

Published in final edited form as:

Read Writ Q. 2013 April 1; 29(2): 145–167. doi:10.1080/10573569.2013.758566.

Neurobiological bases of reading comprehension: Insights from neuroimaging studies of word level and text level processing in skilled and impaired readers

Nicole Landi^{1,2}, Stephen J. Frost², W. Einar Menc^{1,2}, Rebecca Sandak², and Kenneth R. Pugh^{2,3}

¹University of Minnesota, Department of Educational Psychology, Minneapolis, MN

²Haskins Laboratories, New Haven, CT

³Yale University School of Medicine, Department of Pediatrics, New Haven, CT

Abstract

For accurate reading comprehension, readers must first learn to map letters to their corresponding speech sounds and meaning and then they must string the meanings of many words together to form a representation of the text. Furthermore, readers must master the complexities involved in parsing the relevant syntactic and pragmatic information necessary for accurate interpretation. Failure in this process can occur at multiple levels and cognitive neuroscience has been helpful in identifying the underlying causes of success and failure in reading single words and in reading comprehension. In general, neurobiological studies of skilled reading comprehension indicate a highly overlapping language circuit for single word reading, reading comprehension and listening comprehension with largely quantitative differences in a number of reading and language related areas. This paper reviews relevant research from studies employing neuroimaging techniques to study reading with a focus on the relationship between reading skill, single word reading, and text comprehension.

Introduction

The ultimate goal of reading, beyond its initial acquisition stage, is comprehension – typically comprehension of connected text. Successful reading comprehension requires successful processing at all levels. At the lowest level, readers must have accurate word level processing – this includes the conversion of letters into speech sounds (or decoding) and accessing a words meaning. At higher levels readers must be able to string together words to form sentences and understand their language’s syntax in order to get the sentential meaning. And finally, at the text level, readers must be able to link sentences and paragraphs and acquire a global meaning representation for a given text. Some models of reading consider these processes to be largely independent and sequential (e.g., Jackendoff, 1999; Levelt, 1999) while others consider them to be more fully interactive (McClelland, 1987; Macdonald et al, 1994). Regardless, most researchers agree that failure at any of these levels will result in poor reading comprehension (e.g., Perfetti & Hart, 2002). The recent increase in cognitive neuroscience research into reading has led to a greater understanding of the underlying neurobiology of reading success and failure at each of these levels. In this paper we will review this literature with a particular focus on the relationship between the neurocircuitry for single word reading and the neurocircuitry for reading comprehension.

Basics of neuroimaging

In order to orient the reader to the topics reviewed here we provide a brief description of functional neuroimaging principles and methodology. Although several types of neuroimaging are used to study reading including fMRI (functional magnetic resonance imaging), MEG (magnetoencephalography) PET (positron emission topography), EEG (electroencephalography) and more recently NIRS (Near Infrared Spectrography), in this article we focus on studies that have employed fMRI. fMRI is by far the most commonly used neuroimaging method for studying reading, largely because of its precise spatial resolution, which allows us to determine what regions of the brain are involved in a particular cognitive task or skill. Thus, this work follows from a long tradition (beginning with lesion studies in the 19th century) of work that seeks to understand the cortical systems responsible for cognition. fMRI measures the change in blood flow (the hemodynamic response) that occurs when humans engage in an active task. This change in blood flow is closely linked to neural activity; though the precise nature of this relationship is an active area of research, the basic assumption is that when neurons are active they increase their metabolism (glucose consumption) which results in greater oxygenated blood flow to the active region. Critically, the molecule that carries oxygen in the blood, hemoglobin, has particular magnetic properties that allow us to measure its level of oxygenation using the fMRI scanner, which creates a magnetic field. This signal is called the Blood Oxygen Level Dependent (BOLD) signal and it measures the amount of deoxygenated hemoglobin in a voxel (unit of activation, typically 2mm³).

Neurobiological basis of single word reading

Basic reading circuit

Evidence from functional imaging studies indicates that skilled word reading requires the development of a highly organized cortical system that integrates processing of orthographic, phonological, and lexical-semantic features of words (see Pugh et al, 2000a; Sandak et al, 2004a and Sarkari et al, 2002 for reviews). This system broadly includes two posterior areas in the left hemisphere: a dorsal (temporoparietal) system, a ventral (occipitotemporal or OT) and, and a third, anterior area centered in and around the inferior frontal gyrus (IFG).

The dorsal, temporoparietal, system broadly includes the angular gyrus (AG) and supramarginal gyrus (SMG), and the posterior aspect of the superior temporal gyrus (STG; Wernicke's Area). The areas within this system seem to be involved in mapping visual aspects of print on to their phonological form and binding phonological information to semantic representations (Black & Behrmann, 1994). In skilled readers, regions within the left hemisphere temporoparietal system (particularly the SMG) tend to respond with greater activity to pseudowords than to familiar words or pictures (Price et al, 1997; Simos et al, 2002; Xu et al, 2001); the angular gyrus, by contrast generally responds with greater activity to words than pseudowords and a role in semantic integration has been suggested (e.g., Price et al 1997). These findings, along with findings from our developmental studies (Shaywitz et al, 2002) suggests that, in general, the temporoparietal system plays a role in the types of phonological and semantic analyses that are relevant to learning new words.

The ventral system includes a left inferior occipitotemporal/fusiform (OT) region (sometimes referred to as the visual word form area or VWFA because of findings suggesting that this area responds more to word stimuli than to objects and nonwords) and extends anteriorly into the middle and inferior temporal gyri (MTG & ITG). The more anterior areas within the ventral system appear to be semantically tuned (Fiebach et al, 2002; Simos et al, 2002) and the more posterior aspects of this system (OT region) are fast-acting

in response to linguistic (particularly printed) stimuli in skilled readers. Importantly, the functional specificity of the OT region appears to develop late and to be positively correlated with the development of reading skill in children (Booth et al, 2001; Shaywitz et al, 2002).

The anterior system, centered in the IFG, appears to have sub-regions that are utilized for processing of different types of information during reading: the more anterior aspects of IFG have been implicated in semantic retrieval (Poldrack et al, 1999). The more posterior regions of this multi-functional system, along with the insula and opercular area seem to be phonologically tuned; they are activated in silent reading and in naming and during rhyme tasks (see Fiez & Petersen, 1998; Paulesu et al, 1997; Roskies et al, 2001) and, like the temporoparietal system, are more strongly engaged by low-frequency words (particularly, words with inconsistent spelling-to-sound mappings) and more strongly engaged by 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 et al, 2000). However, it should be noted that this region has been linked to a variety of functions including speech production (Indefrey et al, 2001) syntactic processing (Grodzinsky et al, 2000) and more domain general selection processes (see Thompson-Schill, 2005 for a review). The role of the IFG in sentence/syntactic processing is discussed later in this paper.

This general account of single word reading is coarse grained and underspecified but is continually being refined with more and more sophisticated neuroimaging designs that aim to further understand the functional properties of each reading-related region and how they interact (e.g., Frost et al, 2005, Katz et al, 2005, Pugh et al, in press; Sandak et al, 2004a). For example, in one study from our group (Frost et al, 2005) we investigated the relative tradeoffs between phonology and semantics in a neurobiological study based on the work of Strain and colleagues. Strain et al (1995) found that the standard consistency effect on low-frequency words (longer naming latencies for words with multivalent or inconsistent spelling to sound mappings relative to words with singular or consistent mappings) was attenuated for words that were concrete or imageable; thus implying a critical role for top down semantic feedback on difficult-to-decode items. In the Frost et al study, go/no-go naming produced higher activation for high imageable words in middle temporal and posterior parietal sites, including AG, and higher activation for inconsistent relative to consistent words in the IFG. Furthermore, increased imageability was associated with reduced consistency-related activation in IFG but increased posterior activation; which we interpret to be the neural signature of the behavioral trade-off between semantics and phonology revealed behaviorally by Strain and colleagues.

Modification of the neural circuitry for reading

In another line of research from our group we have been investigating the shift from a predominantly dorsal reading circuit to a predominantly ventral reading circuit associated with increased reading skill (Shaywitz et al, 2002). For example, Katz et al (2005) found evidence that this shift can happen on a relatively short time scale as skilled readers acquired greater familiarity for words via repetition. In this study, words that were repeated three times over the course of a scanning session were compared to unrepeated words, in both lexical decision and overt naming. Along with improved behavioral performance, many sites including LH IFG & SMG, supplementary motor area, and cerebellum, showed reduced activation for repeated relative to unrepeated tokens across tasks. Critically, a dissociation was observed within the ventral system: activation in L.OT showed repetition-related reduction, whereas more anterior sites, (e.g., MTG), were stable or even showed increased activation with repetition. Thus, we concluded that a neural signature of increased efficiency

in word recognition is reduced activation in anterior, and posterior ventral sites, with stable or increased activation in more anterior middle and inferior temporal sites. To further refine our understanding of the type of learning that produces such a shift, Sandak et al (2004a) examined whether the type of processing engaged in during word learning mediates how words are learned, and what cortical regions are engaged when these words are subsequently read. Prior to MRI scanning, participants completed a behavioral training session in which they repeatedly saw three sets of pronounceable pseudowords while making orthographic (consonant/vowel pattern), phonological (rhyme) or semantic (category) judgments. After training, participants completed an event-related fMRI session in which they overtly named trained pseudowords, another set of untrained pseudowords, and a set of real words. The results indicated that the type of processing (orthographic, phonological, or semantic) engaged in when learning a new word influences both how well that word is learned (as evidenced by behavioral performance), 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. However, of the three training conditions, 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, in particular reduced OT activation (Katz et al, 2005). Thus, we suggested that for phonologically trained items, learning was facilitated by engaging in phonological processing during training and that this in turn resulted in efficient phonological processing (instantiated cortically as relatively reduced activation in LH 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. Thus learning occurred for both phonologically and semantically trained items but was accomplished via different neurobiological shifts.

These types of studies provide more information on specialization for component processing (e.g., orthography, phonology, semantics) in subsystems within the broad left hemisphere reading circuit, and also how these subsystems engage in tradeoffs as information-processing demands are varied. Many of our current projects are aimed at further refining our understanding of the interactions between subcomponents of word processing with training studies that vary the emphasis on type and amount of training and through analyses such as functional connectivity that aim specifically to identify the relationship among cooperative and competitive systems within the reading circuit in skilled and less skilled readers (Pugh et al., in press).

Neurobiological circuitry associated with impaired word reading

Altered circuitry

Studies of impaired word reading have also helped to refine our understanding of the neurocircuitry for reading. Converging evidence from functional neuroimaging studies of single word reading indicates that a primary neurobiological marker of reading disability (RD) is reduced activation of left hemisphere posterior regions, particularly the temporoparietal and OT regions relative to non-impaired (NI) readers during tasks that make demands on language and printed word processing (Temple et al, 2003; Shaywitz et al, 2002). In fact, research has shown a linear relationship between reading skill and activation of LH reading sites (Shaywitz et al, 2002; Turkeltaub et al, 2003). Together with this failure to reliably engage left hemisphere temporoparietal and occipitotemporal regions, RD readers tend also to show heightened activation of right hemisphere posterior and bilateral frontal regions (see Pugh et al, 2000a; Sarkari et al, 2002 for reviews). A number of explanations

have been proposed for how the tendency to hyper-engage these regions may serve to compensate for deficient linguistic processing in the left hemisphere, including greater reliance on sight-word reading and/or increased involvement of higher level control processing.

Although the pattern of altered function described above is the most commonly identified pattern of neural activity for dyslexic children and adults, there is some evidence that suggests a possible sensory processing deficit, e.g., low-level visual motion processing (Eden et al, 1995; Eden et al, 1996) or low-level auditory processing, (e.g., Tallal, 1980), with alerted circuitry extending beyond language processing areas. One of the more prominent of these theories is the magnocellular deficit hypothesis, which suggests that individuals with dyslexia have a deficit in the magnocellular pathway in the lateral geniculate nucleus (LGN), which is involved in visual motion processing (e.g., Eden et al, 1995; Stein, 2003). Neurobiological evidence for this abnormality comes from a series of studies that have shown that presentation of moving visual stimuli produced less functional activity in V5/MT in dyslexics relative to control participants (Eden et al, 1996) and that amount of activity in V5/MT associated with visual motion processing was directly correlated with reading skill (Demb et al, 1997; Eden et al, 2000). Proponents of this argument admit that the visual motion processing deficit in V5/MT is small and may be limited to specific subtypes of dyslexics (Zeffiro & Eden, 2000). Although these deficits are likely to be relevant for a subtype of the dyslexic population, the behavioral and neurobiological evidence for a lower level sensory deficit in dyslexia, and its causal role in reading difficulties (Frith & Ramus, 2006) is limited. The current review will focus on the linguistic processing regions involved in reading, a research issue more intensively investigated to date.

Effects of intervention on the neural circuitry for reading

Importantly, several studies with school aged children have shown that the altered circuitry in RD can be modified to look more like that of a typically developing readers with certain types of intervention. For example, in a recent MEG study, children with severe reading difficulties showed robust increases in the engagement of the L. temporoparietal region, accompanied by a moderate reduction in the activation of the R. temporoparietal areas after a brief but intensive phonics based remediation program (Simos et al, 2002). Using fMRI, Temple et al, (2003) examined the effects of a commercial intervention aimed at building auditory processing and oral language skills (Fast ForWord Language) on the cortical circuitry of a group of 8- to 12-year-old children with reading difficulties. After intervention, along with increased reading and oral language scores, the authors observed increased LH temporoparietal and inferior frontal activation, and the LH increases correlated significantly with increased reading scores. In another fMRI study, three groups of young children: A treatment RD group that received nine months of an intensive phonologically-analytic intervention and two control groups, typically developing and an untreated RD group, were examined at two time points; pre and post intervention (Shaywitz et al, 2004). When RD groups were compared post treatment, reliably greater activation increases in left hemisphere reading related sites were seen in the treatment group. In particular, differences were seen in L. IFG, and importantly in L. OT. Importantly, left hemisphere ventral increases along with decreasing right hemisphere activation patterns were observed even one year later in a follow up scanning session after treatment was concluded. These initial combined intervention/neuroimaging studies suggest that a critical neurobiological signature of successful intervention in young RD children is increased engagement of major left hemisphere reading-related circuits, and reduced compensatory reliance on right hemisphere homologues.

Other forms of reading impairment

It is important to note that the group of readers that were investigated neurobiologically in Shaywitz et al (2004) were all treatment responders; that is, they all showed behavioral improvements as a function of training. Similarly, in the Temple et al, (2003) study, the greatest increases in LH activity were seen for those children who made the greatest gains behaviorally. What is unknown, is what type of remediation would be successful for those readers that do not respond to these types of interventions. One possibility is that those poor readers who did not respond represented a different subtype of RD reader. Most research on impaired reading has focused on children and adults with phonological and/or decoding impairments (developmental dyslexia type). This focus on developmental dyslexia exists because phonological deficits have long been thought to be the primary source of reading difficulty (see Velutino et al, 2004). However, an understanding of the neurobiology of additional types or subtypes of reading disability may also further our understanding of the neurobiological circuitry necessary for reading. One such possible subtype of readers particularly relevant to the current review are those with specific comprehension impairments (or SCI). Behaviorally, this group has exhibited impaired working memory skills (Cain et al, 2004), impaired semantic processing skills (Nation and Snowling, 1998) and impaired inference making (Cain & Oakhill, 1999) skills, all despite normal IQ and putatively normal decoding skill. The only neurobiological investigation of this group that we know of compared SCI adults to control adults using ERP (Landi & Perfetti, 2007). In this study SCI participants and adult control participants (who differed significantly on comprehension but not on IQ or decoding tasks) made a semantic judgment about two words (do they belong to the same category) and a homophone judgment about two words (do they sound the same if pronounced). The authors found that SCI readers had reduced N400 and P200 on the semantic but not on the phonological processing task, suggesting a semantic processing weakness in this group. Although ERPs alone do not provide information about localization of function, there is some evidence that the neural generators of the N400 are located in Wernicke's area (e.g., Kutas & Van Petten, 1993 – See also Frishkoff et al, 2004, for evidence of a larger network of generators), which suggests that this region is related to the observed processing differences in this group of poor readers and is consistent with the hypothesis that these readers have difficulty with semantic processing. Further investigation of the neurocircuitry of impaired reading, especially for understudied subtypes with more isolated impairments such as SCI readers may help refine our current working model of the neural basis of reading and provide a more solid foundation for neuroimaging studies of comprehension in impaired groups (discussed later in this paper).

With regard to remediation in SCI readers, if they truly have a circumscribed difficulty with comprehension, than we would not expect phonologically based or decoding based intervention to improve their performance or shift their neurocircuitry. One barrier to identifying the type of training that would be most beneficial for this group is that it is still unclear what is causing SCI reader's difficulty with comprehension – a deficit in working memory would suggest a different course of training relative to a deficit in semantic processing. Furthermore, it is difficult to speculate on how their neurocircuitry might be altered as a function of intervention, as currently we don't know how their basic neurocircuitry for language differs from typically developing or traditionally defined RD readers. Knowledge of the basic mechanisms and neurocircuitry that underlie SCI will be beneficial for making links between single word reading, impaired reading and comprehension. There is a growing recognition of the importance of comprehension level deficits in RD (especially in older children) and thus it will be critical to apply the same intensity of research focus that has been applied to decoding in recent years. In With regard to remediation in SCI readers, if they truly have a circumscribed difficulty with comprehension, than we would not expect phonologically based or decoding based

intervention to improve their performance or shift their neurocircuitry. One barrier to identifying the type of training that would be most beneficial for this group is that it is still unclear what is causing SCI reader's difficulty with comprehension – a deficit in working memory would suggest a different course of training relative to a deficit in semantic processing. Furthermore, it is difficult to speculate on how their neurocircuitry might be altered as a function of intervention, as currently we don't know how their basic neurocircuitry for language differs from typically developing or traditionally defined RD readers. Knowledge of the basic mechanisms and neurocircuitry that underlie SCI will be beneficial for making links between single word reading, impaired reading and comprehension. There is a growing recognition of the importance of comprehension level deficits in RD (especially in older children) and thus it will be critical to apply the same intensity of research focus that has been applied to decoding in recent years. In the following section we review the status of research findings on the neurobiological basis of skilled and impaired comprehension.

Neurobiological basis of comprehension

Although the primary focus of most cognitive neuroscience research in reading has been at the single word processing level, recent research has begun to explore the neurobiological bases of reading comprehension. The process of reading comprehension is often characterized as the product of word reading and listening comprehension (Gough & Tunmer, 1986). Thus, one might expect to find areas that are recruited for each of these skills to be recruited for reading comprehension. Although difficult to directly compare because of the greater demands imposed by sentence reading, findings from neuroimaging research generally indicate that the neurocircuitry for reading comprehension is largely overlapping with the circuitry for single word reading and that the circuitry for comprehension is largely modality independent (e.g., Michael et al, 2001).

Neurocircuitry associated with sentence processing

Neuroimaging investigations of comprehension, typically involve either passive single sentence reading or listening followed by a judgment about the grammaticality or meaningfulness of the sentence compared to a baseline comparison task (such as reading or listening to a series of unrelated words or consonant strings). In a classic example of this type study, Bevalier et al (1997) presented participants with alternating blocks of visually presented sentences or a series consonant strings in a passive fMRI paradigm. The authors found greater activity for sentence processing, relative to reading consonant strings, in Broca's area, Wernicke's area, L. STG and MTG bilaterally, as well as the L. IFG and the angular gyrus. This engagement of these areas for sentence processing is relatively consistent across studies; in general, studies show greater activation for sentence reading relative to a control task in the left IFG and the posterior, superior and middle temporal gyri (typically with more activation in the left hemisphere relative to the right hemisphere) (e.g., Caplan et al, 2001; Fredeirici et al, 2003) some studies also report activation in the fusiform gyrus/ occipital temporal region (Cutting et al, 2006) and in the parietal lobes (Booth et al, 2001). Depending on task demands and type of the comparison task, areas that are relatively more active for sentences vary from study to study; for example, areas such as the parietal lobe and the occipital temporal region are less commonly reported than temporal lobe regions and L. IFG, which seem to be constant across studies of sentence comprehension.

Further refining comprehension processes

Some of the most informative studies of comprehension have tried to more specifically isolate comprehension processes. For example, a few studies have tried to directly compare single word reading to sentence comprehension in order to further refine the networks that

are specific to each. Although sentence reading is a much more complicated task than single word reading and brings to bear a number of higher level skills that may not be used in single word reading, it is useful to compare the two using subtractive methodology in order to try to isolate those regions that are used for sentential processing above and beyond those used for decoding and identification of words. Using PET, Stowe et al (1999) presented complex sentences or lists of single words made from scrambling the words from the sentences such that the words seen across conditions were identical – participants were instructed to listen passively. Stowe and colleagues found the left anterior temporal lobe to be more heavily recruited for sentence processing relative to word processing but found no regions with greater activity for words relative to sentences, suggesting that complex sentence reading more heavily recruited all language areas identified in this study. In a related PET study, Bottini et al (1994) had participants read sentences for plausibility or make a lexical decision about a word that was embedded in a string of words. Greater activation was found for sentences relative to words in a number of right hemisphere and left hemisphere regions including a large left frontal region encompassing the IFG, a region in the left parietal lobe, a large portion of the left temporal lobe encompassing the middle and inferior temporal gyri as well as the right and left temporal poles, the right and left subcallosal gyrus and right IFG and right hippocampus. Again these findings suggest overlapping regions for word and sentence processing with qualitative differences (sentence > word) in many language and reading-related areas, along with greater right hemisphere recruitment. Many of these same regions of differences between sentence and single word processing have been identified with fMRI. Cutting et al (2006) contrasted single word processing to sentence reading and identified similar regions of increased activation for sentences. In this examination participants either saw a list of words and made a button press when they viewed a word corresponding to a living object or read a series of sentences and made meaningfulness judgments. Findings included increased left inferior, middle and superior temporal lobe activation as well as right middle temporal lobe activation for sentences relative to words. Cutting and colleagues also found an area in IFG (left anterior IFG) that was preferentially activated for single word tasks (although this activation might in part be driven by the increased semantic processing demands of the single word task in this study, as this part of IFG has been associated with semantic analysis). Thus, there appears to be a critical network for comprehension that is largely overlapping with single word processing but draws somewhat more heavily on a number of reading and language related areas, particularly the left hemisphere temporal lobe regions and L.IFG and several right hemisphere regions. The greater activation in temporal and inferior frontal regions likely reflects the general increased processing demands associated with sentence relative to single word processing, in particular the L. IFG is likely to be more active because of the need for syntactic analysis (particularly for the more complex sentences) either because of the greater working memory demands associated with syntactic processing (Roskies et al, 2001) or the need to select between alternative interpretations (e.g., Thompson-Shill, 2005). The greater role for the right hemisphere may reflect increased resources required above and beyond word processing for sentence processing (Just et al, 1996), the addition of prosodic processing (Buchanan et al, 2000; Damasio & Damasio, 1992), the increased need for processing of subtle semantic information/relationships as in metaphor processing (Bottini et al, 1994) and in some cases the resolution of semantic ambiguity (MacDonald et al, 1994); this remains an important but understudied question.

Semantics and syntax

Additional research has attempted to further specify the neural circuitry for some of the critical subcomponents of sentence comprehension including syntactic processing, semantic processing, working memory and inferential processing. Behaviorally there is evidence to suggest that although these processes work together, they pose somewhat different cognitive

demands on the language system (e.g., Ni et al, 2000) and this partial dissociation as been confirmed with neuroimaging studies. For example, using fMRI, Ni et al (2000) compared processing of syntactically anomalous and semantically anomalous sentences. In this study, across three types of runs, participants heard semantically anomalous or non-anomalous sentences and were asked to make a meaningfulness judgment, syntactically anomalous or nonanomalous sentences and were asked to make a grammaticality judgment or pure tones and were asked to make a pitch discrimination judgment. Ni and colleagues found that activity associated with semantic anomaly was generally more widespread and more bilateral than for syntactic anomaly. Furthermore, confirming findings from lesion studies, they found a region of IFG (Broca's area) to be more active for syntactic anomaly and the posterior part of superior temporal region (Wernicke's area) to be more active for semantic anomaly. This is a rather course distinction of this division of labor but generally, the inferior frontal region encompassing Broca's area seems to be critically related to syntactic processing as this region is repeatedly implicated in tasks that require complex syntactic processing, particularly for anomaly resolution (e.g., Constable et al, 2004; Michael et al, 2001; Peelle et al, 2004).

Working memory

With regard to the involvement of working memory in comprehension, studies that look specifically at working memory typically identify regions of IFG or DLPFC; however, working memory has long been difficult to separate out from syntactic processing in language comprehension studies, as working memory can be heavily taxed in syntactic analysis. For example, one study by Fiebach et al (2004) found Broca's areas activation to increase as a function of length of a syntactically ambiguous region in a sentence and to interact with working memory span (individual difference variable) and sentence complexity, thus suggesting increased activation in this region for increased demands – both for and individual with low span (working memory demands) and for increasing syntactic complexity (sentence processing demands). Cutting et al (2006), using a subtractive analysis, attempted to parcel out activation associated with working memory from that associated with sentence processing and single word reading and found that working memory was more strongly associated with the superior parietal lobe.

Inference making

Research in reading has long acknowledged the importance of inference making during comprehension of sentences and texts. Although there has been a long-standing debate over when and under what circumstances readers draw inferences when they read, most researchers agree that a certain amount of inferential processing is necessary for adequate understanding of discourse. Early neurobiological examinations of inference making revealed a prominent role for the right hemisphere; patients with right hemisphere lesions have trouble drawing inferences and integrating sentences (e.g., Beeman, 1993); also split hemifield presentations has demonstrated an important role for the RH in inferential processing (e.g., Beeman, et al, 2000). One recent neuroimaging study by Mason and Just (2004) used fMRI to directly examine activation during inferential processing by having participants read pairs of sentences that varied in the degree to which they were causally related. In this study participants saw an a outcome sentence such as, "The next day Joey's body was covered with bruises" and either a highly causally related sentence "Joey's big brother punched him again and again" a moderately causally related sentence "Racing down the hill, Joey fell off his bike" or a sentence that was not causally related "Joey went to a neighbor's house to play" (from Mason & Just, 2004). This study was based on an earlier behavioral study by Meyers et al, (1987), which found that memory for these types of sentence pairs followed an inverted U shape function; moderately related sentences were recalled better than highly related or distantly related pairs. Meyers et al, (1987) suggested

that for the moderately causally related pair, a causal inference was drawn, which created a richer representation for the pair, thus enhancing memory. Mason and Just (2004) found a similar inverted U shape function for neural activation in several right hemisphere regions (including the R. inferior parietal lobule and the R. inferior and middle temporal regions), with greater activity for moderately causally related sentences relative to either of the other two types, but no modulation by condition of left hemisphere language processing regions. This recent fMRI finding, along with early RH lesion and split hemifield presentation research, suggests an important role for the right hemisphere in inferential processing. Neuroimaging research on inference making has only emerged recently and thus further research will be necessary to refine our understanding of which regions within the RH are most important for inference making and how RH activation might be modulated for processing of different types of inferential relationships (e.g., causal vs. predictive).

It is clear that there are many subcomponents of comprehension that work together to produce a readers overall understanding of the text but more studies with greater sophistication will be needed to fully identify the relative contribution of each of these sub components.

Beyond the sentence

A small set of studies has examined the underlying brain regions involved in comprehension of longer texts. Findings from these studies implicate many of the same regions for comprehension of longer connected text that are involved in sentence and single word processing, including the L. IFG and temporal lobe regions; however, for longer texts there seems to be even greater involvement of the right hemisphere (see Gernsbacher & Kashak, 2003 for a review). Studies that have directly contrasted sentence processing and discourse processing are of particular importance for understanding discourse or narrative processing (processing of longer connected texts). In general, these investigations have revealed greater right hemisphere and frontal activation for discourse over sentence processing. For example, one study by Plante et al (2006) compared activation in typically developing (TD) and college students with a broad history of learning disabilities (HLD) listening to a series of six unrelated sentences or six sentences that formed a connected narrative (group differences are discussed later in this article). Plante and colleagues identified several regions of interest that were more active for sentence (IFG) or narrative (middle temporal gyrus and precentral sulcus) processing and further compared left and right hemisphere activation. They found greater activation in L. IFG relative to R. IFG for sentences, greater activation for the left relative to the R. MTG and greater R. precentral sulcus relative to left for narratives. These relative differences likely reflect greater attention to syntactic information in the sentence processing condition compared to greater attention to semantic information in the narrative condition. In another study by Robertson et al (2000) participants were visually presented with 11 sentences that formed a narrative or 11 sentences that did not. To create this distinction Robertson and colleagues manipulated the presence of indefinite articles – the presence of a definite article in a series of sentences created a connected narrative whereas the absence of a definite article created a series of unconnected sentences. This study provides an important data point as the two conditions were maximally similar in structure. The findings from this study revealed no differences between conditions in left hemisphere regions that are typically implicated in reading and language processing, but did find differential processing in several right frontal regions (connected > unconnected text) including the right superior and medial frontal gyri. The authors point out that an increased role for the right hemisphere when processing connected text is consistent with lesion data that suggests difficulty with complex language processing after right hemisphere lesions including, prosody and semantics (e.g., metaphor). Thus, overall, it seems that frontal and right hemisphere regions become increasingly involved as texts get longer and require a

more fine-grained analysis of meaning and relatedness, working memory demands increase and prosodic information becomes relevant.

This RH role in more complex text comprehension tasks is a primary area of divergence between the network for sentence and connected text level processing and single word reading, where the RH plays a more limited role (one notable exception is the previously discussed RH compensatory processing in RD).

Modality effects

Interestingly, the comprehension network seems to be largely modality independent: similar networks are activated for auditorally compared with visually presented sentences –in general, exceptions include increased extrastriate activation and greater left lateralization for visually presented sentences (Constable et al, 2004; Michael et al, 2001) and increased STG activation for auditorally presented sentences (Braze et al, under review). Several studies have directly compared auditory and visual sentence processing in the same study to identify more subtle differences. One such study by Michael et al (2001) used fMRI to directly compare auditory and visual sentence processing by having participants listen to or read a sentence and answer a true false question after each sentence. Michael and colleagues also manipulated complexity such that half of the sentences were object relative and half were simpler subject relative sentences. Region of interest analyses indicated several areas of overlap across modalities including a left hemisphere temporal region (encompassing ITG, STG, and MTG) and L. IFG. A modality comparison revealed a number of areas that were differentially active as a function of modality including increased activation in bilateral ITG & STG/MTG, bilateral Heschl's gyrus, & L. IFG for auditory relative to visual processing of sentences and increased activation for visually relative to auditorally presented sentences in extrastriate regions and primary visual regions. With regard to complexity, the temporal cortex regions and the L.IFG were more active for the object relative sentences regardless of modality (again suggesting an important role for the IFG in syntactic analysis). Similar findings were obtained by Constable et al (2004) who also compared auditory and visual processing of more simple (subject relative) and more complex (object relative) sentences and found that the IFG (bilaterally) responded to complexity regardless of modality. Constable and colleagues also found the preferential response in auditory regions for auditorally presented sentences and a preferential response for visual stimuli in inferior parietal sites. These findings suggest that although there are many areas of overlap for visual and auditory sentence processing there are also some significant quantitative differences in many reading and language related areas.

In sum, neurobiological studies of skilled reading comprehension indicate a largely overlapping language circuit for single word reading, reading comprehension and listening comprehension with notable differences being largely quantitative: greater left hemisphere temporal and L. IFG involvement for sentences over words and greater activity in auditory processing regions, (Heschl's gyrus and STG) for auditory relative to visual processing of sentences and greater activity in visual processing regions (extrastriate cortex) for visually relative to auditorally presented sentences. Additionally there is greater involvement of the right hemisphere and prefrontal regions for longer connected narratives relative to single sentences, likely due to the increased need for subtle semantic processing and higher level cognitive processing in maintaining text meaning and drawing inferences.

Impaired reading and comprehension

Examinations of the single word reading with neuroimaging methods in impaired readers have been extremely useful for furthering our understanding of the underlying neurocircuitry. Understanding the way in which poor readers brains respond to processing

connected text, which requires more complex syntactic and semantic processing should provide additional information about the functioning of their impaired systems (e.g., phonological in the case of traditional RD and potentially semantic in the case of SCI) when they are part of a more complex comprehension process (see Meyler et al, in press). Very little research has examined the neurobiological basis of comprehension in poor readers (broadly defined) .

In one recent fMRI study by Meyler et al (in press) that compared good and poor readers in 3rd and 5th grade, participants read sentences and had to decide if they were semantically sensible (e.g., the man fed the dress vs. the man fed the goat). The authors used a whole brain multiple regression analysis and found a significant positive linear relationship between brain activation and increasing reading ability in the L. MTG, R. inferior parietal lobule and L. precentral gyrus – the L. angular gyrus was also correlated with skill in the older group of children (these findings parallel single word studies to an extent). Developmentally, activation in the R. IFG and the R. superior frontal gyrus decreased from 3rd to 5th grade. These findings highlight the importance of the temporoparietal regions and the R. IFG in sentence comprehension. Surprisingly, however, the authors failed to find differences in L. IFG which is routinely active for sentence processing tasks and shows increased activation with increasing difficulty, furthermore, this region is often more active for dyslexic relative to control participants in single word studies (Shaywitz et al, 1998). One potential explanation is the level of reading skill in the Meyler et al study, the poor readers had a variety of reading difficulties, not necessarily dyslexia – the only criteria for poor readers was that they were below the 30th percentile on nonword and word reading assessments and were above the 5th percentile on a vocabulary assessment. Thus, this group likely included mostly “garden variety poor readers” who may also have had lower IQ than the control group. In the previously mentioned study by Plante et al (2006), she compared non-impaired college aged adults to college aged adults with a history of learning disabilities (HLD) who performed significantly worse on a variety of reading and language tasks but had otherwise normal cognitive functioning. Plante and colleagues looked at activation associated with processing of unrelated sentences and of narrative discourse. Participants heard a series of sentences that formed a short story and were later asked a question about the content or they heard a series of unrelated sentences. Plante and colleagues found that during sentence processing, the HLD group, had higher activation in the L. IFG, and reduced activation in the L. SMG during narrative processing. These findings are consistent with findings from another study of German dyslexics who showed greater IFG (in addition to reduced OT and SMG activation) during sentence reading relative to viewing strings of false fonts (Kronbichler et al, 2006). The findings from this group of studies is mixed, largely because of the differences in the types of reading disabled readers – although all of the RD groups discussed all had some word level reading difficulty, their overall RD profile, RD history, age and native languages varied. However, to date there have been no investigations to our knowledge of sentence or discourse processing in RD readers with a well defined, circumscribed reading impairment, thus our current understanding of disabled processing for comprehension is nascent and needs further investigation before the altered circuitry for comprehension can be informative about the relationship between comprehension and reading skill. Furthermore, there have been no neuroimaging investigations that have examined the neurobiology of comprehension in SCI readers – a potentially very important line of research for understanding comprehension processes in general. Although traditionally identified RD readers and SCI readers both have reading comprehension difficulty it is likely to be for very different reasons; dyslexic readers likely suffer from a bottleneck wherein their slow and impaired word reading leads to difficulty with larger texts because of increased working memory demands etc. (Crain & Shankweiler, 1990) and poor comprehenders may have difficulty because of a weakness in a variety of other higher level skills, such as semantic processing (Landi & Perfetti, 2007; Nation &

Snowling, 1998) as discussed above. Again we would expect the neurobiological profile for these two groups to be different if their reading difficulty stems from different sources. In particular we would expect less of a difference in SCI readers neurocircuitry relative to the comparison of traditionally defined RD and TD readers in phonological processing regions as their single word reading is more similar to TD readers. However, like traditionally defined RD readers we would expect large deviances from TD readers during comprehension – but these differences are likely to be of a different nature. One possibility is that these readers will show their primary differences in semantic processing regions (temporal regions, angular gyrus) and in regions that are more heavily recruited for comprehension of longer texts (right hemisphere and prefrontal regions). As mentioned above, a better understanding of the neurobiological profile of SCI (for both single word reading and reading of longer texts) will not only be useful for furthering our understanding of the underlying cognitive processes involved in reading more generally, but will be of critical utility for designing interventions for SCI readers.

Directions for future research

Although the neurocircuitry for single word reading has been relatively well defined for both skilled and impaired readers, the neurocircuitry for reading comprehension (and comprehension in general) is less well understood – particularly for impaired readers. The identification of different subtypes of impaired readers will greatly improve our understanding of the underlying circuitry for comprehension – as subtypes of readers with different profiles (e.g., SCI) are likely to show impairments in different underlying circuits involved in comprehension. For example, those readers with primary impairments at the single word reading level are likely to show larger differences in those regions that are largely overlapping in single word reading and comprehension (e.g., IFG) whereas those readers without word level difficulties are more likely to show differences in areas that are more specific to or taxed more heavily for comprehension (e.g., bilateral temporal regions). Moreover, an understanding of the differences in underlying neurocircuitry for comprehension in impaired readers, particularly those who have specific comprehension impairments, will be important for informing education and remediation beyond the word level because fast and accurate single word reading does not alone make a skilled reader. Another neglected area of cognitive neuroscience research in reading is comprehension development, although there has been extensive behavioral research on the development of comprehension (see Perfetti, Landi & Oakhill, 2005 for a review), and many neuroimaging studies of children that focus on single word processing, most neuroimaging studies of comprehension examine skilled adult readers.

Another shortcoming of past neurobiological research on comprehension is that it has rarely examined reading beyond the single sentence level – in part because of technical limitations involved in neuroimaging design. Reading of larger texts (which makes up the majority of skilled reading activity) uses a somewhat different set of skills – for example a shift from a more simplistic syntactic analysis (e.g., correctly identifying the subject, verb and object) to analysis of the larger meaning and themes of a text. Studies that look at comprehension of larger texts will be critical for understanding some of the more complex aspects of comprehension such as inference making, or comprehension monitoring as well as semantics and working memory. Furthermore, such investigations will provide a closer approximation to naturalistic reading as adult skilled readers rarely read disjoint sentences in isolation. As new techniques and approaches for neuroimaging of more naturalistic behaviors emerge (e.g., fMRI studies that measure activation during a long continuous stimulus such as a movie; Golland et al, 2006), understanding the neurobiology associated with reading or listening to longer narratives becomes a more realistic goal.

Implications for education & practice

Neurobiological studies of word reading and reading comprehension have helped us to further refine our understanding of the component processes involved in these tasks and this knowledge can be useful for guiding appropriate teaching methods. For example, neuroimaging research has highlighted the role of phonological systems for beginning readers, and the role of semantic systems for comprehension. Moreover, neuroimaging research has shown that there is plasticity in the system such that the circuitry for reading can be modulated with appropriate treatment. This line of research has also shown that some children do not respond to evidence based treatment, at both the level of brain and behavior. This work provides concrete evidence that a poor reading system can be re-wired to be a better reading system – and, that even state of the art evidence based treatments do not work for everyone. Critically, ongoing research is looking to identify predictive starting states for appropriate treatment, that is, a way to identify what will likely work for whom based on initial neural response to spoken and written language.

Conclusion

Single word reading and reading of longer texts involve similar networks in the brain – including the L. IFG, L. temporal cortex and L. posterior parietal regions with quantitative differences for some of these regions (greater temporal lobe and IFG activation for sentences and longer connected text relative to single words) and increased involvement of frontal and right hemisphere regions as texts become longer and more complex. Additionally, studies of reading comprehension indicate a large amount of modality independence in the neural network for comprehension, with the exception of visual processing regions (greater activation for visual than auditory presentation) increased STG activation for auditorally presented sentences/texts and greater left lateralization for visually processed sentences. Furthermore, studies that have attempted to isolate component processing have identified regions that are more active for syntactic processing (e.g., IFG) and those that are more active for semantic processing (e.g, Wernicke’s area) within sentence processing and areas that are particularly important for inferential processing (e.g., R.H regions). Finally, however, little research has examined the neurobiological basis of comprehension in struggling readers, for either the more typically identified group of RD readers with phonological deficits or for readers with impairments that are specific to comprehension. Future investigations will need to consider different types or subtypes of reading disability when assessing the neural circuitry for impaired reading as readers with different behavioral profiles, including the poor comprehension profile are likely to show a very different pattern of discrepancy from those with more general language and reading impairments or developmental dyslexia.

References

- Bavelier D, Corina D, Jezzard P, Padmanabhan S, Clark VP, Karni A, Prinster A, Braun A, Lalwani A, Rauschecker J, Turner R, Neville H. Sentences reading: A functional MRI study at 4T. *Journal of Cognitive Neuroscience*. 1997; 9:664–686.
- Beeman M. Semantic processing in the right hemisphere may contribute to drawing inferences from discourse. *Brain and Language*. 1993; 44:80–120. [PubMed: 8467379]
- Beeman MJ, Bowden EM, Gernsbacher MA. Right and left hemisphere cooperation for drawing predictive and coherence inferences during normal story comprehension. *Brain and Language*. 2000; 71:310–336. [PubMed: 10716864]
- Black, SE.; Behrmann, M. Localization in alexia. In: Kertesz, A., editor. *Localization and neuroimaging in neuropsychology*. Academic Press; New York: 1994.

- Booth JR, Burman DD, Van Santen FW, Harasaki Y, Gitelman DR, Parrish TB, Mesulam MM. The development of specialized brain systems in reading and oral-language. *Child Neuropsychology (Neuropsychology, Development and Cognition: Section C)*. 2001; 7:119–41.
- Bottini G, Corcoran R, Sterzi R, Paulesu E, Schenone P, Scarpa P, Frackowiak RS, Frith CD. The role of the right hemisphere in the interpretation of figurative aspects of language. A positron emission tomography activation study. *Brain*. 1994; 117:1241–1253. [PubMed: 7820563]
- Braze D, Shankweiler DP, Mencl WE, Tabor W, Constable RT, Fulbright RK. Sentence Processing by ear and by eye: Homing in on the heteromodal language brain. under review.
- Buchanan TW, Lutz K, Mirzazade S, Specht K, Shah NJ, Ziles K, Lutz J. Recognition of emotional prosody and verbal components of spoken language: an fMRI study. *Cognitive. Brain Research*. 2000; 9:227–38. [PubMed: 10808134]
- Cain K, Oakhill JV. Inference making ability and its relation to comprehension failure. *Reading and Writing*. 1999; 11:489–503.
- Cain K, Oakhill J, Bryant PE. Children's reading comprehension ability: Concurrent prediction by working memory, verbal ability, and component skills. *Journal of Educational Psychology*. 2004; 96:31–42.
- Caplan D, Vijayan S, Kuperberg GR, West C, Waters GS, Greve D, Dale AM. Vascular Responses to Syntactic Processing: Event-Related fMRI Study of Relative Clauses. *Human Brain Mapping*. 2001; 15:26–38. [PubMed: 11747098]
- Constable RT, Pugh KR, Berroya E, Mencl WE, Westerveld M, Ni W, Shankweiler D. Sentence Complexity and Input Modality Effects in Sentence Comprehension: An fMRI Study. *NeuroImage*. 2004; 22:11–21. [PubMed: 15109993]
- Crain, S.; Shankweiler, DP. Explaining failures in spoken language comprehension by children with reading disability. In: Balota, D.; Flores d'Arcais, GB.; Rayner, K., editors. *Comprehension Processes in Reading*. Lawrence Erlbaum; Hillsdale, NJ: 1990. p. 477-508.
- Cutting LE, Clements AM, Courtney S, Rimrodt S, Schafer J, Bisesi J, Pekar JJ, Pugh KR. Differential components of sentence comprehension: Beyond single word reading and memory. *Neuroimage*. 2006; 29:429–38. [PubMed: 16253527]
- Damasio AR, Damasio H. Brain and Language. *Scientific American*. 1992; 267:89–95.
- Demb JB, Boynton GM, Heeger DJ. Brain activation in visual cortex predicts individual differences in reading performance. *Proceedings of the National Academy of Sciences*. 1997; 94:13363–13366.
- Eden G, Brown CP, Jones K, Given B, Zeffiro T. Phonological and visual motion processing in reading impaired children. *Neuroimage*. 2000; 11:S183.
- Eden GF, Stein JF, Wood MH, Wood FB. Verbal and visual problems in reading disability. *Journal of Learning Disabilities*. 1995; 28:272–290. [PubMed: 7775847]
- Eden GF, VanMeter JW, Rumsey JM, Maisog JM, Woods RP, Zeffiro TA. Abnormal processing of visual motion in dyslexia revealed by functional brain imaging. *Nature*. 1996; 382:66–69. [PubMed: 8657305]
- Fiebach CJ, Friederici AD, Mueller K, von Cramon DY. (fMRI). Evidence for dual routes to the mental lexicon in visual word recognition. *Journal of Cognitive Neuroscience*. 2002; 14:11–23. [PubMed: 11798383]
- Fiez JA, Balota DA, Raichle ME, Petersen SE. Effects of lexicality, frequency, and spelling-to-sound consistency on the functional anatomy of reading. *Neuron*. 1999; 24:205–218. [PubMed: 10677038]
- Fiez JA, Peterson SE. Neuroimaging studies of word reading. *Proceedings of the National Academy of Sciences*. 1998; 95:914–921.
- Friederici AD, Ruschemeyer S-A, Hahne A, Fiebach CJ. The Role of Left Inferior Frontal and Superior Temporal Cortex in Sentence Comprehension: Localizing Syntactic and Semantic Processes. *Cerebral Cortex*. 2003; 13:170–177. [PubMed: 12507948]
- Frishkoff GA, Tucker DM, Davey C, Scherg M. Frontal and posterior sources of event-related potentials in semantic comprehension. *Cognitive Brain Research*. 2004; 20:329–354. [PubMed: 15268912]
- Frith U, Ramus F. The role of sensorimotor impairments in dyslexia: A multiple case study of dyslexic children. *Developmental Science*. 2006; 9(3):237–255. [PubMed: 16669791]

- Frost SJ, Mencl WE, Sandak R, Moore DL, Rueckl J, Katz L, Fulbright RK, Pugh KR. An fMRI study of the trade-off between semantics and phonology in reading aloud. *Neuroreport*. 2005; 16:621–624. [PubMed: 15812320]
- Gernsbacher MA, Kaschak MP. Neuroimaging studies of language production and comprehension. *Annual Review of Psychology*. 2003; 54:91–114.
- Golland Y, Bentin S, Gelbard H, Yoav B, Heller R, Nir Y, Hasson U, Malach R. Extrinsic and Intrinsic systems in the posterior cortex of the human brain revealed during natural sensory stimulation. *Cerebral Cortex*. 2006; 17:766–777. [PubMed: 16699080]
- Gough PB, Tunmer WE. Decoding, reading, and reading disability. *RASE: Remedial & Special Education*. 1986; 7:6–10.
- Grodsinsky Y. The neural signature of the language faculty: Suggestions for the future. *Brain and Language*. 2000; 71:82–84. [PubMed: 10716814]
- Indefrey P, Brown CM, Hellwig F, Amunts K, Herzog H, Seitz RJ, Hagoort P. A neural correlate of syntactic encoding during speech production. *Proceedings of the National Academy of Science*. 2001; 98:5933–5936.
- Jackendoff R. Possible stages in the evolution of the language capacity. *Trends in Cognitive Sciences*. 1999; 3:272–279. [PubMed: 10377542]
- Just MA, Carpenter PA, Keller TA, Eddy WF, Thulborn KR. Brain activation modulated by sentence comprehension. *Science*. 1996; 274:114–116. [PubMed: 8810246]
- Katz L, Lee CH, Tabor W, Frost SJ, Mencl WE, Sandak R, Rueckl JG, Pugh KR. Effects of printed word repetition in lexical decision and naming on behavior and brain Activation. *Neuropsychologia*. 2005; 43:2068–2083. [PubMed: 16243052]
- Kronbichler M, Hutzler F, Staffen W, Mair A, Ladurner G, Wimmer H. Evidence for a dysfunction of left posterior reading areas in German dyslexic readers. *Neuropsychologia*. 2006; 44:1822–1832. [PubMed: 16620890]
- Kutas, M.; Van Petten, C. Psycholinguistics Electrified: Event-related potential investigations. In: Gernsbacher, MA., editor. *Handbook of Psycholinguistics*. Academic Press; 1994. p. 83-143.
- Landi N, Perfetti CA. An electrophysiological investigation of semantic and phonological processing in skilled and less-skilled comprehenders. *Brain and Language*. 2007; 102:30–45. [PubMed: 17188346]
- Levelt WJM. Models of word production. *Trends in Cognitive Sciences*. 1999; 3:223–232. [PubMed: 10354575]
- MacDonald MC, Pearlmutter NJ, Seidenberg MS. The lexical nature of syntactic ambiguity resolution. *Psychological Review*. 1994; 101:676–703. [PubMed: 7984711]
- Mason RA, Just MA. How the brain processes causal inferences in text: A theoretical account of generation and integration component processes utilizing both cerebral hemispheres. *Psychological Science*. 2004; 15:1–7. [PubMed: 14717824]
- McCandliss BD, Noble KG. The Development of Reading Impairment: a Cognitive Neuroscience Model. *Mental Retardation and Developmental Disabilities Research Reviews*. 2003; 9:196–204. [PubMed: 12953299]
- McClelland, JL. The case for interactionism in language processing. In: Coltheart, M., editor. *Attention and performance XII: The psychology of reading*. Erlbaum; London: 1987. p. 1-36.
- Myers JL, Shinjo M, Duffy SA. Degree of causal relatedness and memory. *Journal of Memory and Language*. 1987; 26:453–465.
- Meyler A, Keller TA, Cherkassky VL, Lee D, Hoeft F, Whitfield-Gabrieli S, Gabrieli JD, Just MA. Brain activation during sentence comprehension among good and poor readers. *Cerebral Cortex*. in press.
- Michael EB, Keller TA, Carpenter PA, Just MA. fMRI Investigation of Sentence Comprehension by Eye and by Ear: Modality Fingerprints on Cognitive Processes. *Human Brain Mapping*. 2001; 13:239–252. [PubMed: 11410952]
- Nation K, Snowling MJ. Semantic processing skills and the development of word recognition: evidence from children with reading comprehension difficulties. *Journal of Memory and Language*. 1998; 39:85–101.

- Ni W, Constable T, Mencl WE, Pugh KR, Fulbright RK, Shaywitz SE, Shaywitz BA, Gore JC. An Event-Related Neuroimaging Study: Distinguishing Form and Content in Sentence Processing. *Journal of Cognitive Neuroscience*. 2000; 12:120–133. [PubMed: 10769310]
- Paulesu E, Goldacre B, Scifo P, Cappa SF, Gilardi MC, Castiglioni I, Perani D, Fazio F. Functional heterogeneity of left inferior frontal cortex as revealed by fMRI. *Neuroreport*. 1997; 8:2011–2016. [PubMed: 9223094]
- Peelle JE, McMillan C, Moore P, Grossman M, Wingfield A. Dissociable patterns of brain activity during comprehension of rapid and syntactically complex speech: Evidence from fMRI. *Brain and Language*. 2004; 91:315–325. [PubMed: 15533557]
- Perfetti, CA.; Hart, L. The lexical quality hypothesis. In: Verhoeven, L.; Elbro, C.; Reitsma, P., editors. *Precursors of functional literacy*. John Benjamins; Amsterdam/Philadelphia: 2002. p. 189–213.
- Perfetti, CA.; Landi, N.; Oakhill, J. The acquisition of reading comprehension skill. In: Snowling, MJ.; Hulme, C., editors. *The science of reading: A handbook*. Blackwell; Oxford: 2005. p. 227–247.
- Plante E, Ramage AE, Magloire J. Processing Narratives for Verbatim and Gist Information by Adults with Language Learning Disabilities: A Functional Neuroimaging Study. *Learning Disabilities Research & Practice*. 2006; 21:61–76.
- Poldrack RA, Wagner AD, Prull MW, Desmond JE, Glover GH, Gabrieli JD. Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. *Neuroimage*. 1999; 10:15–35. [PubMed: 10385578]
- Price CJ, More CJ, Humphreys GW, Wise RJS. Segregating semantic from phonological processes during reading. *Journal of Cognitive Neuroscience*. 1997; 9:727–733.
- Price CJ, Winterburn D, Giraud AL, Moore CJ, Noppeney U. Cortical localization of the visual and auditory word form areas: A reconsideration of the evidence. *Brain and Language*. 2003; 86:272–286. [PubMed: 12921768]
- Price CJ, Wise RJS, Frackowiak RSJ. Demonstrating the implicit processing of visually presented words and pseudowords. *Cerebral Cortex*. 1996; 6:62–70. [PubMed: 8670639]
- Pugh KR, Frost SJ, Sandak R, Landi N, Rueckl JG, Constable RT, Seidenberg M, Fulbright R, Katz L, Mencl WE. Effects of stimulus difficulty and repetition on printed word identification: An fMRI comparison of non-impaired and reading disabled adolescent cohorts. *Journal of Cognitive Neuroscience*. in press.
- Pugh KR, Mencl WE, Jenner AR, Katz L, Frost SJ, Lee JR, Shaywitz SE, Shaywitz BA. Functional neuroimaging studies of reading and reading disability (developmental dyslexia). *Mental Retardation & Developmental Disabilities Research Reviews*. 2000a; 6:207–213. [PubMed: 10982498]
- Robertson DA, Gernsbacher MA, Guidotti SJ, Robertson RWR, Irwin W, Mock BJ, Campana ME. Functional neuroanatomy of the cognitive process of mapping during discourse comprehension. *Psychological Science*. 2000; 11:255–260. [PubMed: 11273413]
- Roskies AL, Fiez JA, Balota DA, Raichle ME, Petersen SE. Task-dependent modulation of regions in the left inferior frontal cortex during semantic processing. *Journal of Cognitive Neuroscience*. 2001; 13:829–843. [PubMed: 11564326]
- Sandak R, Mencl WE, Frost S, Pugh KR. The neurobiological basis of skilled and impaired reading: Recent findings and new directions. *Scientific Studies of Reading*. 2004b; 8:273–292.
- Sandak R, Mencl WE, Frost SJ, Rueckl JG, Katz L, Moore D, Mason SM, Fulbright RK, Constable RT, Pugh KR. The neurobiology of adaptive learning in reading: A contrast of different training conditions. *Cognitive, Affective, & Behavioral Neuroscience*. 2004; 4:67–88.
- Sarkari S, Simos PG, Fletcher JM, Castillo EM, Breier JI, Papanicolaou AC. The emergence and treatment of developmental reading disability: Contributions of functional brain imaging. *Seminars in Pediatric Neurology*. 2002; 9:227–236.
- Shaywitz B, Shaywitz S, Blachman B, Pugh KR, Fulbright R, Skudlarski P, Mencl WE, Constable T, Holohan J, Marchione K, Fletcher J, Lyon R, Gore J. Development of left occipitotemporal systems for skilled reading following a phonologically based intervention in children. *Biological Psychiatry*. 2004; 55:926–933. [PubMed: 15110736]

- Shaywitz SE, Shaywitz BA, Fulbright RK, Skudlarski P, Mencl WE, Constable RT, Pugh KR, Holohan JM, Marchione KE, Fletcher JM, Lyon GR, Gore JC. Neural systems for compensation and persistence: Young adult outcome of childhood reading disability. *Biological Psychiatry*. 2003; 54:25–33. [PubMed: 12842305]
- Shaywitz SE, Shaywitz BA, Pugh KR, Fulbright RK, Constable RT, Mencl WE, Shankweiler DP, Liberman AM, Skudlarski P, Fletcher JM, Katz L, Marchione KE, Lacadie C, Gatenby C, Gore JC. Functional Disruption in the Organization of the Brain for Reading in Dyslexia. *Proceedings of the National Academy of Sciences*. 1998; 95:2636–2641.
- Shaywitz BA, Shaywitz SE, Pugh KR, Mencl WE, Fulbright RK, Constable RT, Skudlarski P, Jenner A, Fletcher JM, Marchione KM, Shankweiler D, Katz L, Lacadie C, Gore JC. Disruption of posterior brain systems for reading in children with developmental dyslexia. *Biological Psychology*. 2002; 52:101–110.
- Simos PG, Fletcher JM, Bergman E, Breier JI, Foorman BR, Castillo EM, Davis RN, Fitzgerald M, Papanicolaou AC. Dyslexia-specific brain activation profile becomes normal following successful remedial training. *Neurology*. 2002; 58:1203–1213. [PubMed: 11971088]
- Stein J. Visual motion sensitivity and reading. *Neuropsychologia*. 2003; 41:1785–1793. [PubMed: 14527541]
- Stowe LA, Paans AM, Wijers AA, Zwarts F, Mulder G, Vaalburg W. Sentence comprehension and word repetition: a positron emission tomography investigation. *Psychophysiology*. 1999; 36:786–801. [PubMed: 10554592]
- Strain E, Patterson K, Seidenberg MS. Semantic effects in single-word naming. *Journal of Experimental Psychology: Learning, Memory, and Cognition*. 1995; 21:1140–1154.
- Tallal P. Auditory temporal perception, phonics, and reading disabilities in children. *Brain and Language*. 1980; 9:182–198. [PubMed: 7363063]
- Temple E, Deutsch GK, Poldrack RA, Miller SL, Tallal P, Merzenich MM, Gabrieli JDE. Neural deficits in children with dyslexia ameliorated by behavioral remediation: Evidence from functional MRI. *Proceedings of the National Academy of Sciences*. 2003; 100:2860–2865.
- Thompson-Schill, SL. Dissecting the language organ: A new look at the role of Broca's area in language processing. In: Cutler, A., editor. *Twenty-First Century Psycholinguistics: Four Cornerstones*. 2005.
- Turkeltaub PE, Gareau L, Flowers DL, Zeffiro TA, Eden GF. Development of neural mechanisms for reading. *Nature Neuroscience*. 2003; 6(7):767–73.
- Vellutino FR, Fletcher JM, Snowling MJ, Scanlon DM. Specific reading disability (dyslexia): what have we learned in the past four decades? *Journal of Child Psychology and Psychiatry*. 2004; 45:2–40. [PubMed: 14959801]
- Xu B, Grafman J, Gaillard WD, Ishii K, Vega-Bermudez F, Pietrini P, Reeves-Tyer P, DiCamillo P, Theodore W. Conjoint and extended neural networks for the computation of speech codes: The neural basis of selective impairment in reading words and pseudowords. *Cerebral Cortex*. 2001; 11:267–277. [PubMed: 11230098]
- Zeffiro T, Eden G. The neural basis of developmental dyslexia. *Annals of Dyslexia*. 2000; 50:3–30.

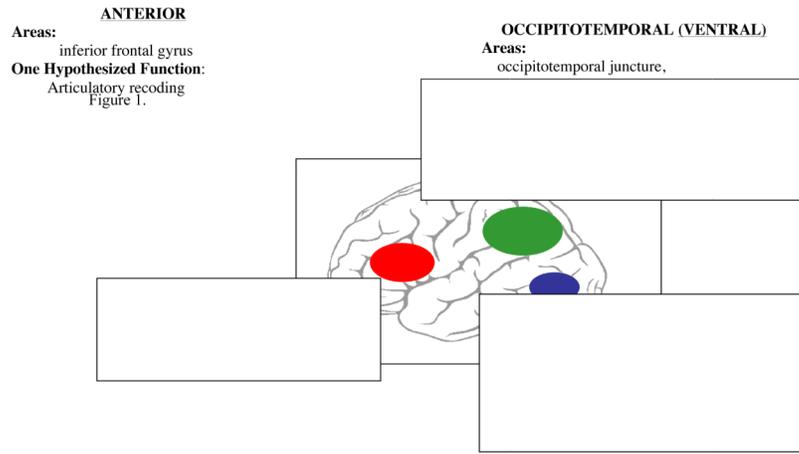


Figure 1. Simplified diagram of the neurocircuitry for single word reading, adapted from Pugh et al. (2000)