technology, particularly the development of functional magnetic resonance imaging, provide evidence of a neurobiological signature for dyslexia, specifically a disruption of two left hemisphere posterior brain systems, one parieto-temporal, the other occipito-temporal, with compensatory engagement of anterior systems around the inferior frontal gyrus and a posterior (right occipito-temporal) system. Furthermore, good evidence indicates a computational role for the left occipito-temporal system: the development of fluent (automatic) reading. The brain systems for reading are malleable and their disruption in dyslexic children may be remediated by provision of an evidence-based, effective reading intervention. In addition, functional magnetic resonance imaging studies of young adults with reading difficulties followed prospectively and longitudinally from age 5 through their mid twenties suggests that there may be two types of reading difficulties, one primarily on a genetic basis, the other, and far more common, reflecting environmental influences. These studies offer the promise for more precise identification and effective management of dyslexia in children, adolescents and adults.

Key Words: Reading, dyslexia, brain imaging, functional magnetic resonance imaging (fMRI)

This paper reviews progress in understanding developmental dyslexia. Our focus is on recent functional magnetic resonance imaging (fMRI) studies of reading and dyslexia, though we briefly review the scientific context that informs these fMRI studies, including definition, history, cognitive mechanisms and outcome.

Definition and History

Developmental dyslexia is characterized by an unexpected difficulty in reading in children and adults who otherwise possess the intelligence and motivation considered necessary for accurate and fluent reading. More formally, "Dyslexia is a specific learning disability that is neurobiological in origin. It is characterized by difficulties with accurate and/or fluent word recognition and by poor spelling and decoding abilities. These difficulties typically result from a deficit in the phonological component of language that is often unexpected in relation to other cognitive abilities and the provision of effective classroom instruction" (Lyon et al 2003).

Historically dyslexia in adults was first noted in the latter half of the nineteenth century and developmental dyslexia in children was first reported in 1896 (Morgan 1896). Our understanding of the neural systems for reading had its roots as early as 1891 when Dejerine (1891) suggested that a portion of the posterior brain region (which includes the angular gyrus and supramarginal gyrus in the inferior parietal lobule, and the posterior aspect of the superior temporal gyrus) is critical for reading. Another posterior brain region, this more ventral in the occipito-temporal area, was also described by Dejerine (1892) as critical in reading.

Epidemiology

Recent epidemiologic data indicate that, like hypertension and obesity, dyslexia fits a dimensional model. In other words, within the population, reading ability and reading disability occur along a continuum, with reading disability representing the lower tail of a normal distribution of reading ability (Gilger et al 1996; Shaywitz et al 1992). Dyslexia is perhaps the most common neurobehavioral disorder affecting children, with prevalence rates ranging from 5 to 17.5 percent (Interagency Committee on Learning Disabilities 1987; Shaywitz 1998). Longitudinal studies, both prospective (Francis et al 1996; Shaywitz et al 1995) and retrospective (Bruck 1992; Felton et al 1990; Scarborough 1990), indicate that dyslexia is a persistent, chronic condition; it does not represent a transient "developmental lag (Figure 1)." Over time, poor readers and good readers tend to maintain their relative positions along the spectrum of reading ability (Shaywitz et al 1995).

Heritability

Dyslexia is both familial and heritable (Pennington and Gilger 1996). Family history is one of the most important risk factors, with 23 percent to as much as 65 percent of children who have a parent with dyslexia reported to have the disorder (Scarborough 1990). A rate among siblings of affected persons of approximately 40 percent and among parents ranging from 27 to 49 percent (Pennington and Gilger 1996) provides opportunities for early identification of affected siblings and often for delayed but helpful identification of affected adults. Replicated linkage studies of dyslexia implicate loci on chromosomes 2, 3, 6, 15 and 18 (Fisher and DeFries 2002). Whether the differences in the genetic loci represent polygenic inheritance, different cognitive paths to the same phenotype or different types of dyslexia is not clear.

Cognitive Influences: Theories of Developmental Dyslexia

A number of theories of dyslexia have been proposed, including: the phonological theory (Liberman et al 1989; Ramus et al 2003); the rapid auditory processing theory (Tallal 1980, 2000; Tallal et al 1993); the visual theory (Livingstone et al 1991; Lovegrove et al 1980); the cerebellar theory (Nicolson and Fawcett 1990; Nicolson et al 2001); and the magnocellular theory (Galaburda et al 1994; Livingstone et al 1991; Stein 2003; Stein and Walsh 1997). The reader is referred to Ramus et al (2003) for a review and critique of the various theories.

Among investigators in the field there is now a strong consensus supporting the phonological theory. This theory recognizes that speech is natural and inherent, while reading is acquired and must be taught. To read, the beginning reader must recognize that the letters and letter strings (the orthography)

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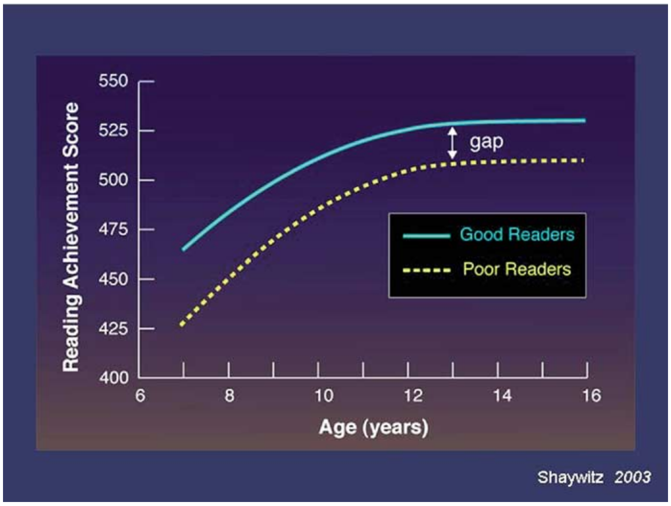

Figure 1. Trajectory of reading skills over time in nonimpaired and dyslexic readers. Ordinate is Rasch scores (W scores) from the Woodcock-Johnson reading test (Woodcock and Johnson 1989) and abscissa is age in years. Both dyslexic and nonimpaired readers improve their reading scores as they get older, but the gap between the dyslexic and nonimpaired readers remains. Thus dyslexia is a deficit and not a developmental lag. Figure derived from data in (Francis et al 1996) and reprinted from (Shaywitz 2003) with permission.

represent the sounds of spoken language. In order to read, a child has to develop the insight that spoken words can be pulled apart into the elemental particles of speech (phonemes) and that the letters in a written word represent these sounds (Shaywitz 2003); such awareness is largely missing in dyslexic children and adults (Bruck 1992; Fletcher et al 1994; Liberman and Shankweiler 1991; Shankweiler et al 1979; Shaywitz 2003; Torgesen 1995; Wagner and Torgesen 1987). Results from large and well-studied populations with reading disability confirm that in young school-age children (Fletcher et al 1994; Stanovich and Siegel 1994) as well as in adolescents (Shaywitz et al 1999) a deficit in phonology represents the most robust and specific correlate of reading disability (Morris et al 1998; Ramus et al 2003). Such findings form the basis for the most successful and evidence-based interventions designed to improve reading; such interventions detailed in the Report of the National Reading Panel include five critical elements: phonemic awareness; phonics; fluency; vocabulary and comprehension (Report 2000).

Implications of the Phonologic Model of Dyslexia

Reading comprises two main processes - decoding and comprehension (Gough and Tunmer 1986). In dyslexia, a deficit at the level of the phonologic module impairs the ability to segment the spoken word into its underlying phonologic elements and then link each letter(s) to its corresponding sound. As a result, the reader experiences difficulty, first in decoding the word and then in identifying it. The phonologic deficit is domain-specific; that is, it is independent of other, nonphonologic, abilities. In particular, the higher order cognitive and linguistic functions involved in comprehension, such as general intelligence and reasoning, vocabulary (Share and Stanovich 1995), and syntax (Shankweiler et al 1995), are generally intact. This pattern - a deficit in phonologic analysis contrasted with intact higher-order cognitive abilities - offers an explanation for the paradox of otherwise intelligent, often gifted, people who experience great difficulty in reading (Shaywitz 1996, 2003).

According to the model, a circumscribed deficit in a lower-order linguistic function (phonology) blocks access to higher-order processes and to the ability to draw meaning from text. The problem is that the affected reader cannot use his or her higher-order linguistic skills to access the meaning until the printed word has first been decoded and identified. Suppose, for example, an individual who knows the precise meaning of the spoken word "apparition;" however, she will not be able to use her knowledge of the meaning of the word until she can decode and identify the printed word on the page and it will appear that she does not to know the word's meaning.

Outcome

Deficits in phonological coding continue to characterize dyslexic readers even in adolescence; performance on phonological processing measures contributes most to discriminating dyslexic and average adolescent readers, and average and superior readers as well (Shaywitz et al 1999). Children with dyslexia neither spontaneously remit nor do they demonstrate a lag mechanism for "catching up" in the development of reading skills. That is not to say that many dyslexic readers do not become quite proficient in reading a finite domain of words that are in their area of special interest, usually words that are important for their careers. For example, an individual who is dyslexic in childhood but who, in adult life becomes interested in molecular biology might then learn to decode words that form a minivocabulary important in molecular biology. Such an individual, while able to decode words in this domain still exhibits evidence of his early reading problems when he has to read unfamiliar words, which he then does accurately but not fluently and automatically (Ben-Dror et al 1991; Bruck 1992, 1994; Lefly and Pennington 1991; Shaywitz et al 1999). In adolescents, the rate of reading as well as facility with spelling may be most useful clinically in differentiating average from poor readers. From a clinical perspective, these data indicate that as children approach adolescence, a manifestation of dyslexia may be a very slow reading rate; in fact, children may learn to read words accurately, but they will not be fluent or automatic, reflecting the lingering effects of a phonologic deficit (Lefly and Pennington 1991). Because they are able to read words accurately (albeit very slowly) dyslexic adolescents and young adults may mistakenly be assumed to have "outgrown" their dyslexia. Data from studies of children with dyslexia who have been followed prospectively support the notion that in adolescents, the rate of reading as well as facility with spelling may be most useful clinically in differentiating average from poor readers in students in secondary school, and college and even graduate school. It is important to remember that these older dyslexic students may be similar to their unimpaired peers on untimed measures of word recognition yet continue to suffer from the phonologic deficit that makes reading less automatic, more effortful, and slow. For these readers with dyslexia the provision of extra time is an essential accommodation; it allows them the time to decode each word and to apply their unimpaired higher-order cognitive and linguistic skills to the surrounding context to get at the meaning of words that they cannot entirely or rapidly decode. With such accommodations, many students with dyslexia are now successfully completing studies in a range of disciplines, including medicine. It is important to appreciate that phonologic difficulties in dyslexia are independent of intelligence, consequently, many highly intelligent boys and girls have reading problems which are often overlooked and even ascribed to "lack of motivation."

In counseling their patients who are dyslexic, physicians should bear in mind that a range of outcomes characterize adults with a childhood history of dyslexia. Indeed, many, including physicians, are often unaware that dyslexic individuals have been successful in a range of professions and disciplines and are represented in our most distinguished authors, poets, educators, attorneys, physicians, and scientists. For example, at least two Nobel laureates, Niels Bohr and Baruj Benacceraf were also dyslexic. While there is accumulating empiric data to guide interventions in children, the kinds of rigorous studies to determine the most effective interventions for adolescents and adults are just underway. Similarly, while the same five elements identified by the National Reading Panel (Report 2000) for children are also important for older individuals, the issue of how to implement such programs at older ages is not fully resolved. What is currently known about reading programs and interventions for adolescents and adults with dyslexia is discussed in Shaywitz (2003).

Neurobiological Studies

To a large degree these advances in understanding the cognitive basis of dyslexia have informed and facilitated studies examining the neurobiological underpinnings of reading and dyslexia. Thus, a range of neurobiologic investigations using postmortem brain specimens (Galaburda et al 1985), and more recently, brain morphometry (Brown et al 2001; Eliez et al 2000; Filipek 1996) and diffusion tensor MRI imaging (Klingberg et al 2000) suggests that there are differences in the temporo-parieto-occipital brain regions between dyslexic and nonimpaired readers.

Functional Brain Imaging

Rather than being limited to examining the brain in an autopsy specimen, or measuring the size of brain regions using static morphometric indices based on CT or MRI, functional imaging offers the possibility of examining brain function during performance of a cognitive task. This review focuses on functional magnetic resonance imaging which measures changes in metabolic activity and blood flow in specific brain regions while subjects are engaged in cognitive tasks. The term functional imaging has also been applied to the technology of magnetic source imaging using magnetoencephalography, an electrophysiologic method with strengths in resolving the chronometric properties of cognitive processes. This technique allows examination of neural function at the time scale of milliseconds in contrast to fMRI which typically allows measurements on the order of seconds. We refer to some MEG studies in discussing results of fMRI studies and the reader is referred to more detailed reviews of MEG by Papinicolaou and his associates (Papanicolaou et al 2003).

Functional Magnetic Resonance Imaging (fMRI)

Functional Magnetic Resonance Imaging (fMRI) promises to supplant other methods for its ability to map the individual brain's response to specific cognitive stimuli. Since it is noninvasive and safe, it can be used repeatedly, properties which make it ideal for studying humans, especially children. The principles of fMRI depend on the principle of autoregulation of cerebral blood flow. When an individual is asked to perform a discrete cognitive task, that task places processing demands on particular neural systems in the brain. To meet those demands requires activation of neural systems in specific brain regions and those changes in neural activity are, in turn, reflected by changes in brain metabolic activity, which in turn, are reflected, for example, by changes in cerebral blood flow and in the cerebral utilization of metabolic substrates such as glucose. The signal used to construct MRI images changes by a small amount (typically of the order 1 - 5 %), in regions that are activated by a stimulus or task. The increase in signal results from the combined effects of increases in the tissue blood flow, volume and oxygenation, though the precise contributions of each of these is still somewhat uncertain. MR image intensity increases when deoxygenated blood is replaced by oxygenated blood. A variety of methods can be used to record the changes that occur but one preferred approach makes use of ultrafast imaging, such as echo planar imaging, in which complete images are acquired in times substantially shorter than a second. Echo planar imaging can provide images at a rate fast enough to capture the time course of the hemodynamic response to neural activation and to permit a wide variety of imaging paradigms over large volumes of the brain. Clearly this is a great simplification of the technology and details of fMRI are reviewed in (Anderson and Gore 1997; Frackowiak et al 2004; Jezzard et al 2001).

Recent Progress Using Functional MRI to Study the Brain Organization for Reading

Functional MRI has proven to be a powerful tool for understanding the brain organization for reading. Studies have examined a number of domains, each of which are detailed below.

Identification and Localization of Specific Systems and Their Differences in Good and Poor Readers

A number of research groups, including ourselves, have used fMRI to examine the functional organization of the brain for reading in nonimpaired (NI) and dyslexic (DYS) readers. We (Shaywitz et al 1998) found significant differences in brain activation patterns between DYS and NI readers, differences which emerged during tasks that made progressive demands on phonologic analysis. Thus, during nonword rhyming in dyslexic readers, we found a disruption in a posterior region involving the superior temporal gyrus and angular gyrus with a concomitant increase in activation in the inferior frontal gyrus anteriorly.

When studying adults with dyslexia there is always the concern that the findings may represent the consequences of a lifetime of poor reading and so it is important to study children in order to examine the neural systems for reading during the acquisition of literacy. We (Shaywitz et al 2002) used functional magnetic resonance imaging (fMRI) to study 144 right handed children (both boys and girls) as they read pseudowords and real words. We found significant differences in brain activation patterns during phonologic analysis in nonimpaired compared to dyslexic children. Specifically, nonimpaired children demonstrate significantly greater activation than do dyslexic children in left hemisphere sites including the inferior frontal, superior temporal, parieto-temporal and middle temporal–middle occipital gyri and right hemisphere sites including an anterior site around the inferior frontal gyrus and two posterior sites, one in the parieto-temporal region, the other in the occipito-temporal region (Figure 2). These data converge with reports from many investigators using functional brain imaging which 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; Rumsey et al 1992; Salmelin et al 1996; Seki et al 2001; Shaywitz et al 2002; Temple et al 2000) as well as during nonreading visual processing tasks (Demb et al 1998; Eden et al 1996) and indicate that dysfunction in left hemisphere

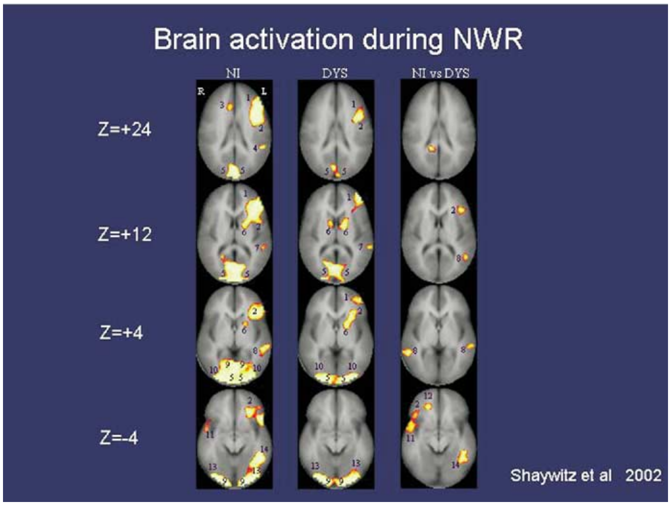

Figure 2. Composite maps (columns 1 and 2) demonstrating brain activation in nonimpaired (NI) and dyslexic (DYS) readers as they determined whether two visually-presented pseudowords rhymed (NWR, nonword rhyme), and composite contrast maps (column 3) comparing directly the brain activation of the two groups. The colored regions in Columns 1 and 2 statistical parametric maps and represent relative activation compared to a baseline task. In columns 1 and 2, red-yellow indicates areas that had significantly greater activation ($p = .05$) in the NWR task compared to the line task, and in column 3, red-yellow indicates brain regions that were more active in NI compared to 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: (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. Figure from Shaywitz et al (2002) with permission.

posterior reading circuits is already present in dyslexic children and cannot be ascribed simply to a lifetime of poor reading.

Compensatory Systems in Dyslexic Readers

The study design also allowed for the examination of compensatory systems which develop in dyslexic readers. Two kinds of information were helpful in examining this issue. One involved the relationship between brain activation and age. During the most difficult and specific phonologic task (nonword rhyming) older compared to younger, dyslexic readers engaged the left and right inferior frontal gyrus, in contrast to nonimpaired readers where few differences emerged between older and younger readers. Another clue to compensatory systems comes from the findings of the relationship between reading skill and brain activation. As noted above, a significant positive correlation exists between reading skill and activation in the left occipito-temporal word form area. We also found a negative correlation between brain activation and reading skill in the right occipito-temporal region, that is, the poorer the reader, the greater the activation in the right occipito-temporal region. Thus compensatory systems seem to involve areas around the inferior frontal gyrus in both hemispheres as well as the right hemisphere analogue of the left occipito-temporal word form area.

Computational Roles of the Component Systems

Accumulating evidence has begun to assign specific computational roles to the components of the reading system. Evidence primarily from studies of acquired alexia describes neuroanatomic lesions most prominently centered about the angular gyrus, a region considered 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). Thus, it is reasonable to suggest that this temporo-parietal reading system may be critical for analyzing the written word, that is, transforming the orthography into the underlying linguistic structures. Perhaps the best evidence for a computational role linked to a specific reading system comes from evidence indicating that a second posterior reading system, located in left occipito-temporal area, is critical for the development of skilled reading and functions as an automatic, instant word recognition system, the visual word form area (Cohen et al 2000, 2002; McCandliss et al 2003). Not only does brain activation in this region increase as reading skill increases (Shaywitz et al 2002) (Figure 3); this region responds preferentially to rapidly presented stimuli (Price et al 1996), responds within 150 msec after presentation of a stimulus (Salmelin et al 1996), and is engaged even when the word has not been consciously perceived (Dehaene et al 2001). The third 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 2004).

Plasticity of Neural Systems for Reading

Given the converging evidence of a disruption of posterior reading systems in dyslexia, an obvious question relates to the plasticity of these neural systems, that is, whether they are malleable and can be changed by an effective reading interven-

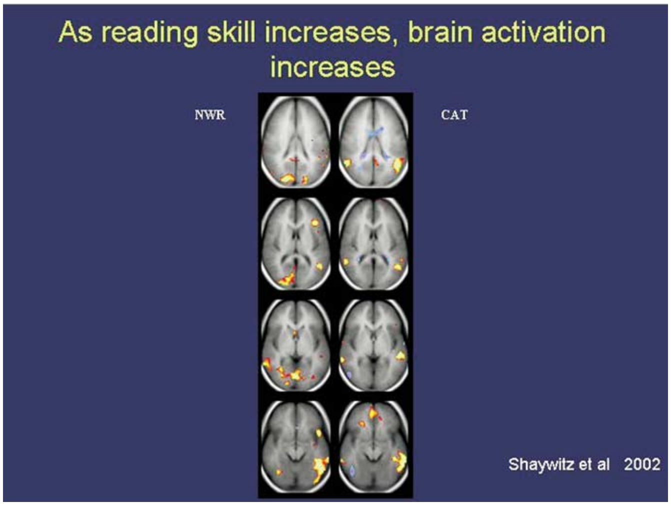

Figure 3. Correlation map between reading skill as measured by the Word Attack reading test (Woodcock and Johnson 1989) performed out of magnet during two activation tasks, judging whether two pseudowords rhymed (NWR) and judging whether two real words were in the same category (CAT). At each voxel, 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). Figure from Shaywitz et al (2002), with permission.

tion. In a recent report (Shaywitz et al 2004) we hypothesized that the provision of an evidence-based, phonologically mediated reading intervention would improve reading fluency and the development of the neural systems serving skilled reading. Second and third graders were recruited for three experimental groups: experimental intervention (EI, $n = 37$); community intervention (CI, $n = 12$) and community controls, i.e., nonimpaired readers (CC, $n = 28$). Children in the community intervention met criteria for reading disability and received a variety of interventions commonly provided within the school; specific, systematic, explicit phonologically-based interventions comparable to the experimental intervention were not used in any of the reading programs that were provided to the community group. The experimental intervention provided second and third grade poor readers with 50 minutes of daily, individual tutoring that was explicit and systematic and focused on helping children understand the alphabetic principle (how letters and combinations of letters represent the small segments of speech known as phonemes). Children were imaged on three occasions, pre-intervention, immediately post-intervention, and one year after the intervention was complete.

Children who received the experimental intervention improved their reading accuracy, reading fluency, and reading comprehension. Compared to CI, both CC, and EI demonstrate increased activation in left hemisphere regions including the inferior frontal gyrus and the posterior aspect of the middle temporal gyrus. CC and EI are very similar. One year after the experimental intervention had ended (Figure 4), compared to their pre-intervention images, EI were activating bilateral inferior frontal gyri, left superior temporal sulcus, the occipital temporal region involving the posterior aspects of the middle and inferior temporal gyri and the anterior aspect of the middle occipital gyrus, the inferior occipital gyrus, and the lingual gyrus.

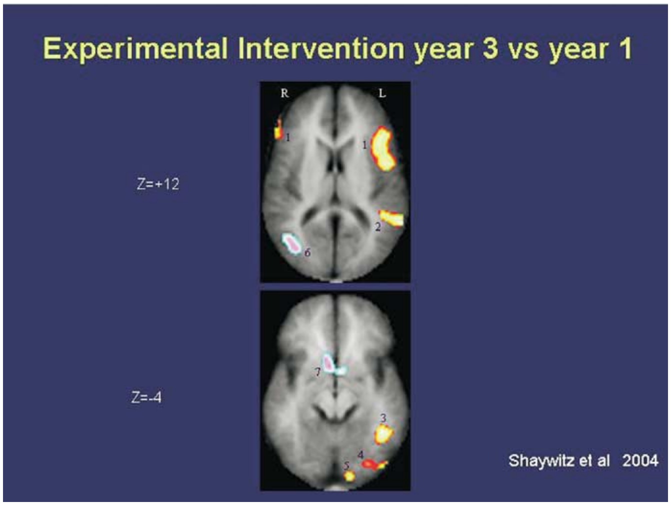

Figure 4. Composite maps indicating the difference in activation between year 3 and year 1 in the experimental intervention (EI) study group ($n = 25$). Red-yellow indicates brain regions that were more active ($p = .05$) in the third year; blue-purple indicates brain regions that were more active ($p = .05$) in the first year. The slice locations are 12, and −4 in Talairach space. Brain regions (Talairach x,y,z, coordinates in parenthesis) more active in the third year compared to the first were (1) bilateral inferior frontal gyri (± 41, 23, 12), (2) the left superior temporal sulcus (51, −42, 12), (3) the occipital temporal region involving the posterior aspects of the middle and inferior temporal gyri and the anterior aspect of the middle occipital gyrus (42, −49, −4), (4) the inferior occipital gyrus (34, −71, −4), and (5) the lingual gyrus (13, −88, −4). The brain regions more active in the first year compared with the third year were (6) the right middle temporal gyrus (−35, −69, 12) and (7) the caudate nucleus (−7, 10, −4). Figure from Shaywitz et al (2004), with permission.

These findings suggest that the nature of the remedial educational intervention is critical to successful outcomes in children with reading disabilities and that the use of an evidence-based phonological reading intervention facilitates the development of those neural systems that underlie skilled reading. Our findings indicate that a phonologically based reading intervention leads to the development of neural systems both in anterior (inferior frontal gyrus) and posterior (middle temporal gyrus) brain regions.

Previous studies (Aylward et al 2003; Richards et al 2000; Simos et al 2002; Temple et al 2000, 2003) on the effects of a reading intervention on neural systems in reading disability were informative but limited to smaller studies in adults and magnetoencepalography and magnetic resonance spectroscopy in children and an fMRI study in solely reading disabled children without a nonexperimental comparison group. This is the first imaging study of a reading intervention in either children or adults that reports its effects on reading fluency, a critical but often neglected reading skill (Report 2000). It is also the largest imaging study of a reading intervention and the first report of the effects of a reading intervention on fMRI in children that examined not only reading disabled children who received an experimental reading intervention but also examined reading disabled children who did not receive such an intervention. Thus the provision of an evidence-based reading intervention at an early age improves reading fluency and facilitates the development of those neural systems which underlie skilled reading.

Types of Reading Disability

Functional magnetic resonance imaging has also been helpful in beginning to distinguish types of reading disability. We (Shaywitz et al 2003) took advantage of the availability of a cohort who are participants in the Connecticut Longitudinal Study, a representative sample of now young adults who have been prospectively followed since 1983 when they were age 5 years and who have had their reading performance assessed yearly throughout their primary and secondary schooling (Shaywitz et al 1990, 1992, 1999). Three groups of young adults, ages 18.5 –22.5 years, were classified as: 1) persistently poor readers (PPR, $n = 24$) if they met criteria for poor reading in 2nd or 4th grade and again in grade 9 or 10; 2) accuracy improved (compensated) readers (AIR, $n = 19$) if the subject satisfied criteria for poor reading in 2nd or 4th grade and not in grade 9 or 10; 3) nonimpaired readers (NI, $n = 27$) were selected on the basis of not meeting the criteria for poor reading in any of the grades 2-10. Findings during pseudoword rhyming in both groups of poor readers (AIR, PPR) were similar to those observed in previous studies, that is, a relative underactivation in posterior neural systems located in the superior temporal and the occipitotemporal regions. But when reading real words, brain activation patterns in the AIR and PPR readers diverged. As they had for rhyming pseudowords, compared to NI, AIR demonstrated relative underactivation in left posterior regions (Figure 5, column 2). In contrast, during real word reading PPR subjects activated posterior systems (Figure 5, column 3); thus, there were no differences between NI and PPR in the posterior reading systems, findings that were both new and unexpected. Despite the significantly better reading performance in NI compared to PPR on every reading task administered, left posterior reading systems were activated during reading real words in both NI and PPR. Two lines of evidence indicate that the PPR readers were

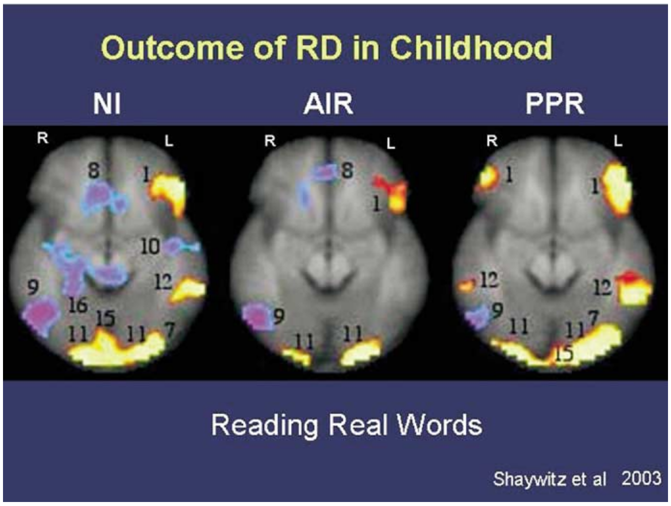

Figure 5. Composite maps demonstrating brain activation in nonimpaired (NI), accuracy improved (AIR), and persistently poor (PPR) readers during the nonword rhyme (NWR) reading task. Red-yellow indicates areas that had significantly greater activation ($p = .05$) in the reading task compared to the line task. Blue-purple indicates areas that had significantly greater activation ($p = .05$) in the line task compared to the reading task. The slice locations correspond to a z levels of –4 in the Talairach and Tournoux atlas (Talairach and Tournoux 1988). Following standard MRI nomenclature, the right side of the axial slice corresponds to the left hemisphere. The legend for regional brain activation is as follows: (1) inferior frontal gyrus, (2) precentral gyrus, (3) insula, (4) superior temporal gyrus and superior temporal sulcus, (5) middle temporal gyrus and superior temporal sulcus, (6) cuneus, (7) middle occipital gyrus, (8) anterior cingulate sulcus and adjacent aspects of the cingulate gyrus and superior frontal gyrus, (9) posterior middle temporal gyrus and anterior middle occipital gyrus, (10) anterior aspect of the superior temporal gyrus, (11) inferior occipital gyrus, (12) middle temporal gyrus, (13) superior frontal gyrus, (14) posterior cingulate gyrus, (15) lingual gyrus, (16) medial occipital temporal gyrus (parahippocampal region), and (17) basal ganglia. Figure modified from Figure 1 in Shaywitz et al (2003), with permission.

reading real words very differently from NI readers, reading the very simple real words primarily by memory. One piece of evidence was that PPR readers were accurate while reading high frequency words, but far less accurate when reading low frequency and unfamiliar words. A second bit of evidence emerged from functional connectivity analysis (McIntosh et al 1996, 1997) which indicated that NI readers demonstrated connectivity between left hemisphere posterior and anterior reading systems (Figure 6, column 1). In contrast, PPR subjects (Figure 6, column 2) demonstrated functional connectivity between left posterior reading systems and right prefrontal areas often associated with working memory and memory retrieval (Fletcher et al 1997; MacLeod et al 1998).

Insight into some of the factors responsible for compensation on the one hand and persistence on the other comes from an examination of early childhood measures. The two groups of disabled readers (AIR and PPR) began school with comparable reading skills and sharing similar family socioeconomic status but with PPR exhibiting poorer cognitive ability and tending to attend more disadvantaged schools. These findings suggest that despite similar socioeconomic risk factors for reading disability early in life, the presence of compensatory factors such as stronger cognitive ability and perhaps, better schools, allowed the AIR to minimize, in part, the consequences of their phonologic deficit so that as adults AIR were indistinguishable from NI on a measure of reading comprehension and a measure of prose literacy. These findings are consonant with a large body of evidence indicating that the impact of dyslexia can be modified by the availability of compensatory resources, for example, semantic knowledge (Snowling et al 2000), use of context (Frith and Snowling 1983; Nation and Snowling 1998), and verbal ability (Torgesen et al 2001) to compensate for phonologic deficits. In adults, verbal abilities, as measured by verbal IQ, directly predict reading accuracy, with phonologic factors influencing reading indirectly through their effects on verbal IQ (Berninger et al 2001). The current study extends such findings by demonstrating that childhood cognitive ability may be an important influence on the development of reading skills in later childhood and into adult life. Beginning reading is most related to phonologic skills and within a few years other language skills, for example semantic knowledge, gain in importance. The current findings suggest that greater cognitive abilities may provide some degree of compensation for a reading difficulty; intuitively this makes sense since a larger vocabulary and better reasoning skills are helpful when a struggling reader is trying to decipher unknown words. If the word is in his spoken language vocabulary the beginning reader may recognize the word even if he can only partially sound it out. Strong reasoning abilities also help this reader to use the context around an unknown word to figure out its meaning. The imaging findings noted earlier which demonstrate a greater number of ancillary systems in AIR compared to PPR may represent the neural correlates of this compensation.

Finally, for the first time, results from functional brain imaging studies distinguish two potential types of reading disability. These are consistent with Olson's suggestion of two possible etiologies for childhood reading disability: a primarily genetic type with IQ scores over 100 and a more environmentally influenced type with IQs below 100 (Olson 1999; Olson et al

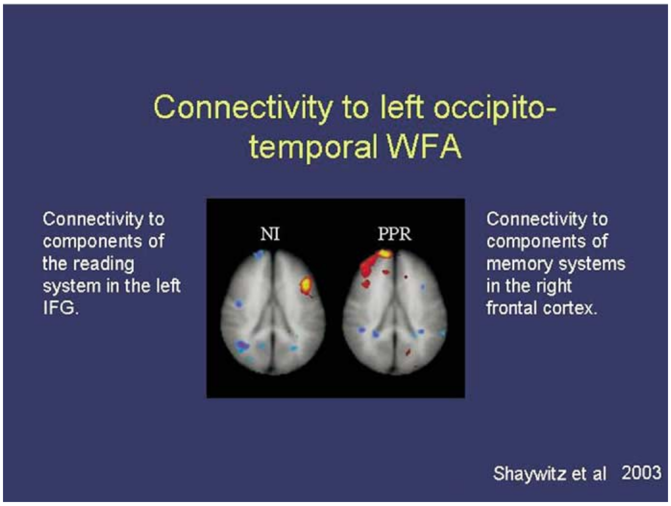

Figure 6. Group connectivity profiles between the "seed voxel" in the left occipito-temporal region (Talairach coordinates −55, −36, −5) and other brain regions during the CAT (real word) reading task. Red-yellow indicates significant positive correlations ($p < .02$); blue-purple indicates negative correlation. The images correspond to $z = +24$ in Talairach space. In the nonimpaired readers (on left), a strong positive correlation is observed between the left occipito-temporal region and the left inferior frontal gyrus (Broca's area), a traditional language region. In contrast, for persistently poor readers, the occipito-temporal region is correlated with regions in the right superior, middle and inferior frontal gyri, brain regions believed to play a role in attention and memory. Figure from Shaywitz et al (2003), with permission.

1999; Wadsworth et al 2000). Though clearly both genetic and environmental factors play a role in reading in all children, it is intriguing to speculate that the AIR subjects may represent a predominantly genetic type while the PPR group, with significantly lower IQ and a trend to attend more disadvantaged schools may represent a more environmentally influenced type of dyslexic reader. Another possibility is that both types, AIR and PPR, have a genetic predisposition, but in the case of AIR the genetic predisposition is modified somewhat by positive environmental influences and higher cognitive abilities. These findings have important educational implications and are of special relevance for teaching children to read. Consistent with our knowledge of the components of reading, children need to be able to sound out words in order to decode them accurately and then, they need to know the meaning of the word – to help decode and comprehend the printed message. Both the sounds and the meanings of words must be taught. These findings suggest that it may be beneficial to provide early interventions aimed at stimulating both phonologic and verbal abilities in children at-risk for reading difficulties associated with disadvantage.

Conclusions and Implications

Within the last two decades overwhelming evidence from many laboratories has converged to indicate the cognitive basis for dyslexia: dyslexia represents a disorder within the language system and more specifically within a particular subcomponent of that system, phonological processing. Recent advances in imaging technology and the development of tasks which sharply isolate the subcomponent processes of reading now provide for the first time, a neurobiological signature for dyslexia: a disruption of left hemisphere posterior brain systems in dyslexic readers while performing reading tasks. Furthermore, good evidence suggests a neurobiological target for skilled reading: the left occipito-temporal word form area. The discovery of neural systems serving reading has significant implications. At the most fundamental level, it is now possible to investigate specific hypotheses regarding the neural substrate of dyslexia, and to verify, reject or modify suggested cognitive models. From a more clinical perspective, the identification of neural systems for reading offers the promise for more precise identification and diagnosis of dyslexia in children, adolescents and adults.

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 2004) 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 occipito-temporal 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. These data now suggest an explanation for these observed clinical findings. In dyslexic readers disruption of parieto-temporal and, in particular, occipito-temporal left hemisphere posterior reading systems underlies the failure of skilled reading to develop, while a shift to ancillary systems in left and right anterior regions and right posterior regions supports accurate, but not automatic word reading.

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