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The Neurobiological Basis of Skilled and Impaired Reading: Recent Findings and New Directions

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In recent years, significant progress has been made in the study of reading and reading disability with the use of functional neuroimaging techniques. There is substantial converging evidence that skilled word recognition requires the development of a highly integrated cortical system that includes left hemisphere dorsal, ventral, and anterior subsystems. This article highlights key findings regarding the functional role of these regions during skilled reading, the developmental trajectory toward this mature reading circuitry in normally developing children, deviations from this trajectory in populations with reading disabilities, and the ways in which successful reading remediation alters the brain organization for reading. We present one possible interpretation of these findings and report some recent findings from our lab that continue to refine our understanding of the functional properties of each component region and the ways in which these areas interact. The article concludes with a discussion of important areas of inquiry to be addressed in future work.

For neuroimaging data to add to researchers' understanding of reading development, links must be established between cognitive processes and the neural systems that support them. Therefore, neuroimaging research must be informed by cognitive theory and research from the outset. Behavioral studies have characterized some of the critical cognitive processes necessary to acquire fluent reading and the ways in which these processes are deficient in individuals with reading disabilities. To learn to read, a child must develop an appreciation of the segmental nature of speech and come to realize that spoken words are composed of the small-

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est of these segments, the phonemes (i.e., develop *phonemic awareness*). The beginning reader must also understand that written words possess an internal phonological structure that is the same as that of spoken words. It is phonemic awareness and the understanding that the constituents of a printed word (its letters) bear a relationship to phonemes that allow a reader to connect printed words to the corresponding words in his or her speech lexicon. Fluent adult readers access a word's entry in the mental lexicon very rapidly (on the order of 200 msec), and as much recent work indicates, efficient orthographic-to-phonological assembly plays a critical role in this skill (e.g., Lukatela & Turvey 1994; Perfetti & Bell, 1991).

Reading is a complex skill, and there are many reasons why some children fail to learn to read. For example, it has been argued that the reading difficulties experienced by some children may result from difficulties with processing speed (Wolf & Bowers, 1999), rapid auditory processing (Tallal, 1980), general language deficits (Scarborough & Dobrich, 1990), or visual deficits (Cornelissen & Hansen, 1998), among other things. However, there is growing consensus that one of the primary causes of reading failure is the difficulty that some children have in mastering phonemic awareness skills (e.g., Fletcher et al., 1994; Shankweiler et al., 1995; Stanovich & Siegel, 1994). Research has indicated that early phonemic awareness is one of the best predictors of subsequent reading success and that it is causally related to reading skill; instruction in phonemic awareness promotes the acquisition of reading skills (Ball & Blachman, 1991; Foorman, Francis, Fletcher, Schatschneider, & Mehta, 1998; Torgesen, Morgan, & Davis, 1992). Phonological-processing deficits persist into adulthood (Bruck, 1992), and in many cases, poor readers struggling with word identification also manifest difficulties in comprehending written sentences; this is thought to reflect a sort of bottleneck in processing resulting from slow, labored, and error-prone word identification processes (Perfetti, 1985).

Recently, neuroimaging techniques have been used to study reading development, reading disability, and intervention (for reviews, see Eden & Zeffiro, 1998; Pugh, Mencl, Jenner, et al., 2000; Sarkari et al., 2002). There is substantial converging evidence that skilled word recognition requires the development of a highly organized cortical system that integrates processing of orthographic, phonological, and lexico–semantic features of words. Broadly, this system includes two posterior subsystems in the left hemisphere (LH): a ventral (occipitotemporal) and a dorsal (temporoparietal) system and a third area, anterior to the other two (the inferior frontal gyrus). In the following sections, we briefly review some key findings regarding the functional role of these regions during reading and deviations in cohorts with reading disabilities, and we outline our interpretation of these findings, integrating them with a current working model of the functional neuroanatomy of reading (Pugh, Mencl, Jenner, et al., 2000). This interpretation is but one possible model, and as becomes evident in this article, continues to evolve and be refined as new data are obtained.

THE CORTICAL READING SYSTEMS AND THEIR ROLES IN SKILLED READING

The ventral system includes an LH inferior occipitotemporal/fusiform area and extends anteriorly into the middle and inferior temporal gyri (MTG and ITG, respectively). It has been suggested that the occipitotemporal/fusiform region functions as a presemantic visual word form area (VWFA) by some researchers (cf. Cohen et al., 2002, but see Price, Winterburn, Giraud, Moore, & Noppeney, 2003, for an alternative account); of importance, the functional specificity of this region appears to be late developing and critically related to the acquisition of reading skill (Booth et al., 2001; S. E. Shaywitz et al., 2002). Because of its critical role in skilled reading, we refer to this region more neutrally as the occipitotemporal (OT) "skill zone." More anterior foci within the ventral system extending into the middle to inferior temporal gyri (MTG and ITG) appear to be semantically tuned. The ventral system, particularly more posterior aspects, is also fast acting in response to linguistic stimuli in skilled readers but not in individuals with reading disabilities (Salmelin, Service, Kiesila, Uutela, & Salonen, 1996). It should be noted that there is some disagreement in the literature about the precise localization of critical subregions composing the ventral system (Pammer et al., 2003; Price et al., 2003). Nevertheless, recent studies examining both timing and stimulus-type effects suggest that moving anteriorly through this system, subregions respond to word and wordlike stimuli in a progressively abstracted and linguistic manner (Pammer et al., 2003; Tarkiainen, Cornelissen, & Salmelin, 2003). Very early in processing, the most posterior aspects of this system (i.e., extrastriate components) respond indiscriminately to any type of letter string (Tarkiainen et al., 2003); subsequently, the putative VWFA shows a heightened response to pseudowords relative to words (in addition, both words and pseudowords show heightened activation relative to nonpronounceable consonant strings in this region; Cohen et al., 2002; S. E. Shaywitz et al., 2002; S. E. Shaywitz et al., 1998); and, at later stages of processing, the more anterior aspects of the ventral system (MTG–ITG) show a heightened response to real words relative to other types of letter strings (Fiebach, Friederici, Mueller, & von Cramon, 2002; Simos, Breier, et al., 2002; Tagamets, Novick, Chalmers, & Friedman, 2000; see Salmelin & Helenius, 2004/this issue, for a more thorough review of these findings).

The more dorsal temporoparietal system broadly includes the angular gyrus and supramarginal gyrus (SMG) in the inferior parietal lobule, as well as the posterior aspect of the superior temporal gyrus (Wernicke's area) Among their other functions (e.g., attentionally controlled processing), the areas within this system seem to be involved in mapping visual percepts of print onto the phonological and semantic structures of language (Black & Behrmann, 1994). In skilled readers, certain regions within the LH temporoparietal system (particularly the SMG) respond with greater activity to pseudowords than to familiar words (Price, Wise, &

Frackowiak, 1996; Simos, Breier, et al., 2002; Xu et al., 2001). This finding suggests that the temporoparietal system plays a role in the types of phonological analyses that are relevant to learning new material.

An anterior system centered in posterior aspects of the inferior frontal gyrus (IFG) appears to be associated with phonological recoding during reading, among other functions (e.g., phonological memory, syntactic processing); the more anterior aspects of IFG seem to play a role in semantic retrieval (Poldrack et al., 1999). The phonologically relevant components of this multifunctional system have been found to function in silent reading and in naming (see Fiez & Petersen, 1998, for review; Pugh et al., 1997) and, like the temporoparietal system, are more strongly engaged by low-frequency words and pseudowords than by high-frequency words (Fiebach et al., 2002; Fiez & Peterson, 1998). We have speculated that this anterior system operates in close conjunction with the temporoparietal system to decode new words during normal reading development (Pugh, Mencl, Jenner, et al., 2000).

Of these three systems, the dorsal and anterior systems predominate during initial reading acquisition in normally developing children with an increased ventral response as proficiency in word recognition increases. We observed (S. E. Shaywitz, Shaywitz, Pugh, et al., 2002) that normally developing children younger than 10½ years of age show strong engagement of dorsal and anterior systems but limited engagement of the ventral system during reading tasks. In contrast, children older than 10½ years of age tend to show increased engagement of the ventral system, which in turn is associated with increasingly skilled reading (greater activation in these regions was strongly correlated with higher reading scores). On the basis of these developmental findings, we speculate that a beginning reader on a successful trajectory uses a widely distributed cortical system for print processing including temporoparietal, frontal, and right hemisphere (RH) posterior areas. As reading skill increases, these regions play a diminished role, whereas LH ventral sites become more active and, presumably, more central to the recognition of printed (word) stimuli (for similar findings, see Booth et al., 2001; Turkeltaub et al., 2003).

ALTERED CIRCUITS IN READING DISABILITY

There are clear functional differences between readers who do not have an impairment (NI readers) and those with reading disabilities (RD) with regard to activation patterns in dorsal, ventral, and anterior sites during reading tasks. In readers with disabilities, a number of functional imaging studies have revealed LH posterior functional dysfunction at both dorsal and ventral sites during phonological-processing tasks (Brunswick, McCrory, Price, Frith, & Frith, 1999; Paulesu, et al., 2001; Pugh, Mencl, Jenner, et al., 2000; Salmelin et al., 1996; S. E. Shaywitz et al., 1998; Temple et al., 2001). This disruption is instantiated as a relative underengagement of these regions specifically when processing linguistic stimuli (words and pseudowords) or during tasks that require decoding. This functional anomaly in posterior LH regions has been observed consistently in children (S. E. Shaywitz et al., 2002) and adults (Salmelin et al., 1996; S. E. Shaywitz et al., 1998). Hypoactivation in three key dorsal and ventral sites, including cortex within the temporoparietal region, the angular gyrus, and the ventral OT skill zone, is detectable as early as the end of kindergarten in children who have not reached important milestones in learning to read (Sarkari et al., 2002). Indeed, the ventral disruption has been seen as a critical signature of RD across several languages (Paulesu et al., 2001; Salmelin et al., 1996).

Of particular importance is the finding that in both children and adults this posterior functional anomaly was largely confined to those tasks that tapped word and pseudoword processing only; these group differences were seen in both activation patterns within (S. E. Shaywitz et al., 1998) and interactions among these regions (Horwitz, Rumsey, & Donohue, 1998; Pugh, Mencl, Shaywitz, et al., 2000; further discussion of *functional connectivity* is presented later in this article). This strongly implies that LH posterior systems, although poorly developed (functionally), are not fundamentally disrupted in readers with RD. This suggests that there may be no underlying developmental "lesion" in readers with RD that precludes alteration of these circuits if the appropriate retraining procedures can be found.

Examinations of the interactions among brain regions in younger populations also implicate the LH inferior occipitotemporal region as critical in skilled reading. The most common method of operationalizing and quantifying these interactions is in terms of correlations among brain areas, termed *functional connectivity* (Friston, 1994; McIntosh, Bookstein, Haxby, & Grady, 1996). These correlations can be obtained within a single participant, identifying areas with activation patterns that correlate over time (Hampson, Peterson, Skudlarski, Gatenby, & Gore, 2002). Here, we describe analyses of correlations obtained across a group of participants, identifying areas that tend to coactivate from participant to participant (Horwitz et al., 1998). Of importance, a region that does not show a simple activation difference between two tasks may still display meaningful differences in functional connectivity (Grady, McIntosh, Beig, & Craik, 2001). This approach may thus uncover system-level differences unseen by traditional univariate analyses. S. E. Shaywitz et al. (2003) examined functional magnetic resonance imaging (fMRI) data from 27 good readers, 19 readers who demonstrated partial compensation after an early diagnosis of developmental dyslexia, and 24 persistently poor readers, from 18 to 22 years of age. Our initial analysis of the OT skill zone showed that good readers activated this region while reading either real words or pseudowords, whereas those with partially compensated dyslexia did not. Surprisingly, the persistently poor reader group did show activation here in response to real words but not to pseudowords, suggesting the use of a more memory-based reading strategy. We then used functional connectivity analysis to assess whether this region is part of a different functional network for good versus poor readers. Results indicated that good readers showed strong connectivity between the occipitotemporal area and Broca's area, suggesting that orthographic processing had become integrated with phonological processing in this group. For persistently poor readers, however, we observed strong connectivity not to Broca's area but instead to areas within the right prefrontal cortex that are typically associated with long-term memory recall (Fletcher et al., 1997).

Connectivity analysis in another sample of 144 good and poor readers, from 7 to 18 years of age, further corroborated these findings (Mencl et al., 2003; S. E. Shaywitz et al., 2002). In this data set, we initially discovered that only the older (ages 12–18) good readers displayed significant connectivity between the OT skill zone and Broca's area; younger good readers (ages 7–11) and those with dyslexia did not. A multivariate analysis was then used to identify shifts in functional connectivity patterns as a function of age and reading ability. Good readers showed an age-related difference that included (a) increased connectivity between the occipitotemporal area and Broca's area, implying integration of orthographic and phonological processing, and (b) decreased connectivity between the occipitotemporal area and the anterior cingulate gyrus, suggesting more automatic processing. Readers with dyslexia showed a distinctly different developmental trend, including (a) increased connectivity between the LH occipitotemporal area and a set of RH areas, consistent with the notion of compensatory processing strategies (see discussion later in this article), and (b) increased connectivity between the anterior cingulate gyrus and IFG bilaterally, again suggesting a more effortful and attentionally guided reading strategy.

POTENTIALLY COMPENSATORY PROCESSING IN READING DISABILITY

Behaviorally, poor readers compensate for their inadequate phonological awareness and knowledge of letter–sound correspondences by overrelying on contextual cues to read individual words; their word reading errors tend to be visual or semantic rather than phonetic (see Perfetti, 1985, for a review). These behavioral markers of reading impairment may be instantiated cortically by compensatory activation of frontal and RH regions. In our studies (S. E. Shaywitz et al., 1998, 2002), we observed processing in readers with RD that we interpret as compensatory. We found that on tasks that made explicit demands on phonological processing (pseudoword- and word-reading tasks), readers with RD showed a disproportionately greater engagement of IFG and prefrontal dorsolateral sites than did NI readers (for similar findings, see also Brunswick et al., 1999; Salmelin et al., 1996). Evidence of a second, potentially compensatory, shift—in this case, to posterior RH regions—comes from several findings. Using magnetoencephalography (MEG), Sarkari et al. (2002) found an increase in the apparent engagement of the RH temporoparietal region in children with reading disabilities. More detailed examination of this trend, using hemodynamic measures, indicates that hemispheric asymmetries in activity in posterior temporal and temporoparietal regions (the middle temporal and the angular gyri) vary significantly among reading groups (S. E. Shaywitz et al., 1998): There was greater RH than LH activation in readers with reading disabilities but greater LH than RH activation in readers without impairment. Rumsey et al. (1999) examined the relationship between RH activation and reading performance in their adult participants with RD and NI participants and found that RH temporoparietal activation was correlated with standard measures of reading performance only for readers with RD (see also S. E. Shaywitz et al., 2002).

We hypothesize that the reason readers with RD tend to strongly engage inferior frontal sites is their increased reliance on covert pronunciation (articulatory recoding) in an attempt to cope with their deficient phonological analysis of the printed word. In addition, their heightened activation of the posterior RH regions with reduced LH posterior activation suggests a process of word recognition that relies on letter-by-letter processing in accessing RH-localized visuo–semantic representations (or some other compensatory process) rather than relying on phonologically structured word recognition strategies. These differential patterns, especially the increased activation in frontal regions, might also reflect increased effort during reading; underengagement of LH posterior areas, particularly ventral sites, would not be thought to reflect this increased effort, but rather the failure to engage these areas likely precipitates any change in effort.

NEUROBIOLOGICAL EFFECTS OF SUCCESSFUL READING REMEDIATION

Converging evidence from other studies supports the notion that gains in reading skill resulting from intense reading intervention are associated with a more "normalized" localization of reading processes in the brain. In a recent MEG study, 8 young children with severe reading difficulties underwent a brief but intensive phonics-based remediation program (Simos, Fletcher, et al., 2002). After intervention, the most salient change observed on a case-by-case basis was a robust increase in the apparent engagement of the LH temporoparietal region, accompanied by a moderate reduction in the activation of the RH temporoparietal areas. Similarly, Temple et al. (2003) used fMRI to examine the effects of an intervention (FastForWord®) on the cortical circuitry of a group of 8- to 12-year-old children with reading difficulties. After intervention, increased LH temporoparietal and inferior frontal increases were observed. Moreover, the LH increases correlated significantly with increased reading scores. In sum, the neurobiological signature of successful intervention in younger children appears to be increased engagement of major LH reading-related circuits (see B. Shaywitz et al., in press, for similar results).

A PRELIMINARY MODEL OF THE NEUROBIOLOGY OF WORD RECOGNITION

We proposed a theory of word recognition based on the neurobiological data in which lexical selection is determined largely by the ventral system when the stimulus is familiar and task demands are appropriate, and largely by the dorsal system, in close conjunction with the inferior frontal gyrus, when the stimulus is novel or low frequency (Pugh, Mencl, Jenner, et al., 2000). In this early conceptualization the two systems were thought to correspond (but only loosely) to the two routes of classical dual-route theory (Coltheart, Curtis, Atkins, & Haller, 1993). Although neuroimaging evidence might be taken to support the existence of multiple "routes," there are, as yet, no compelling data to suggest that the faster ventral route involves direct activation of meaning as proposed by standard versions of dual-route theory. The phonological representation of the word might still be involved either in mediating the activation between orthography and lexical meaning or, alternatively, as an obligatory consequence after the direct activation of meaning by orthography (R. Frost, 1998).

Our initial neurobiological theory proposed that processing in the dorsal system proceeds relatively slowly, producing phonological representations generated by subword analysis (i.e., a result of grapheme–phoneme analysis, onset–body analysis, or other subword phonological analysis). The dorsal system appears to act in concert with the IFG in integrating orthographic and phonological features of words. Direct evidence supporting a critical role of the dorsal system in subword phonological analysis comes from electrocortical stimulation studies. For example, Simos et al. (2000) found that electrical interference within a small portion of the posterior superior temporal gyrus consistently impaired patients' ability to decode pseudowords. Whereas this ability relies primarily on the slower (dorsal) system, the ability to read real words with exceptional spellings, which could be accomplished by the faster (ventral) system, remained unaffected. There is additional, albeit indirect, evidence that the IFG and at least one other component of the dorsal system (the SMG) support subword phonological analysis. Activity in both regions is stronger for (a) pseudowords compared with real words (Xu et al., 2001), (b) tasks that require phonological analysis such as rhyme judgment (Pugh et al., 1996), and (c) tasks that involve phonological priming (Mencl et al., 2004). Moreover, during reading tasks, beginning and early readers show dorsal and anterior activity but do not show substantial ventral activity, unlike more skilled readers (Booth et al., 2001; S. E. Shaywitz et al., 2002; Turkeltaub et al., 2003). When present, activity in ventral occipitotemporal regions, which shows strong LH lateralization in adults, appears to be bilaterally symmetrical in children, a finding consistent with the notion of a progressive specialization of the ventral system in the LH with reading experience (Simos et al., 2001). In response to a printed word, the ventral system responds more rapidly than the dorsal, suggesting that it is a faster acting system (Breier, Simos, Zouridakis, & Papanicolaou, 1999; Salmelin et al., 1996; Simos et al., 2001). As noted earlier, greater activation to real words than to pseudowords within the ventral system, particularly at middle and inferior temporal sites, has also been reported in several studies (Fiebach et al., 2002; Tagamets et al., 2000). And, as noted earlier, reading-related activation in ventral regions increases with age and reading skill (S. E. Shaywitz et al., 2002). A detailed discussion of the data supporting a functional distinction between the dorsal and ventral circuits can be found in Pugh, Mencl, Jenner, et al. (2000).

FURTHER PARTITIONING THE THREE MAJOR SYSTEMS

This initial, speculative taxonomy of three broad LH systems (dorsal, ventral, and anterior) and their computational processing roles is obviously very coarse-grained and underspecified. Indeed, each of these component systems consists of distinct subregions that most likely engage in different types of processing. To refine our basic theoretical framework, we recently conducted a series of experiments aimed at obtaining a more detailed understanding of the information-processing characteristics of the major LH reading-related regions. One line of studies involved a series of manipulations of theoretically relevant psycholinguistic variables aimed at refining our understanding of the functional properties of the subregions and how they operate in relation to one another. A second line of experiments was aimed at obtaining a better understanding of the neurobiological foundations of adaptive learning in the context of reading. We feel that this set of studies provides important constraints on our understanding of the functional neuroanatomy of reading; however, we must note that some of these studies are currently under review; therefore, appropriate conservatism should be used when interpreting them.

Phonological Priming

We recently completed an fMRI study of phonological and orthographic priming effects in printed word recognition (Mencl et al., 2004). Participants performed a primed lexical decision task. Primes were either (a) both orthographically and phonologically similar to the targets (*bribe–TRIBE*), (b) orthographically similar but phonologically dissimilar (*couch–TOUCH*), or (c) unrelated (*lunch–SCREEN*). Results indicate that Condition (b) evoked more activation than Condition (a) in several LH cortical areas hypothesized to underlie phonological processing: This modulation was seen in IFG, Wernicke's area, and the SMG. Notably, this phonological priming effect was also obtained within the early-activating LH OT skill zone, consistent with the claim that phonological coding influences lexical access at its earliest stages (but see the Development of Multimodal Imaging Technologies section later in this article).

Trade-Offs Between Phonology and Semantics

In many previous studies researchers have attempted to identify the neural substrates of orthographic, phonological, and semantic processes in cohorts of readers without impairment (Fiebach et al., 2002) and readers with RD (Rumsey et al., 1997). Readers with RD have acute problems in mapping from orthography to phonology and appear to rely on semantic information to supplement deficient decoding skills (Plaut & Booth, 2000). NI readers, too, appear to show a trade-off between these component processes. Strain, Patterson, and Seidenberg (1996) provided behavioral confirmation of this, demonstrating that the standard consistency effect on low-frequency words (longer naming latencies for words with inconsistent spelling-to-sound mappings such as *PINT* relative to words with consistent mappings such as *MILL*) is attenuated for words that are highly imageable–concrete. Of importance, this interaction reveals that semantics can facilitate the processes associated with orthographic-to-phonological mapping in word recognition. Using fMRI, we sought to identify the neurobiological correlates of this phenomenon (S. J. Frost et al., 2003). A go/no-go naming paradigm was used in a block-design fMRI protocol. Word stimuli represented the crossing of frequency, imageability, and spelling-to-sound consistency. Higher activation for high-imageable words was found in middle temporal and posterior parietal sites. In contrast, higher activation for inconsistent relative to consistent words was found in the inferior frontal gyrus (a critical area for articulatory recoding), replicating findings by Fiez, Balota, Raichle, and Petersen (1999) and Herbster, Mintun, Nebes, and Becker (1997). Critically, analyses revealed that imageability was associated with reduced consistency-related activation in IFG but increased posterior parietal activation; this appears to be the principal neural signature of the behavioral trade-off between semantics and phonology revealed by Strain and colleagues. This finding serves as an important step in the linking of neurobiological and computational models of reading.

Adaptive Learning

Previous studies have demonstrated that both increased familiarity with specific words and increased reading skill are associated with a shift in the relative activation of the cortical systems involved in reading, from predominantly dorsal to predominantly ventral. In another line of research, we are carrying out functional neuroimaging experiments to provide a more precise characterization of the means by which practice with unfamiliar words results in this shift and to gain insights into how these systems learn to read new words. In one study from our lab group (Katz et al., 2004) we found evidence for this shift as skilled readers acquired familiarity for words via repetition. In that study, we examined repetition effects (comparing activation for thrice-repeated tokens relative to unrepeated words) in both lexical decision and overt naming. Across tasks, repetition was associated with facilitated processing as measured by reduced response latencies and errors. Many sites, including IFG, SMG, supplementary motor area, and cerebellum, showed reduced activation for highly practiced tokens. Critically, a dissociation was seen within the ventral system: The OT skill zone showed practice-related reduction (like the SMG and IFG sites), whereas more anterior ventral sites, particularly MTG, were stable or even showed increased activation with repetition. Thus, we concluded that a neural signature of increased efficiency in word recognition is more efficient processing in dorsal, anterior, and posterior ventral sites, with stable or increased activation in more anterior middle and inferior temporal sites. A second experiment (Sandak et al., in press) tested the hypothesis that the type of processing engaged in when learning a new word mediates how well that word is learned, and the cortical regions engaged when that word is subsequently read. We suspected that repetition alone is not sufficient to optimize learning; rather, we hypothesized that the quality of the lexical representations established when new words are learned is affected by the type of processing engaged in during learning. Specifically, we predicted that relative to attending to the orthographic features of novel words, learning conditions that stress phonological or semantic analysis would speed naming and, in turn, would result in cortical activation patterns similar to those characteristic of increased familiarity with words (as seen in Katz et al., 2004). Prior to magnetic resonance imaging scanning, participants completed a behavioral session in which they acquired familiarity for three sets of pronounceable pseudowords while making orthographic (consonant–vowel pattern), phonological (rhyme), or semantic (category) judgments. Note that in the semantic condition, participants learned a novel semantic association for each pseudoword. Following training, participants completed an event-related fMRI session in which they overtly named trained pseudowords, untrained pseudowords, and real words.

As predicted, we found that the type of processing (orthographic, phonological, or semantic) engaged in when learning a new word influences both how well that word is learned and the cortical regions engaged when that word is subsequently read. Behaviorally, phonological and semantic training resulted in speeded naming times relative to orthographic training. Of the three training conditions, we found that only phonological training was associated with both facilitated naming and the pattern of cortical activations previously implicated as characteristic of increased efficiency for word recognition (Katz et al., 2004). We suggest that for phonologically trained items, learning was facilitated by engaging in phonological processing during training; this in turn resulted in efficient phonological processing (instantiated cortically as relatively reduced activation in IFG and SMG) and efficient retrieval of presemantic lexical representations during subsequent naming (instantiated cortically as relatively reduced activation in the OT skill zone). Semantic training also facilitated naming but was associated with increased activation in areas previously implicated in semantic processing, suggesting that the establishment and retrieval of semantic representations compensated for less efficient phonological processing for these items.

IMPLICATIONS OF OUR RECENT FINDINGS

We had initially speculated that the temporoparietal and anterior systems are critical in learning to integrate orthographic, phonological, and semantic features of words whereas the ventral system develops, as a consequence of adequate learning during reading acquisition, to support fluent word identification in normally developing readers but not in the reading development of individuals with RD (Pugh, Mencl, Jenner, et al., 2000). Our recent experiments examining phonological priming, phonological–semantic trade-offs, and critical factors associated with adaptive learning in reading have yielded findings that require us to refine our initial taxonomy. These data allow for the development of a more fine-grained picture of the functional neuroanatomy and subspecializations within these systems. Across these studies identical sets of voxels in the SMG (within the temporoparietal system), the IFG (within the anterior system), and the OT skill zone (within the ventral system) showed (a) increased activation for pseudowords relative to words, (b) strong phonological priming effects, and (c) repetition-related reductions that were most salient in the phonologically analytic training condition. This pattern strongly suggests a phonological "tuning" in these subregions. (It is particularly noteworthy that the developmentally critical OT skill zone—the putative VWFA—by these data appears to be phonologically tuned. It makes good sense that this region should be so structured given the failure to develop this system in RD when phonological deficits are one of the core features of this population.) By contrast, the angular gyrus (within the temporoparietal system) and the middle–inferior temporal gyri (within the ventral system) appear to have more abstract lexico–semantic functions across our studies (see Price, More, Humphreys, & Wise, 1997, for similar claims).

From these findings, we speculate that subregions within SMG and IFG operate in a yoked fashion to bind orthographic and phonological features of words during learning; these systems also operate in conjunction with the angular gyrus where these features are further yoked to semantic knowledge systems distributed across several cortical regions. Adequate binding, specifically adequate orthographic–phonological integration, enables the development of the presemantic OT skill zone into a functional pattern-identification system. As words become better learned, this area becomes capable of efficiently activating lexico–semantic subsystems in MTG–ITG, enabling the development of a rapid ventral word identification system. Individuals with RD, with demonstrable anomalies in temporoparietal function (and associated difficulties with phonologically analytic processing on behavioral tests), fail to adequately "train" ventral subsystems (particularly the OT skill zone) and thus develop compensatory responses in frontal and RH systems. In our view, this revised account better lends itself to the architectural assumptions put forward in interactive models (e.g., Harm & Seidenberg, 1999) than to classic dual-route models. The findings on stimulus-type effects, and especially the data on adaptive learning, do not readily support the notion of independent dorsal and ventral reading pathways, with each coding different information. Instead, they suggest a set of phonologically or semantically tuned subsystems that are widely distributed across both dorsal and ventral cortex and appear to act cooperatively during fluent word reading and in adaptive learning. In our view a crucial next step is to begin to attend to the ways in which neurobiological findings and computational models may constrain one another.

NEW DIRECTIONS

In recent years, significant progress has been made in the study of reading and RD with the use of functional neuroimaging techniques. A good deal is now known about the distributed neural circuitry for reading in skilled adult readers, the developmental trajectory toward this mature reading circuitry in normally developing children, deviations from this trajectory in RD, and the ways in which intensive training for struggling younger readers alters brain organization for reading. Further advancement in developing an adequate theory of the neurobiology of reading demands considerable progress in a number of domains.

Development of Multimodal Imaging Technologies

The development of a neurobiologically grounded, computational model of reading requires that information be obtained regarding not only the localization of reading-related neural systems but also the relative timing for and connectivity among these systems. This can be accomplished by taking the best aspects of several imaging modalities and systematically combining them. Hemodynamic information from fMRI and positron-emission tomography yields excellent localization; however, the millisecond-level temporal resolution for neural activity obtained with EEG or MEG provides crucial information as well. Much work on optimizing communication between these approaches is under way (cf. Dale et al., 2000). Given that hemodynamic and electrophysiological methods yield distinct but necessarily related types of information, finding a way to use both approaches in a mutually constraining fashion would be ideal. As an illustration of the pressing need for this fusion of technologies, consider the question of the role of phonological processing in skilled reading. Some cognitive studies suggest that phonological coding plays a role at the earliest stages of lexical access, though the issue continues to be debated (cf. Coltheart et al., 1993; R. Frost, 1998). As noted earlier, we have identified phonologically driven activation in the OT skill zone in our priming experiment (Mencl et al., 2004). Given that the OT skill zone operates very early in word processing, such a finding is logically consistent with the early phonology hypothesis. However, given the time scale on which fMRI measures operate, we cannot know whether the observed phonologically modulated hemodynamic response occurred early or late in processing (i.e., as a result of feedback from other language regions to the OT skill zone). By combining hemodynamic and electrophysiological measures during task performance, we may be able to shed light on the theoretically important issue of whether phonology mediates fast time-scale processing in LH ventral cortex.

Moreover, it is possible for a clinical deficit to be associated with differences not only in where activation occurs but also in when it occurs. For instance, using MEG, Salmelin, Schnitzler, Schmitz, and Freund (2000) found that whereas participants who stutter and control participants engaged the same broad cortical regions for speech production, the relative timing of neural activation across these areas was reversed in the two groups. This illustration reinforces the need for multimodal integration in this field, optimizing the relative strengths of each imaging technology in a theoretically conjoined manner. In a similar vein, researchers need to determine how distributed neural systems function together as linked processing circuits. Work in RD (Horwitz et al., 1998; Pugh, Mencl, Shaywitz, et al., 2000) using functional connectivity analyses has been promising. However, this approach is still in its early stages of development. Moreover, studies using both hemodynamic and electrophysiological data to isolate correlated activation can be combined with emerging findings from diffusion-weighted tensor imaging, which reveals axonal tracts connecting distributed neural subsystems across cortex. Indeed, a recent study using diffusion-weighted imaging analysis documented structural anomalies in white matter tracts within the LH temporoparietal region, suggesting a possible neural basis for the often seen functional anomalies in readers with disabilities (Klingberg et al., 2000). In addition, new developments in spectroscopic imaging techniques can support more careful analyses of the basic operations of regions targeted by functional studies to investigate the etiology of abnormal development. More deeply, reading disability is a genetically linked syndrome (Grigorenko et al., 1997; Pennington et al., 1991). Links between genetic polymorphisms, brain structure and function, and cognitive deficits promise to constitute the core scientific foundation for our understanding of neurodevelopmental disorders in the coming years.

Extending Research on Intervention, Populations, and Skilled Reading

To date, there appears to be substantial convergence that successful reading interventions in at-risk children result in increased response in critical LH posterior regions (B. Shaywitz et al., in press; Simos, Fletcher, et al., 2002; Temple et al., 2003). Each of these studies has used training programs that emphasize phonological awareness training to differing degrees. However, several pressing questions remain. First, will similar remediation effects be obtained for older populations with persistent reading difficulties? Moreover, are there specific etiological factors that distinguish children who demonstrate only minimal gains with treatment from responders? If so, might alternative instructional approaches be more effective for these children? These are complex issues and demand large-scale studies in which researchers compare and contrast various interventions and examine interactions with individual-differences or subtype dimensions. Such contrastive research will greatly extend the utility of brain-based developmental research.

In addition, there is a real need to find better markers of abnormal trajectories in very young (preschool age) children, as well as to develop appropriate early interventions. Whereas it is known that the development of phonemic awareness is strongly and causally related to the development of reading skill (e.g., Bradley & Bryant, 1985; Wagner & Torgesen, 1987), little is known about the cognitive primitives underlying the development of phonemic awareness. Some researchers have suggested that deficits in phonemic awareness in children with reading impairment may arise from a more basic deficit in speech perception (e.g., Mody, Studdert-Kennedy, & Brady, 1997) or auditory temporal processing (e.g., Tallal, 1980). However, in a recent longitudinal study of first-grade children (not specifically selected as at-risk for reading difficulties), Sandak (2002) found that the development of phonological awareness was not strongly related to earlier performance on measures of speech perception or auditory temporal processing. Future behavioral and neuroimaging work must continue to examine the development of phonological awareness and reading to advance researchers' understanding of the etiology of RD. One possibility that may prove fruitful is the idea that frontal-lobe-controlled processes (e.g., response inhibition, executive function, sequencing, planning, and working memory) function as building blocks for the development of phonemic awareness and reading skills.

In addition to extending our understanding of RD and the remediation thereof, there is a need for future research to continue to focus on the cognitive and neurobiological processes underlying skilled reading. Great strides have been made in the last decade, but many critical issues remain to be adequately addressed. For example, the vast majority of the research on the neurobiology of reading has focused on lexical- and sublexical-level processing. This is a very reasonable starting place given that reading comprehension is closely related to word reading fluency (Shankweiler et al., 1999). However, a complete account of the neurobiology of reading will include a better understanding of sentence reading, reading comprehension, spelling, and so on (e.g., Caplan, 2004/this issue; Keller, Carpenter, & Just, 2001). Finally, whereas much behavioral research has compared reading processes across languages and orthographies, most neuroimaging research to date has been carried out on participants reading or listening to English words or pseudowords (but see Nakamura et al., 2002; Paulesu et al., 2001; Tan et al., 2000). Given the significant variability in orthographic form, orthographic regularity, methods of reading instruction, and manifestations of reading disability across languages and cultures, more work is needed in the area of cross-linguistic studies of reading, both in order to identify the neurobiological universals of reading and to understand how the functional organization of reading varies with language-specific features.

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