LSHSS

Tutorial

Cognitive Neuroscience of Dyslexia

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Purpose: This review summarizes what is known about the structural and functional brain bases of dyslexia.
Method: We review the current literature on structural and functional brain differences in dyslexia. This includes evidence about differences in gray matter anatomy, white matter connectivity, and functional activations in response to print and language. We also summarize findings concerning brain plasticity in response to interventions.
Results: We highlight evidence relating brain function and structure to instructional issues such as diagnosis and prognosis. We also highlight evidence about brain differences in early childhood, before formal reading instruction in school, which supports the importance of early identification and intervention.
Conclusion: Neuroimaging studies of dyslexia reveal how the disorder is related to differences in structure and function in multiple neural circuits.

Developmental dyslexia is characterized by a persistent reading difficulty that cannot be explained by sensory deficits, cognitive difficulties, lack of motivation, or lack of reading instruction (Lyon, Shaywitz, & Shaywitz, 2003). About 5%–17% of children are estimated to have developmental dyslexia. Reading difficulties in individuals with dyslexia are persistent: 75% of students identified with reading problems in third grade continue to read poorly in high school (Francis, Shaywitz, Stuebing, Shaywitz, & Fletcher, 1996). Reading difficulties in individuals with dyslexia also have broad consequences: Individuals with dyslexia face higher rates of academic anxiety (Jordan, McGladdery, & Dyer, 2014), increased likelihood of dropping out of school (Bruck, 1987), and decreased enrollment in postsecondary institutions (Horn & Bobbitt, 1999). In postsecondary settings, over 70% of students with dyslexia compared with 10% of typical readers reported difficulty in skills important for academic achievement, such as note-taking, organizing essays, and expressing ideas in writing (Mortimore & Crozier, 2006).

Although the cause or causes of dyslexia are not yet known, it is a highly heritable disorder (heritability of ~60%; Friend, DeFries, & Olson, 2008) that runs in families. Animal studies and postmortem investigations suggest that genetic differences may affect the development of brain regions that are important for reading (Galaburda, LoTurco, Ramus, Fitch, & Rosen, 2006). Several candidate risk genes have been identified (e.g., ROBO1, DCDC2, and others; see Galaburda et al., 2006, for a review), but there is only a weak link between any particular gene, reading abilities, and dyslexia (Bishop, 2015).

Neuroimaging studies of dyslexia have identified differences in structure and function that are associated with reading difficulty from childhood through adulthood. Although dyslexia is often diagnosed once reading difficulties become apparent around 7 or 8 years old, there is strong evidence that dyslexia is the consequence of differences in prereading abilities that are the building blocks of learning to read and in the brain regions that support those abilities. The present review summarizes current knowledge about structural and functional brain bases of typical reading and dyslexia, so as to allow readers to better interpret emerging primary research in this field. We also discuss future directions, considerations, and implications for assessment and remediation.

Cognitive Neuroscience of Typical Reading

Reading is a complex behavior that necessitates successful development of multiple brain structures and functions associated with language, vision, attention, and thought. Here, we review converging results about the brain functions and structures that support typical reading as elucidated by magnetic resonance imaging (MRI). Functional MRI (fMRI) allows for a measure of brain activation as the result of particular task demands. Increases and decreases in functional activation during reading or reading-related tasks can

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Editor-in-Chief: Tiffany Hogan

Received January 23, 2018
Revision received April 25, 2018
Accepted May 8, 2018
https://doi.org/10.1044/2018_LSHSS-DYSLC-18-0020
Publisher Note: This article is part of the Clinical Forum: Dyslexia.

Disclosure: *The authors have declared that no competing interests existed at the time of publication.*

be correlated with reading behaviors to determine their functional significance. Activation is measured in terms of the blood oxygen level–dependent (BOLD) signal. This signal measures blood use in the brain and is thought to indirectly index activity in a population of nearby brain cells (e.g., increased BOLD is associated with an increased neural activity; Arthurs & Boniface, 2002). Importantly, changes in neural activation during a task can be localized to specific regions of the brain, identifying the location of circuits that underlie reading. In a complimentary way, structural MRI allows for assessment of the characteristics of gray matter (made up of neuronal cell bodies) and white matter (made up of large bundles or tracts of myelinated axons that connect regions of the brain) in the absence of task demands.

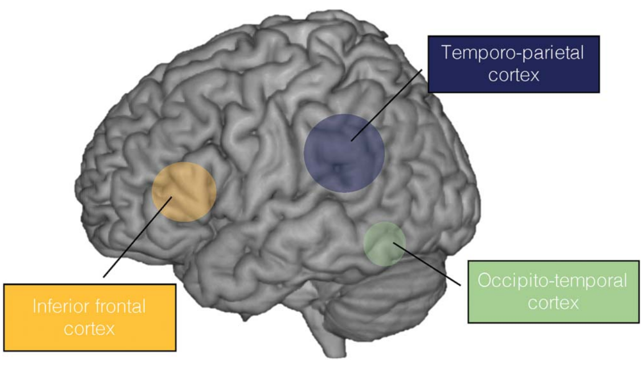
Brain Function and Typical Reading

A network of left-hemisphere regions is thought to support reading, with particular patterns of neural activation dependent on specific task demands (Fiez & Petersen, 1998; Price & Mechelli, 2005). Mature reading relies on a network of left-hemisphere language regions of the brain including frontal, temporo-parietal, and occipito-temporal regions (Price, 2012; see Figure 1). Although all regions must work in concert as a network to support reading, each specific region is particularly important in one or a few discrete reading operations such as phonological processing, visual word detection, or ascertaining meaning. Localized damage to each of these regions has been associated with acquired reading difficulty (Fiez & Petersen, 1998). This "reading network" specializes throughout development, and activation in this network is related to reading ability (Dehaene et al., 2010).

Occipito-Temporal Cortex

The left occipito-temporal cortex is thought to be important in the automatic visual processing of word strings or print (McCandliss, Cohen, & Dehaene, 2003). Activation in this region may be specific to word forms (vs. objects, faces, and other visual percepts), and it is often referred to as the "visual word form area" or VWFA. Word-form–specific activation in this region is consistent across languages and orthographies, that is, representations of sounds by written or printed symbols (Bolger, Perfetti, & Schneider, 2005; Price, 2012). FMRI studies find VWFA activation for both "opaque" orthographies (those for which sound–letter correspondence is inconsistent, e.g., English) and "transparent" orthographies (those for which sound–letter correspondence is consistent, e.g., Spanish; Bolger et al., 2005). Activation in this region is also higher for written words than for spoken words and increases as pseudoword strings become more word-like (Price, 2012). The VWFA appears to be organized in a gradient-like manner, with increased activation for more word-like stimuli in more anterior (or closer to the front of the brain) regions (Vinckier et al., 2007). Damage to this region can result in acquired alexia (the complete loss of the ability to read) in typically developing individuals (Cohen et al., 2003).

Figure 1. Brain regions that make up the reading network and show consistent functional and structural differences in individuals with dyslexia.



Importantly, development of VWFA specialization for letters or words depends on the educational experience of learning to read, both for children and also for illiterate adults (Dehaene et al., 2010; Saygin et al., 2016). There is evidence that VWFA sensitivity (responding to print vs. very different percepts, such as faces) develops quite early in the process of learning to read (Cantlon, Pinel, Dehaene, & Pelphrey, 2011), whereas VWFA specificity (responding to real letters vs. letter-like symbols) emerges more slowly as a product of many years of reading expertise (Blackburne et al., 2014; Centanni, King, Eddy, Whitfield-Gabrieli, & Gabrieli, 2017). This suggests that adultlike specialization for print continues to develop in this part of the brain far into schooling.

Temporo-Parietal Cortex

Most children initially learn spoken language through audition (hearing) and learn to relate spoken or heard words to meaning. Learning to read can be summarized as associating visual print to spoken words and thus to meaning (i.e., cross-modal translation from sight [print] to sound [spoken words]). This process depends on phonological awareness or the ability to recognize and manipulate individual sounds that make up words. These sound units must be mapped onto printed words (orthography) during reading (Pugh et al., 2001, for a review).

Temporo-parietal regions of the brain are generally involved in cross-modal integration. Increasing engagement of left temporo-parietal regions is associated with learning to read, a process that relies on the development of phonological skills (Turkeltaub, Gareau, Flowers, Zeffiro, & Eden, 2003). The cross-modal integration subserved by this region is least important for common (high-frequency) or sight words that with practice become largely recognized by the VWFA. Left temporo-parietal regions, however, remain highly activated for reading of uncommon (low-frequency) words or pseudowords (Pugh et al., 2001) that demand rule-based decoding, that is, "sounding out." Pseudowords tax systems involved in mapping print to sound, as individuals need to sound out words that they have not encountered in the past. Although pseudowords are not a part of typical reading, the same processes used during pseudoword reading are likely engaged throughout education as students expand their vocabularies and learn to map new words in print to language sounds and meanings. Engagement of temporo-parietal cortices is therefore dissociable from engagement of the VWFA, which responds more strongly for familiar words as compared with pseudowords (Price, 2012).

Inferior Frontal Cortex

The role of the left inferior frontal cortex in reading is more complex than the roles of occipito-temporal and temporo-parietal cortices. Activation in the left inferior frontal cortex has been associated with many aspects of language and reading, including verbal working memory, phonological and semantic processing, silent reading, and speech planning (Fiez & Petersen, 1998; Poldrack et al., 1999; Price, 2012). Given the canonical role of the inferior frontal cortex (including Broca's area) in speech-motor production, it may be that silent reading tasks activate circuits important in covert or silent articulatory behaviors (Price, 2012). In fact, older children show less reliance on inferior frontal regions during phonological tasks than do younger children (Hoeft, Meyler, et al., 2007). This age-related difference in activation may be associated with a shift away from inferior frontal regions to other regions of the brain as phonological processing matures and children rely less on articulatory behaviors (Hoeft, Meyler, et al., 2007). Increasing activation in this area has been shown to scale with phonological task difficulty and therefore may be thought of as an index of effort (S. E. Shaywitz et al., 1998). In fact, increased activation in the inferior frontal cortex is consistently seen in individuals who are deaf during phonological judgments of print (e.g., judging whether words rhyme; Aparicio, Gounot, Demont, & Metz-Lutz, 2007; MacSweeney, Brammer, Waters, & Goswami, 2009; MacSweeney, Waters, Brammer, Woll, & Goswami, 2008). Increased activation in this region in individuals who are deaf may reflect increased effort or increased reliance on rule-based or articulatory mechanisms for determining whether words rhyme (Aparicio et al., 2007; MacSweeney et al., 2009, 2008).

Although occipito-temporal, temporo-parietal, and inferior frontal regions are consistently associated with reading, these regions act in concert with other multiple brain regions including primary auditory and visual regions to guide reading behaviors. Coordination and connections between these regions are also important in determining functional specialization of regions important for reading later in life (Saygin et al., 2016).

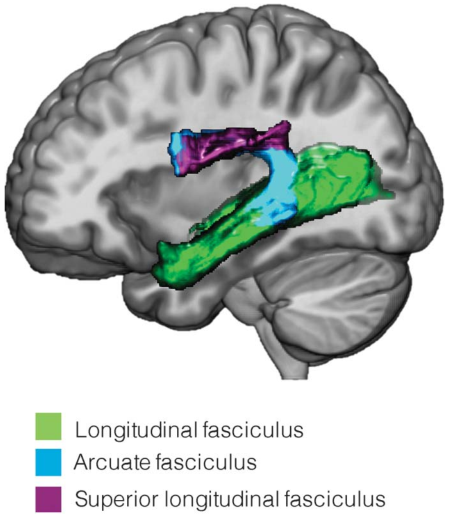
Brain Structure and Typical Reading

Neuroimaging analyses have also elucidated structural correlates of typical reading (He et al., 2013; Hoeft, Ueno, et al., 2007; Wandell & Yeatman, 2013). MRI allows for high-resolution images of the brain, which can be analyzed using various techniques that measure gray and white matter volume as well as the strength of white matter connections between distant regions. In typical readers, greater gray-matter volumes throughout the "reading network," including in temporo-parietal and occipito-temporal regions, are correlated with better reading ability (Hoeft, Ueno, et al., 2007) and with phonological and rapid naming performance (He et al., 2013). Similarly, developmental increases in white matter volume in the left temporo-parietal cortex between kindergarten and third grade have been associated with better reading outcomes (Hoeft, Ueno, et al., 2007).

Connections between cortical regions implicated in reading are important because they help orchestrate the separate parts of the brain into an interactive reading network. Reading-related cortical regions are connected through multiple white-matter tracts including the left arcuate fasciculus, left inferior longitudinal fasciculus, and left superior longitudinal fasciculus (see Figure 2). The strength of connectivity in these tracts increases with age (Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012) and can be predictive of reading outcomes in typically developing children (Myers et al., 2014). Each tract appears to contribute to a different aspect of reading skills and development (Saygin et al., 2013; Wandell & Yeatman, 2013). Diffusion tensor imaging presents an opportunity to examine the characteristics or strength of white matter connections between key regions in the brain. Moreover, properties of white matter tracts can be correlated with reading behaviors to assess the functional significance of each tract.

The left arcuate fasciculus connects temporo-parietal regions involved in cross-modal integration to frontal regions and supports phonological processing (Wandell & Yeatman, 2013). Learning to read, whether in adulthood or childhood, has been associated with stronger connectivity

Figure 2. White matter tracts showing structural differences in dyslexia.



in the left arcuate fasciculus (Thiebaut de Schotten, Cohen, Amemiya, Braga, & Dehaene, 2014), and better phonological awareness is associated with stronger connectivity in this tract as well (Yeatman et al., 2011). The inferior longitudinal fasciculus connects the temporal and occipital lobes, including the VWFA. This tract is thought to be important in mapping visual word information with meaning (Wandell & Yeatman, 2013). Greater integrity of the inferior longitudinal fasciculus is associated with better reading skills (Wandell & Yeatman, 2013) and visual processing of words (Catani, Jones, Donato, & Ffytche, 2003), but not with phonological awareness (Saygin et al., 2013). The superior longitudinal fasciculus connects the parietal and frontal lobes and may be important for mapping phonemic representations to motor representations.

The Cognitive Neuroscience of Dyslexia

Here, we review the most consistent neuroimaging findings about dyslexia. Studies of dyslexia find primarily reduced functional activation, reduced gray matter, and reduced strength of white matter tracts in the left hemisphere. These findings are consistent in both children and adults with dyslexia and persist even when comparisons are made to individuals matched for literacy abilities or reading skills (such as a 10-year-old with dyslexia who is 3 years behind in reading compared with a typically reading 7-year-old).

Reading in Dyslexia

Multiple hypotheses have been proposed regarding core deficits in dyslexia, ranging from deficits in lower-level primary sensory systems to dysfunction in higher-order linguistic systems (Gabrieli, 2009). Behaviorally, dyslexia is most often characterized by impaired phonological awareness, the ability to identify and manipulate units of spoken language. This is primarily true in alphabetic languages (languages in which sounds are represented by written print or symbols), which rely on sound–word knowledge (Siok, Perfetti, Jin, & Tan, 2004). Reduced phonological skills for spoken words are evident not only in children and adults with dyslexia but also in prereading children who are at a heightened risk for reading disability to emerge once reading instruction has begun (Dandache, Wouters, & Ghesquière, 2014; Kirby, Roth, Desrochers, & Lai, 2008; Ozernov-Palchik et al., 2017; Scarborough, 1998; Wagner et al., 1997). Phonologically based training can improve reading in individuals with dyslexia as such training directly addresses this frequent cause of dyslexia (I. S. Brown & Felton, 1990; Foorman, Francis, Fletcher, Mehta, & Schatschneider, 1998; Torgesen, 2000).

Beyond phonological deficits, individuals with dyslexia often struggle with fluent reading, finding it slow and laborious (Lyon et al., 2003). Whereas phonological awareness can be trained via explicit instruction, fluency difficulties in dyslexia are persistent and may become more cumbersome for older children and adolescents as reading becomes increasingly complex in the academic setting (Gabrieli, 2009). Importantly, the automaticity that characterizes expert reading can be measured even in prereaders using rapid naming tasks (i.e., rapid naming of familiar items; see Norton & Wolf, 2012, for a review). It is estimated that 60%–75% of individuals who struggle with reading also have rapid naming deficits (Norton & Wolf, 2012). Both fluency and phonological awareness are important predictors of future reading outcomes (Wolf et al., 2002) and may contribute differently to reading success (Katzir et al., 2006; Wolf et al., 2002). Diagnoses of dyslexia take into account both phonology and fluent reading behaviors.

In addition, although dyslexia has historically been defined as a discrepancy between a typical IQ and a lower-than-expected reading ability, there is evidence that reading difficulties may be unassociated with IQ (Tanaka et al., 2011). Both low- and high-IQ individuals with reading difficulty show a similar pattern of brain differences when compared with typically developing readers (Tanaka et al., 2011). This implies that the ability to read (or at least to accurately read individual words aloud) is independent of intelligence as measured by tests of IQ.

Brain Function in Dyslexia

Neuroimaging studies of dyslexia suggest that reading difficulty is associated with differences in structure and function in the same neural circuits that are engaged by typical readers, including left-lateralized temporo-parietal, occipito-temporal, and inferior frontal cortices (Paulesu, Danelli, & Berlingeri, 2014). These findings provide evidence that dyslexia may be one end of a continuum of reading ability. However, reduced activation in these brain regions has been reported even when individuals with dyslexia are compared with younger readers who are matched for reading ability (Hoeft, Meyler, et al., 2007). This suggests that the etiology of dyslexia is not merely the result of delayed maturation.

The Occipito-Temporal Cortex

Individuals with dyslexia show underactivation in the left occipito-temporal cortex or the VWFA in response to words or word-like materials and lack the typical functional organization within this region that is associated with increased sensitivity to real words as opposed to false words (Olulade, Koo, LaSasso, & Eden, 2014; Richlan, Kronbichler, & Wimmer, 2009; Vinckier et al., 2007). Reduced activation in this region is a persistent difference across both children and adults with dyslexia (Pugh et al., 2001), suggesting that dyslexia may be associated with an early failure to recruit this region for reading in the course of development (Richlan, Kronbichler, & Wimmer, 2011). Activation differences in this region may be associated with rapid naming and word identification deficits reported in dyslexia (Norton & Wolf, 2012), although other regions have been associated with rapid naming deficits in dyslexia as well.

The Temporo-Parietal Cortex

In children and adults with dyslexia, the left temporo-parietal cortex is consistently underactivated during phonological processing tasks (Temple et al., 2001), consistent with the proposed role of this region in grapheme-to-phoneme mapping (mapping printed letters to individual sounds). Temporo-parietal hypoactivation is found in dyslexia even when compared with skill-matched children, suggesting that reduced activation may be related to dyslexia specifically and not to reading ability (Hoeft, Meyler, et al., 2007). Typically, activation in this region increases as a function of increased effort in mapping print to phonology. However, readers with dyslexia do not show increased activation in this region as a function of increased effort (S. E. Shaywitz et al., 1998). Importantly, remediation leading to improved oral language and reading abilities has been associated with increased activation in the left temporo-parietal cortex in children with dyslexia (Temple et al., 2003).

The Inferior Frontal Cortex

In contrast to the decreased activation noted in the left occipito-temporal and temporo-parietal regions, studies often find increased engagement of the left inferior frontal region in dyslexia (Hoeft, Meyler, et al., 2007; S. E. Shaywitz et al., 1998). Increased activation in this region could be associated with compensatory processes that may rely on covert or subvocal reading or an increased effort (Hoeft, Meyler, et al., 2007; Price, 2012). Whereas typical readers show age-dependent decreases in activation in this region, readers with dyslexia show hyperactivation across ages (Hoeft, Meyler, et al., 2007). However, increased engagement of this region may be associated with reading ability rather than dyslexia per se. When compared with younger individuals matched for reading ability, there were no differences in activation in the inferior frontal cortex in individuals with dyslexia (Hoeft, Meyler, et al., 2007). Other studies have reported mixed results regarding the left inferior frontal cortex in dyslexia including decreased activation in this region (Richlan et al., 2009) or differences in the location of activation within this region between individuals with and without dyslexia (Temple et al., 2001).

Brain Structure in Dyslexia

Dyslexia is characterized by structural differences throughout the reading network. Studies examining gray matter volume in dyslexia often find decreased gray matter in the left temporo-parietal cortex and VWFA (W. E. Brown et al., 2001; Hoeft, Meyler, et al., 2007; Kronbichler et al., 2008). Thus, reduced gray matter in dyslexia is found in regions that also typically display functional differences (Hoeft, Meyler, et al., 2007).

Reduced strength of white matter connections between brain regions that are important for reading is also found in children and adults with dyslexia (e.g., Hoeft et al., 2011; Langer et al., 2017; Myers et al., 2014; Vandermosten et al., 2012; Wang et al., 2017). Reduced strength of connectivity in white matter tracts (specifically the left arcuate fasciculus, superior longitudinal fasciculus, and inferior longitudinal fasciculus) has been associated with phonological and orthographic impairments and dyslexia (Hoeft et al., 2011; Langer et al., 2017; Myers et al., 2014; Vandermosten et al., 2012), and characteristics of these white matter tracts predict reading outcomes longitudinally (Wang et al., 2017). Crucially, stronger connections in right-lateralized white matter tracts, such as the superior longitudinal fasciculus, characterized children with dyslexia who showed greater improvements in reading (Hoeft et al., 2011), and greater rates of growth in this tract were found in children with a family history of dyslexia who went on to become typical readers compared with those who were later diagnosed with dyslexia (Wang et al., 2017). This implies that right-lateralized white matter pathways may support an alternative right-hemisphere network for reading in children with dyslexia (Wang et al., 2017). Some studies have also found stronger connections in the corpus callosum, which connects the left and right hemispheres, in individuals with dyslexia (Dougherty et al., 2007; Robichon & Habib, 1998). Hyperconnectivity between hemispheres may be a cause or consequence of the overreliance on right-lateralized brain regions often reported in dyslexia (Gabrieli, 2009).

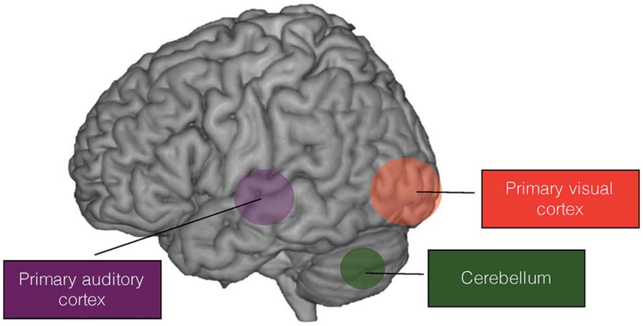
Beyond the Canonical Reading Regions: Other Consistent Findings in Dyslexia

Beyond the canonical reading network, primary sensory regions and subcortical structures including the cerebellum also contribute to typical reading, learning to read, and issues that are sometimes concomitant with dyslexia (visual or auditory impairments and/or motor difficulties; Nicolson & Fawcett, 1999; Stein, 2001; Tallal, 1980; see Figure 3).

Primary Visual and Auditory Systems

Some hypotheses about the etiology of dyslexia focus on basic visual and auditory differences (Stein, 2001; Tallal, 1980). Evidence for visual deficits in dyslexia originally comes from postmortem anatomical findings of cellular variances in regions of the thalamus that are important for the processing of fast visual information including motion (the magnocellular pathway; see Stein, 2001, for a review). Many behavioral studies report visual processing deficits in

Figure 3. Brain regions outside the canonical reading network that show functional and structural differences in individuals with dyslexia.



dyslexia (e.g., Geiger & Lettvin, 1987; Slaghuis, Lovegrove, & Davidson, 1993). Neuroimaging supports behavioral evidence for visual deficits: Activation in brain regions associated with visual perception of the movement of nonverbal stimuli is reduced in dyslexia (Eden et al., 1996; Demb, Boynton, Best, & Heeger, 1998). Furthermore, visual processing streams terminate in parietal regions that are consistently associated with dyslexia (Stein & Walsh, 1997). Although visual system differences are often identified in dyslexia, there is evidence to suggest that they may be a consequence rather than a cause of impoverished reading, as functional differences in visual processing regions between children with and without dyslexia disappear when children are matched for skill and, furthermore, can change as a function of reading intervention (Olulade, Napoliello, & Eden, 2013). Impaired perception of rapidly presented auditory nonverbal stimuli has also been associated with reading disability and reading behaviors (e.g., Boets et al., 2011; Richardson, Thomson, Scott, & Goswami, 2004; Tallal, 1980). One functional neuroimaging study reported that training in rapid auditory processing improved reading performance and brain responses to rapid auditory nonverbal stimuli (Gaab, Gabrieli, Deutsch, Tallal, & Temple, 2007). Although perhaps not present in all individuals with dyslexia, these deficits may occur in some individuals with dyslexia.

The Cerebellum

Cerebellar differences are also often reported in neuroimaging studies of dyslexia (Eckert et al., 2003; Nicolson & Fawcett, 1999; Stoodley & Stein, 2013). The cerebellum is functionally and anatomically connected to temporoparietal and frontal regions important for phonological processing, verbal working memory, and semantics (Stoodley, 2012). It might be the case that certain dyslexia subtypes, such as those individuals who have both phonological and fluency deficits, are more likely to have cerebellar differences (Nicolson, Fawcett, & Dean, 2001). The cerebellum is thought to be important in procedural learning and timing functions, which are important for a large number of linguistic functions including fluency and may additionally underlie the implicit motor difficulties that are sometimes reported in dyslexia (Stoodley, 2016; Stoodley, Harrison, & Stein, 2006). Different regions of the cerebellum are engaged during language and reading tasks than are engaged during motor processing (Stoodley, 2012). Reduced activation and structure in dyslexia are consistently found in “nonmotor,” language-engaged cerebellar regions (Stoodley, 2016).

Predictors of Dyslexia and Evidence for Early Differences

Studies in children and adults with a history of dyslexia are unable to determine with certainty whether neural differences are a cause or consequence of reading impairments in dyslexia. However, neuroimaging evidence from infants and young prereading children at risk for dyslexia suggest that differences exist in the brain even before the onset of learning to read (i.e., that at least some brain differences are causal; Langer et al., 2017; Leppänen et al., 2002; Molfese, 2000; Raschle, Chang, & Gaab, 2011; Torppa, Lyytinen, Erskine, Eklund, & Lyytinen, 2010; van Viersen et al., 2017). Studies of risk for dyslexia have taken two main approaches: Some studies have examined neural structure and function in children and infants who have a family history of dyslexia and are therefore at an increased risk of developing dyslexia. Dyslexia is highly heritable (heritability of ~60%; Friend et al., 2008), and including family history of dyslexia and parental phonological awareness into predictive models of future reading proficiency increases model accuracy (Heath et al., 2014). Other studies examine neural correlates of behaviors known to be highly associated with later dyslexia diagnoses (e.g., poor phonological awareness). Determining the neural correlates of these risk factors may be especially important for early identification of high risk for dyslexia, as currently dyslexia can only be diagnosed after the onset of formal reading instruction.

Behaviorally, weaknesses in phonological awareness, expressive and receptive vocabulary, letter knowledge, and rapid naming in children with and without a family history of dyslexia predict reading ability before the onset of reading instruction (Schatschneider, Fletcher, Francis, Carlson, & Foorman, 2004; Torppa et al., 2010; van Viersen et al., 2017). Beyond behavior, differences in neural function and structure are evident in very young children at risk for dyslexia (e.g., prereading siblings of individuals with dyslexia and/or children of adults with dyslexia). At-risk prereaders have structural and functional differences in the left-hemisphere reading network, including temporo-parietal and occipito-temporal cortices, consistent with differences reported in adults and children with dyslexia (Raschle et al., 2011; Raschle, Zuk, & Gaab, 2012). These differences are evident even in infancy. For example, 6-month-old infants at a familial risk for dyslexia display differences in very early left-hemisphere neural responses to language sounds (Leppänen et al., 2002). Infants at risk for dyslexia also exhibit differences in the structure of the left arcuate fasciculus, a white matter tract associated with dyslexia in children and adults (Langer et al., 2017). Early structural differences in infants at risk for dyslexia may be related to both current and future neurobiological and behavioral differences. Neural responsiveness to speech and nonspeech sounds in newborn infants, tested within 36 hr of birth, predicted whether children would be diagnosed with dyslexia at 8 years old (Molfese, 2000), and measures of white matter integrity in the arcuate fasciculus in infants between 5 and 18 months old correlated with expressive language skills, which are associated with future reading skills (Langer et al., 2017).

Brain Plasticity Associated With Remediation

Neuroimaging studies in both children and adults with dyslexia suggest that the brain can be plastic or can change as a result of experience (Aylward et al., 2003; Eden et al., 2004; Gaab et al., 2007; Hoeft et al., 2011; Krafnick, Flowers, Napoliello, & Eden, 2011; B. A. Shaywitz et al., 2004; Temple et al., 2003). Brain changes occurring as a result of remediation or intervention have been measured primarily with fMRI (to assess changes in functional activation patterns before and after remediation; Aylward et al., 2003; Eden et al., 2004; Gaab et al., 2007; B. A. Shaywitz et al., 2004; Temple et al., 2003), but also with structural measures (to assess how gray and white matter change as a result of remediation; Keller & Just, 2009; Krafnick et al., 2011). Research studies of remediation for individuals with dyslexia typically involve systematic, explicit, and intensive instructions in phonological awareness and decoding for a few hours per day over a limited period (e.g., 8 weeks). These remediation programs can evoke brain plasticity that can be described as *normalization* (bringing functional and structural patterns closer to what is seen in typical readers) or *compensation* (altering functional or structural patterns in neural networks that are outside the typical reading network).

In children, remediation has increased activation in left-hemisphere temporo-parietal and inferior frontal cortices that are typically underactive in dyslexia (Aylward et al., 2003; Gaab et al., 2007; B. A. Shaywitz et al., 2004; Temple et al., 2003). Increased activation in these regions was concurrent with improved performance on many reading and reading-related measures, including measures of phonological awareness (Aylward et al., 2003; Gaab et al., 2007; Temple et al., 2003) and fluency (B. A. Shaywitz et al., 2004). It is noteworthy that such plasticity occurs not only in children, but also in adults, whose increased activation in the left temporo-parietal cortex accompanied improved phonological processing after a reading intervention (Eden et al., 2004; Krafnick et al., 2011). Remedial educational practices in these studies brought brain patterns in dyslexia closer to those seen in typical readers.

Compensatory plasticity as a result of remediation is most often observed in right-hemisphere language homologues (Eden et al., 2004; Temple et al., 2003). Increased activation in these regions is associated with an improved oral language ability (Temple et al., 2003) and improved reading performance (Eden et al., 2004; Temple et al., 2003) and may reflect alternate strategies used by children and adults with dyslexia to decode print. The potential importance of such compensatory right-hemisphere plasticity is supported by evidence that greater right-hemisphere prefrontal activation, and greater right-hemisphere white matter connectivity between parietal and frontal regions, has been associated with greater reading gains in children with dyslexia (Hoeft et al., 2011). These findings suggest that remediation-related improvements in reading may reflect development of alternative right-hemisphere neurocognitive pathways that differ from the typical dependence on a left-hemisphere reading circuit.

Fewer studies have examined the effects of remediation on brain structure, but there is evidence of increases in gray matter volume or thickness and strengthened white matter connectivity as a result of remediation (Keller & Just, 2009; Krafnick et al., 2011; Romeo et al., 2017). Structural brain plasticity was also found in regions outside the canonical reading network, including the hippocampus and cerebellum (Krafnick et al., 2011). Few studies have examined how remediation-driven plasticity persists, but one study found that changes in the brain lasted at least a year after remediation had ended (Meyler, Keller, Cherkassky, Gabrieli, & Just, 2008).

Variations in Dyslexia

Educational and remediation efforts should consider factors that vary across children with dyslexia. Four of these factors are additional difficulties (comorbidities) that often accompany dyslexia, the differential nature of how language relates to print across languages, bilingualism, and socioeconomic status (SES).

Comorbidities with other disorders including attention-deficit/hyperactivity disorder, math disorders, and speech disorders may add to the complexity of behavioral assessments, remediation efforts, and neuroimaging results. Attention-deficit/hyperactivity disorder, reading disorders, math disorders, and speech disorders co-occur at a far higher rate than would be expected by chance (e.g., Landerl & Moll, 2010; Shalev, 1997) and may impair reading even if unrelated to phonological decoding or other behaviors associated with dyslexia. Little is known at present about how these comorbidities alter neural systems implicated in dyslexia.

The neural correlates of dyslexia can also differ depending on the demands of a given language. Two important ways in which printed language differs across languages are (a) whether reading involves alphabetic or logographic decoding and (b) the degree to which sound–letter correspondences are more or less transparent. There are differing demands associated with reading alphabetic languages (languages in which letters represent sounds such as English) versus logographic languages (languages in which a character represents a whole word or phrase such as Chinese). These differential demands may alter the brain organization for reading. For example, whereas French and Italian individuals with dyslexia hypoactivate the left temporo-parietal cortex (Paulesu et al., 2001), one study suggests that Chinese adults with dyslexia do not show left temporo-parietal hypoactivation (Siok et al., 2004; but see Hu et al., 2010, for evidence of more similar hypoactivation in dyslexia in English and Chinese). In addition, orthographically transparent languages such as Italian or German have much more consistent sound–letter correspondence than languages such as English that have many inconsistent relations between sounds and letters. Thus, impaired phonological awareness may be a weaker predictor of future reading outcomes in languages for which sound–letter correspondence is more transparent and consistent (Ziegler, Perry, Ma-Wyatt, Ladner, & Schulte-Körne, 2003). On the other hand, the observation of decreased fluency in dyslexia is more consistent across languages (Ziegler et al., 2003).

In individuals who are bilingual, or fluent readers in more than one language, reading-related brain activation can differ (even within similar anatomical structures) in each language depending on the component skills necessary to decode the writing systems (Das, Padakannaya, Pugh, & Singh, 2011; Jamal, Piche, Napoliello, Perfetti, & Eden, 2012; Meschyan & Hernandez, 2006). Although bilingual individuals activate similar brain regions during reading in both languages, activation patterns differ as a function of orthographic transparency (Jamal et al., 2012; Meschyan & Hernandez, 2006). English–Spanish bilingual individuals show increased inferior frontal activation when reading in English, an opaque language in which one grapheme may map onto more than one phoneme and vice versa, than when reading in Spanish, in which graphemes and phonemes have a more direct one-to-one relationship (Jamal et al., 2012). Furthermore, brain activation patterns associated with reading in bilingual individuals may also be modulated by the age of second language acquisition (Das et al., 2011). Although few studies have used neuroimaging to examine bilingualism in dyslexia, behavioral studies in bilingual children with and without dyslexia find that reading accuracy deficits are exacerbated in their opaque language as compared with their transparent language (e.g., English vs. Hindi and/or French vs. Spanish; Gupta & Jamal, 2007; Lallier, Valdois, Lassus-Sangosse, Prado, & Kandel, 2014).

Finally, SES is a strong predictor of reading ability and may affect reading disability and its remediation (Noble & McCandliss, 2005). Studies have found that SES interacts with both structure and function in the brains of individuals with dyslexia (Noble, Wolmetz, Ochs, Farah, & McCandliss, 2006; Romeo et al., 2017). Gains in remediation for dyslexia may be greater in individuals from low-SES backgrounds (Romeo et al., 2017), an important consideration for recruitment of participants in research and future educational endeavors.

Conclusions and Future Directions for Research and Education

Dyslexia is a complex disorder associated with reading difficulty despite adequate reading instruction. Neuroimaging research suggests that dyslexia is associated with differences in a network of regions implicated in typical reading development. Neural signatures that may signal future reading difficulty exist even in infancy, a sign that identification of reading problems could be possible before a child fails to learn to read and falls behind.

There is a considerable debate about how a deepening understanding of the brain basis of dyslexia may or may not be useful in light of current educational practices and policies (Bowers, 2016; Gabrieli, 2016). Although neuroimaging studies have revealed that dyslexia reflects functional and structural brain differences that diverge from typical brain development starting in infancy, reading instruction is not targeted at particular neural systems. Rather, instruction targets behavioral abilities, such as phonological awareness as a component of single-word decoding.

One area in which neuroimaging studies may contribute particular educational value is in the prediction of response to instruction that would promote personalized or individualized instruction (Gabrieli, Ghosh, & Whitfield-Gabrieli, 2015). In one study of children with dyslexia around the age of 14 years, none of 17 conventional tests of reading and reading-related abilities predicted which particular children would or would not show gains in reading over the next 2.5 years (Hoeft et al., 2011). Neuroimaging methods, however, could predict with considerable accuracy which individual child would or would not make gains in reading over that same period (Hoeft et al., 2011). Similarly, brain measures in kindergarteners correlated better with reading level than did behavioral measures of those same children in fifth grade (Maurer et al., 2009). These studies suggest that brain differences among children may make them more or less likely to benefit from particular kinds of instruction.

These kinds of neuroimaging findings indicate that we ought to be able to distinguish among children and differentiate instruction to meet their needs. Currently, children with dyslexia are given a form of remediation that, under optimal conditions, appears to be effective for about half of the children who receive the remediation (e.g., Romeo et al., 2017). Whether or not a form of instruction is effective, however, is currently only known after a period of prolonged failure in the children who do not respond. Neuroimaging studies indicate that such variable response to reading instruction can be predicted before such instruction begins. In that case, children could be guided at the outset to alternative forms of remediation that are more likely to be beneficial for each child. Although current educational measures are not effective in identifying instruction-relevant variation, neuroimaging findings show that such identification is possible. Coupled with advances in neuroimaging, there would likely need to be some sort of translation of neuroimaging findings to practical educational measures. However, neuroimaging provides a framework for advances in educational measures that may allow each child to receive the sort of reading instruction that best accommodates his or her mind and brain.

Acknowledgments

This work was supported by the National Science Foundation (Division of Research on Learning Grant 164450 to John D. E. Gabrieli) and a Simons Center for the Social Brain Postdoctoral Fellowship to Anila M. D'Mello. The authors thank Sara Beach and Gigi Luk for helpful comments on this article.

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