WHERE AND WHEN MEANING OCCURS IN THE BRAIN:

EVIDENCE FOR A NEUROBIOLOGICAL MODEL OF READING COMPREHENSION ABILITY

By

Katherine S. Aboud

Dissertation
Submitted to the Faculty of the
Graduate School of Vanderbilt University
in partial fulfillment of the requirements
for the degree of
DOCTOR OF PHILOSOPHY
in
NEUROSCIENCE
December 14, 2019
Nashville, Tennessee

Approved:
Laurie E. Cutting, Ph.D.
Gavin R. Price, Ph.D.
Alexandra P. Key, Ph.D.
Bennett A. Landman, Ph.D.
David H. Zald, Ph.D.

DEDICATION

This work is dedicated to my sister, Christa, for her sincerity and wit; my mom, Laura, for making every day a bright one; my dad, Bruce, for his advice on life and robots; my son, Sami, for keeping me in the moment; and my husband, Asaad, for being hilarious and always having my back.

ACKNOWLEDGEMENTS

This body of work has been supported by a huge team of researchers and staff, who are not only excellent scientists and organizers, but also amazing people. The lab members at Vanderbilt's Education and Brain sciences Research Lab (EBRL) have put in countless hours to assist in organizing this study, collecting data, and training me in all stages of the research process. Julie Delheimer, Lanier Sachs, and Laura Barquero each provided selfless assistance in guiding me through the IRB, subject recruitment, and data collection stages of research for this project, in addition to almost single-handedly running the show for ever other project I've been involved in. My fellow PhD students and post-doctoral fellows in the lab have enriched my entire experience in the PhD program, both in terms of interesting thoughts and meaningful friendships, and have directly contributed to the present work through their insight and constant encouragement. In particular, Neena Saha and Sage Pickren have challenged me to actively connect my research questions to real-world applications in education. Tin Nguyen has provided countless hours of statistical support, general morale boosting, and wonderful conversations on art and philosophy. Dr. Stephanie Del Tufo freely gave of her time and mentorship to support my in-depth statistical and logic questions. Dr. Laura Barquero provided encouraging mentorship and friendship throughout my years at EBRL, and taught me how to be a conscientious scientist.

Outside of EBRL, the broader Vanderbilt community of researchers and staff have provided vital assistance for my growth as a researcher. The Vanderbilt University Institute of Imaging sciences and the team of MRI technicians were responsible for assisting in all of the MRI data collection. This includes support from their grant 1S10OD021771-01 for the 3T MRI, housed in the Vanderbilt Center for Human Imaging. The Vanderbilt Institute for Clinical and

Translational Research (VICTR) also provided funding to the current project; VICTR is funded by the National Center for Advancing Translational Sciences (NCATS) Clinical Translation Science Award (CTSA) Program (5UL1TR002243-03). The Vanderbilt Kennedy Center and the EEG system supported by the Neuroimaging Core C provided access and technical support for its EEG system, all of which was supported by the U54 HD083211 grant. Dr. Key, a member of my committee, provided indispensable training in EEG collection and analysis. Her kind mentorship allowed me to pursue my goal of training in multiple imaging modalities. The other members of my committee also provided incredible support throughout my PhD experience. Dr. Gavin Price, the chair of my committee, encouraged my growth in rigorous, theoretically driven hypotheses, and emphasized the need for clinically-driven neuroimaging research. Dr. Bennett Landman taught me how to be truly inter-disciplinary and to not be afraid of big data. Dr. David Zald constantly contributed thoughtful advice, and encouraged me to pursue multiple avenues of inquiry for every research question. Also, I'd like to give a special thanks to Dr. Catie Chang for her support and mentorship related to the joint ICA pipeline.

Lastly, this line of research would not have occurred without the amazing support from my mentor, Dr. Laurie Cutting. Dr. Cutting provided the mentorship, research support (including R01 HD044073, R01 HD067254, and others), and intellectual encouragement for me to become an independent researcher. Her guidance has constantly pushed me to become a more critical thinker without sacrificing the accessibility of the findings. She has also shown me that it is, in fact, feasible to be an excellent scientist and a happy, generous person.

TABLE OF CONTENTS

Page

CHAPTER

LIST OF TABLES

Table **Page**

*See Appendix for additional tables

LIST OF FIGURES

LIST OF ABBREVIATIONS

RC	Reading comprehension
BR	Basic reading
TD	Typically developing reader
DYS	Dyslexia
S-RCD	Specific reading comprehension deficits
OT	Occipitotemporal cortex
VWFA	Visual word form area
SMG	Supramarginal gyrus
MTG	Middle temporal gyrus
STG	Superior Temporal gyrus
TP	Temporal pole
IFG	Inferior frontal gyrus
dlPFC	Dorsolateral prefrontal cortex
dmPFC	Dorsomedial prefrontal cortex
MFG	Middle frontal gyrus
SFG	Superior frontal gyrus
ACC	Anterior cingulate cortex
PCC	Posterior cingulate cortex
PCU	Precuneus
AG	Angular gyrus
IPL	Intraparietal lobule
DMN	Default mode network

Chapter 1

Introduction: Neurobiological studies of reading comprehension ability

Motivation

Reading comprehension (RC) ability is a critical skill that predicts long-term educational and occupational outcomes (Ricketts, Sperring, & Nation, 2014; Ritchie & Bates, 2013). Yet 20% of adults in the U.S. are unable to understand the meaning of a written sentence (U.S. Department of Education, 2019). While word decoding, or the ability to "sound out" words, has received considerable attention over the past several decades, we now know that adequate RC requires appropriate integration across multiple processing domains (Ferstl, Neumann, Bogler, & von Cramon, 2008; Kendeou, van den Broek, Helder, & Karlsson, 2014; Sesma, Mahone, Levine, Eason, & Cutting, 2009). Consequently, while some reading difficulties result from poor word decoding, an estimated 10% of readers with typical IQ and word decoding ability still have poor RC ability (Stothard & Hulme, 1995). These specific reading comprehension deficits (S-RCD) may stem from language difficulties as early as 15 months old (Justice, Mashburn, & Petscher, 2013), but often first become apparent in early adolescence (10-14 year olds), when typical reading curriculum shifts from a focus on reading fluency (i.e. "learning to read") to an emphasis on extracting meaning from texts (i.e. "reading to learn"; Yovanoff, Duesbery, Alonzo, & Tindal, 2005). Even within the range of typical RC ability, decoding ability only accounts for 27% of RC ability in second grade, and decreases to 2% in eighth grade (Catts, Hogan, & Adlof, 2005; Hogan, Adlof, & Alonzo, 2014).

Behavioral studies have found that RC ability independent of decoding (heretofore referred to just as RC ability) is related to measures of vocabulary knowledge (Cain & Oakhill, 2006; Kate Nation, Snowling, & Clarke, 2007; Spencer, Quinn, & Wagner, 2014), integration of semantic information within and across sentences (Oakhill, Cain, & Bryant, 2003; Oakhill & Cain, 2012), and executive functions such as working memory and planning/organizational ability (Cutting et al., 2009; Nation et al., 1999), with some studies additionally showing relationships to grammar (Catts, Adlof, & Ellis Weismer, 2006; Nation, Clarke, Marshall, & Durand, 2004). This wide range of behaviors associated with individual differences in RC have led to significant debate on the fundamental nature of RC ability and related deficits, including whether RC ability is more strongly associated with single word or multi-word/discourse processes, and more dependent on semantic or executive systems (as discussed in Landi & Ryherd, 2017). Importantly, behavioral approaches are limited in their ability to address these questions. First, neural processes do not always map to behavioral differences in subpopulations or conditions: neuroimaging has been found to differentiate conditional responses in the absence of reaction time differences (Duncan et al., 2009), and identify reader sub-groups who do not demonstrate behavioral differences (Aboud, Barquero, & Cutting, 2018). Second, one behavioral output can be the result of many different underlying neural processes (see Discussion). Lastly, behavioral measurements are often conflated (for instance working memory and decoding), making their independent contributions to RC ability difficult to parse (Stuebing et al., 2015). Consequently, understanding the complex and flexible neural interactions that support RC and RC ability require the use of neuroimaging approaches.

In the present paper, I first briefly summarize the neurocognitive processes that support general RC (for full reviews, see Introductions for Chapters 2 and 3), and then use this framework to present a systematic review of studies that have explicitly examined RC ability in the brain. I then address the limitations of the field, and what future studies need to achieve to develop a neurobiological model of RC ability.

The Neurobiology of Reading Comprehension (RC)

RC requires dynamic coordination of multiple brain systems. Once orthographic-to-phonological mapping occurs in the fusiform, inferior frontal (IFG), and supramarginal gyri (SMG; Richlan, Kronbichler, & Wimmer, 2011), the meaning of a word relies on systems in the temporal lobe (Davey et al., 2015; Peter Hagoort, 2013; Lau, Phillips, & Poeppel, 2008; Visser, Jefferies, Embleton, & Lambon Ralph, 2012). The temporal poles (TP) are thought to act as amodal semantic hubs that consolidate widespread cortical activations associated with semantic re-activation from long-term memory (Jefferies, 2013). The left middle temporal gyrus (MTG) may be involved in these retrieval processes, while also playing a role in restricting semantic re-activation to the current context/goal (Davey et al., 2016; Hagoort, 2013; Whitney, Kirk, O’Sullivan, Lambon Ralph, & Jefferies, 2012). The frontal cortex, specifically bilateral IFG play a more active role in combinatorial processes that unify individual words into a multi-word context (Davey et al., 2016; Friederici, 2011; Peter Hagoort, 2005). The ventral IFG is widely thought to support semantic combinations of words (i.e. “semantic integration”), while the dorsal IFG appears to more specifically support the logical structures of a sentence (i.e. “syntax”) (Friederici & Gierhan, 2013).

At the highest level of reading, adequate RC requires the building, maintenance, and updating of an internal, cross-sentence representation of a text (i.e. the “situation model”). Studies that examine story comprehension versus sentence and word reading show a consistent set of domain-general processing areas whose internal correlations have been found to encode story-level information (Baldassano et al., 2017a; Ferstl et al., 2008; Mar, 2011; Simony et al., 2016). Specifically, the default mode network (DMN) is a set of coordinated brain areas that supports internalized cognition. Regions within the DMN have been found to individually play diverse roles in discourse comprehension: the left angular gyrus (AG) supports long time-scale conceptual integration of ideas (Baldassano et al., 2017a; Seghier, 2013); bilateral AG activation, right-dominant, supports social cognition required to understand character mindsets(Saxe, Moran, Scholz, & Gabrieli, 2006; Saxe & Wexler, 2005); the medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC) support self-centric mentalization processes (Saxe et al., 2006); and the precuneus (PCU) is thought to encode the coherence and boundaries of narrative events (Whitney et al., 2009). Lastly, from the word- to discourse-levels there appears to be an important role for lateral prefrontal regions that support executive functions (Aboud et al., 2018; Aboud, Bailey, Del Tufo, Barquero, & Cutting, 2019). These areas, in particular the left dorsolateral prefrontal cortex (dlPFC), have been proposed to facilitate each of the neurocognitive processes required for adequate RC (Aboud et al., 2018).

While fMRI studies have provided excellent spatial understanding of *where* reading processes occur, event-related potentials (ERPs) allow for identification of *when* these diverse array of processes occur. Two ERP components have been of particular interest in studies of language above the phonological-orthographic level. The N400 component is a negative waveform that peaks approximately 300-500 ms after a stimulus (Kutas & Hillyard, 1980). During RC, the N400 is followed by the P600, a positive waveform that peaks approximately 600-800 ms after a stimulus (Lee Osterhout & Holcomb, 1992). Importantly, the amplitudes of these two components are dependent on specific dimensions of the preceding stimulus. In the context of reading, words that are harder to integrate into the preceding semantic context have greater N400 negativity, a phenomenon referred to as the N400 effect. Numerous studies have revealed that the N400 effect is sensitive to semantic incongruency at the word, sentence, and discourse-levels, and shows additive effects if there are multiple levels of incongruency (Stafura & Perfetti, 2014; Van Petten, Weckerly, Mclsaac, & Kutas, 1997; for full review see Kutas & Federmeier, 2011). Localization studies reveal that the N400 does not stem from a unified spatial source, but instead likely reflects a task-dependent wave of activation across language areas (Kutas & Federmeier, 2011). This has led some to suggest that the N400 reflects the iterative communication between semantic retrieval and integration processes (Peter Hagoort, 2013). Notably, the N400 is not sensitive to the syntactic difficulty of a sentence. Conversely, the P600 is strongly impacted by syntactic difficulty/incongruency of a sentence (Gouvea, Phillips, Kazanina, & Poeppel, 2010; Lee Osterhout & Holcomb, 1992). Interestingly, recent literature has also found that semantic incongruency at the sentence level (i.e. whether a sentence is “silly” or makes sense) also produces a strong P600 effect. These findings have led to considerable debate about the role of the P600 in language processing. Some theories maintain that the P600 is a syntactic component that is activated for silly sentences because the reader is attempting to re-appraise the syntactic structure to make sense of the sentence meaning (Lee Osterhout, Kim, & Kuperberg, 2012). Others propose that the P600 is a more general re-appraisal component that can be impacted by syntactic or semantic information, and potentially localize to different circuits accordingly (Leckey & Federmeier, 2019). Still others propose that the P600 is primarily a semantic integration component (Brouwer, Fitz, & Hoeks, 2012; Brouwer & Hoeks, 2013). Localization studies suggest that the P600 have pointed to variable structures, including fronto-parietal areas (Kielar, Panamsky, Links, & Meltzer, 2015), and temporal areas (Kielar et al., 2015; Service, Helenius, Maury, & Salmelin, 2007; Yang, Perfetti, & Liu, 2010); consequently, more study is needed to identify the potentially diverse sources and functions for the P600.

Current MRI and ERP research emphasize the fact that adequate RC requires complex and timely communication across brain regions. In the present systematic review, we report the state-of-the-art neurobiological understanding of individual differences in RC ability. We then propose what steps the field needs to take to identify the specific neural mechanisms that underlay individual differences in RC ability, independent of word decoding. Finally, we map out how the current dissertation will address the gaps in the literature, and move towards a comprehensive neurobiological model of individual differences in RC ability.

Methods

To identify studies that used neuroimaging to examine RC ability, we used six inclusion criteria. First, only peer-reviewed studies were included. Second, the studies were required to use either event-related potentials (ERP) or MRI. Third, the studies had to include a metric of RC ability that was examined in the neuroimaging analysis (of note, measurements in which RC ability was conflated with another cognitive behavior were excluded; e.g. reading span working memory tasks or component measures of reading that combined decoding and RC). Fourth, stimuli (in functional modalities) were limited to reading tasks, language tasks, or resting state. Fifth, subjects could not have a clinical or psychiatric pathology, developmental disorder, language disorder, or hearing/speech disorder. ADHD and dyslexia were not automatically excluded. ADHD groups were included due to high comorbidity with RC ability. While RC deficits related to dyslexia are outside the scope of this review, papers that met the search criteria and included populations with dyslexia were not immediately excluded. If the study's methods allowed for distinctions between word reading ability and RC ability, they were included in the final list, and are discussed within this context. For our sixth inclusion criteria, we required that all studies had no quality “flags”. In particular, studies had to have results reported at p-corrected < 0.05, including multiple comparison corrections for univariate brain analyses or extensive behavioral correlations. Additionally, as we were interested in whole-brain patterns related to RC ability, we excluded papers that restricted examinations to single regions of interest.

To identify studies that met the inclusion criteria, we followed a three-step process (see Figure 1.1). First, searches were conducted in three online databases, *ProQuest*, *PubMed*, and *Web of Science* for all available years. The following Boolean operations were used (with the peer-reviewed option checked, and duplicate entries excluded) within the fields of “anywhere but full text” (“noft”; ProQuest), MeSH terms (PubMed), and Topic (“TS”; Web of Science):

<<“magnetic resonance imaging” OR “MRI” OR "ERP" OR "event-related potentials"> AND <"skilled comprehenders" OR "poor comprehenders" OR “comprehension ability” OR “comprehension abilities” OR “comprehension skill” OR “comprehension expertise” OR “specific reading comprehension” OR “S-RCD” OR “SRCD” OR “comprehension disorder” OR “comprehension deficits” OR “comprehension deficit”> NOT autism NOT schiz* NOT lesion NOT aphasia NOT bilingual NOT deaf NOT “specific language impairment” NOT stroke NOT traumatic brain injury NOT Parkinson’s NOT Alzheimer’s>.

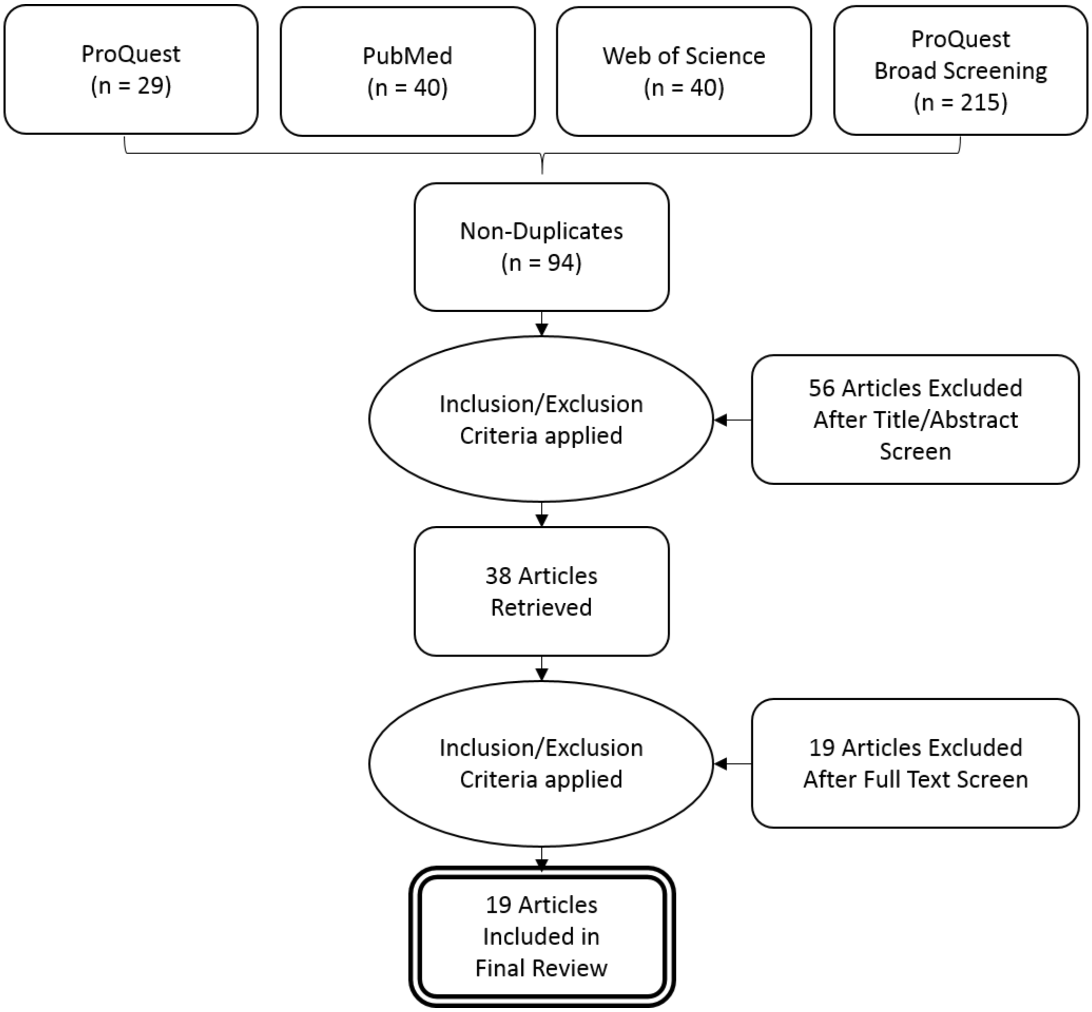


Figure 1.1: Flowchart of literature search for the systematic review.

Our search yielded 62 unique results. In our second identification step, we reviewed abstracts and, if necessary, methods sections to identify whether papers met the six inclusion criteria mentioned above. This second step resulted in 22 articles. We read these articles in full, again applying the defined inclusion/exclusion criteria, which resulted in the inclusion of 13 articles (see Appendix for study details). As a final stage, we ran one additional search in ProQuest that was identical to the search described above, but with the inclusion of the term “reading comprehension”, and the exclusion of the term “dyslexia”. This search was meant to ensure that studies were not excluded if they had unique phrases indicating the examination of RC ability in the brain. This search resulted in 215 unique studies. After an abstract review, 16 studies were selected for a full read-through, and, of these, 6 studies were found to meet all criteria. As a result, 19 studies total were included in the final review. The studies represented a diverse array of examination for RC ability in the brain. The primary dimensions in which the studies varied were: (1.) imaging modality (fMRI or ERP), (2.) reading task (word or sentence/passage), and (3.) population (typical readers, readers with S-RCD, resilient readers with dyslexia; children, adolescents, and adults). Across all of the studies, there was considerable variability on how basic reading (i.e. decoding) processes were treated. Consequently, the treatment of basic reading is included as a discussion point throughout the review.

Review of the Neurobiology of RC Ability

Functional MRI studies of word reading

The fMRI studies on word reading reveal associations between RC ability and language, memory, and executive areas of the brain, even at the single word level. Cutting et al. (2013) was the first neuroimaging study to examine populations with S-RCD. The study examined typically developing (TD) readers, readers with dyslexia (DYS) and readers with S-RCD as they read single words that were either low or high frequency (i.e. harder or easier semantic retrieval, respectively). Functional connectivity analysis revealed that readers with S-RCD showed several differences in IFG function compared to TD. During hard retrieval (i.e. low vs. high frequency word reading), S-RCD had (1.) greater coupling between the left IFG and hippocampus and motor areas, and (2.) less adaptive recruitment of the right IFG to support the left IFG during difficult semantic processing. S-RCD also showed qualitatively lower activations in the left TP compared to TD.

Unlike DYS, as compared to TD, S-RCD did not show any significant differences in brain regions associated with orthographic or phonological processing. These findings were the first to reveal that S-RCD has a unique neural signature compared to TD and DYS, which involves activation differences in semantic retrieval areas during word reading.

In parallel findings within a typical adult population, Malins et al. (2016) found associations between higher RC ability and activations in the left IFG (dorsal and ventral), as well as in the left fusiform and left precentral gyrus during more difficult semantic retrieval (non-primed versus primed word pairs). These findings did not control for word decoding ability, which potentially accounts for associations with the fusiform gyrus and the IFG. In contrast, Welcome & Joanisse (2012) found that RC ability was anti-correlated with the anterior cingulate cortex (ACC) and the left MTG. These activations were qualitatively different from correlations with orthographic and phonological processing ability. Consistent with models in which the left MTG is the semantic retrieval “hub”, lower activation in the left MTG may signal increased efficiency in word retrieval processes for adults with higher RC ability. However, it is important to note that the study did not report a baseline comparison to the word judgment task in the correlation analysis, and consequently, the findings appear to be conflated with domain-general judgment processes.

In the most recent study on RC ability and word reading, Ryherd et al. (2018) examined brain activations in older adolescents as they read and listened to words and passages. Using a Partial Least Squares (PLS) approach, they found that higher RC ability mapped onto greater activation in a wide range of areas in visual words (and passages), including memory regions (parahippocampal gyrus), visual areas, orthographic areas (fusiform gyrus), and language areas including bilateral temporal poles (TP), MTG and left IFG (notably, the TP was not identified in the tables, but was present in the figures; see Discussion). Lower RC corresponded with increased activation in executive areas, specifically the left dlPFC and ACC, as well as the anterior insula. Word reading ability was within the normal range for the population, but was not controlled for in the analyses.

Summary of functional MRI studies of word reading

Despite different methodologies and populations, word reading studies on RC ability showed some consistencies. First, children, adolescents, and adults showed anomalous activation patterns of the IFG in lower comprehenders. Notably, these relationships were significant for both passive (Ryherd et al., 2019) and active (Cutting et al., 2019) word reading paradigms, and so appear to be generalizable in terms of population and task. Associations with the temporal lobes were less consistent: adolescents and adults showed a relationship between RC ability and bilateral/left MTG, but this relationship was positive for adolescents and negative for adults. These differences could reflect developmental changes in neural requirements for efficient RC, but inconsistencies cannot be easily resolved due to differences in populations and stimuli (passive word reading versus word judgement). The TP only appeared in one study, but were not included as a region of interest in Malins et al. (2016). However, Cutting et al. (2013) did show qualitatively greater activation in this area for TD versus S-RCD. As the TP are often under-examined in fMRI studies due to coverage constraints and lack of distinction from other temporal structures (as discussed in (Pobric, Jefferies, & Ralph, 2007), more study is needed to understand the role of the TP in RC ability during word-level reading (see Chapters 2 and 4). Studies additionally revealed associations with RC ability and non-language areas, including (1.) the hippocampus in children and adolescents, and (2.) domain-general frontal areas (ACC, dlPFC, and dmPFC). These findings suggest that there may be a role for executive and memory processes in RC ability at the single word level.

ERP studies of word reading

ERP studies of word reading and RC ability are limited to typical adult readers, and largely assume in-tact decoding processes. Within that context, however, there are several consistent findings, including a close association between RC ability and both the N400 and P600 effects during word reading. Perfetti, Wlotko, & Hart (2005) examined word learning processes in typical college students with a range of RC ability. Students were trained in unfamiliar rare words, then performed a semantic judgement task in which the trained words, familiar words, and rare untrained words were paired with a second semantically related or unrelated word. Analysis with RC ability revealed that the expected N400 effect for unprimed versus primed words was larger in skilled versus unskilled comprehenders. Interestingly, stronger comprehenders additionally showed a greater P600 effect in trained versus untrained words compared to weaker comprehenders. The researchers suggest that this reflects a stronger memory trace for recently learned words in the P600 for stronger comprehenders, providing one of the first links between the P600 and RC ability. The sensitivity of the P600 to learning effects, as well as the fact that the P600 was observed after a single word presentation, argues against the possibility that the observed P600 effect was driven by multi-word syntactic processes. In a follow-up study, Balass, Nelson, & Perfetti (2010) replicated the relationship between RC ability and the N400 effect, and found that the N400 and P600 effects were driven by newly learned semantic properties of the word, particularly when the orthographic and semantic dimensions of the new word were learned together, suggesting a specific role for these effects in written language.

Other studies have failed to find a relationship between the N400 effect and RC ability in typical adult readers during word reading (Stafura & Perfetti, 2014a), with one study revealing that RC ability only correlated with word-priming effects in which there was a forward association (i.e. the first word primes the second word), but was absent during backwards association (Stafura, Rickles, & Perfetti, 2015). Interestingly, this effect is reversed during word priming effects that are embedded in a sentence (see Discourse Comprehension).

In the final ERP word reading study identified for this review, Landi & Perfetti (2007) had typical adult readers with a range of RC ability perform word pair and picture pair priming tasks. The word task included categorical (e.g. horse and dog) and associative (e.g. horse and mane) semantic relationships. They found that RC ability only corresponded with N400 effects in the word priming task, not the picture priming or phonological tasks. Secondly, higher RC corresponded with N400 effects across categorical and associative pairs vs unprimed word pairs. Interestingly, higher RC showed a greater N400 reduction for associative than categorical priming, suggesting associative semantic priming facilitates easier semantic retrieval than categorical priming. Conversely, lower RC showed reduced (but present) N400 effects across all tasks, and less benefit from associative priming compared to categorical. The authors also noted general late positivity differences in the P600 range between RC groups, with stronger comprehenders have greater positivity regardless of task. Finally, the authors found strong associations between an early positivity (the P200) and RC ability, with stronger readers showing a greater P200 effect for semantically related vs. unrelated pairs. Overall these findings demonstrate global reductions of semantic processes in lower comprehenders that are specific to language (as evidenced by a lack of group difference in picture priming), and indicate that these effects may have earlier onsets than the traditional N400 window.

Summary of ERP studies of word reading

ERP studies on word reading and RC ability reveal that stronger comprehenders show a greater N400 effect that is driven by semantic properties of the words, and which is assisted by associative more than categorical semantic relationships. Additionally, stronger comprehenders have a greater P600 effect at the single word level which is modulated by semantic content and training. The interpretation of the P600 effect as a memory trace parallels the hippocampal/parahippocampal findings in Cutting et al. (2009) and Ryherd et al. (2018), as do the N400 findings, since the N400 has been associated with both IFG and MTG (Kutas & Federmeier, 2011).

Functional MRI studies of discourse comprehension

Similar to word reading paradigms, only a handful of studies have examined relationships between RC ability and discourse-level processes (including sentences and connected passages), and a wide range of methodologies provide limited granularity in terms of specific brain region contributions to RC ability. In adult readers, Shankweiler et al. (2008) provided a thorough examination into how RC ability corresponded with activations during visual and auditory sentence comprehension, and provided some potential insight in the role of frontal versus temporal contributions to RC ability. Subjects read or listened to visual or auditory sentences that were incongruent or congruent (including both syntactic and semantic incongruence). They found that incongruent visual sentences elicited greater activations primarily in bilateral IFG, the left angular gyrus, and bilateral frontal regions in readers with higher RC (MFG and SFG; see Appendix for additional areas). Interestingly, they did not find associations with the MTG or other temporal areas. Conversely, the primary correlation with RC ability in the spoken sentences (incongruent versus congruent) was in the left MTG, with some correlation in left frontal areas as well. The strongest comprehenders were also found to have the highest speech-print convergence (i.e. overlapping activation across RC modalities) in the left dorsal IFG. The authors proposed that with increased RC ability (and reading ability in general), language processes have less modal distinctions, and instead begin to converge in frontal speech circuits. This study consequently suggests a prominent role for the left IFG in RC ability, with modality-specific associations in temporal areas.

In another study, Horowitz-Kraus et al. (2013) examined adolescents as they listened to narratives, and, similar to Shankweiler et al.'s (2008) auditory results, found positive associations between temporal activations (left MTG and left TP) and RC ability. In a separate approach, however, Horowitz-Kraus et al. (2015, 2013) found that both frontal and temporal/temporoparietal areas during passage comprehension at age 6 predicted better RC later in life. The interpretation of these differences are unclear, but raise important questions regarding the early versus later developmental biomarkers of RC ability, and differential contributions of frontal versus temporal areas to RC ability. Making these distinctions will likely require increasingly nuanced paradigms and spatiotemporally sensitive neuroimaging approaches. For example, Ryherd et al. (2018) found widespread associations between RC ability and fronto-temporal language and executive areas during passage reading in adolescents, and these findings overlapped with word-reading and RC ability associations. However, this study's methodological approach restricted passage and word differences to loadings on a shared spatial component; consequently, some areas may not have been highlighted through this methodology.

Finally, a few studies have specifically examined how RC ability corresponds with domain-general networks during discourse comprehension. Smallwood et al. (2013) found that typical adult readers with higher RC ability had greater correlations between a DMN mentalization area (the posterior cingulate cortext; PCC) and a language region (right IFG), and lower correlations between the PCC and striatum. This finding indicates that connectivity between domain-general comprehension areas (DMN) and domain-specific language areas is important for RC outcomes, not just domain-specific alone.

A recent study by Aboud et al. (2019) also highlights the importance of domain-general interactions in RC ability. In this study, the authors examined the relationship between RC ability and different types of discourse (stories versus scientific texts) in adolescent readers. They found that in more difficult text environments (i.e. science texts), lower comprehenders showed decreased communication between a widespread executive control network (the frontoparietal control network) and the comprehension network (the DMN). These findings remained significant even after controlling for word fluency ability. The authors suggested that poorer comprehenders have decreased online executive facilitation of comprehension processes. This study did not, however, examine passage versus word reading, making it difficult to parse the specific reader-text properties that drove the differences. Still, these early explorations into the relationship with RC ability and passage reading suggest that executive and language systems playing a role in RC ability outcomes at the discourse level.

Summary of functional MRI studies of discourse comprehension

Studies on the association between RC ability and discourse processes highlight the importance of the language network as well as domain-general processing areas. Similar to word reading studies, the left IFG appears to play a prominent role in RC ability. Additionally, RC ability appears to be more closely related to temporoparietal activation and other DMN areas in both visual and auditory paradigms. Notably, no studies in discourse and RC ability compare discourse versus word-level processes to capture true “discourse-level” findings, and few controlled for decoding ability. Future studies need to examine multiple levels of reading in a single paradigm.

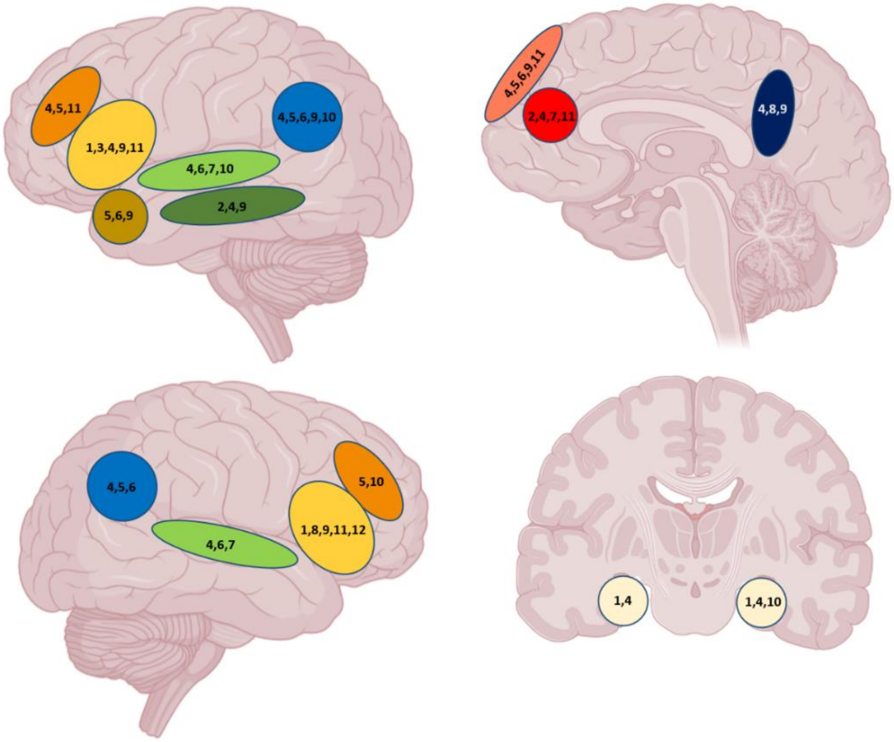


Figure 1.2: Brain regions in language, executive, and memory areas associated with RC ability across more than one functional/structural MRI study (study number corresponds with Appendix Table), including: bilateral IFG (yellow), bilateral dlPFC (orange), medial frontal cortex (including MFG and SFG; pink), ACC (red), medial posterior areas (including PCC and PCU; dark blue), left MTG (dark green), bilateral STG (light green), left TP (gold); bilateral IPL (including SMG and AG; blue), bilateral hippocampus (white). Not shown: left fusiform (found in papers 3, 4, 6, and 9). The most consistent findings were associations between RC ability and bilateral IFG, medial frontal areas and left IPL.

ERP studies of discourse comprehension

In the ERP literature, several studies have found that the relationship between RC ability and the N400 effect is attenuated in sentence reading, while the P600 effect still plays an important role. Stafura & Perfetti (2014) presented adult subjects with pairs of sentences, in which the first sentence either primed or did not prime the first content word of the second sentence. They found that the highest skilled readers showed only trending reductions for the N400 effect in both strong and weakly primed pairs, while skilled readers and less skilled readers did not show significant conditional differences. Interestingly, none of the RC ability comparisons reached significance for the N400 effect. In a follow-up study, Stafura et al. (2015) examined the influence of backward association versus forward association in similar sentence pairs. Backward association is thought to support memory processes, while forward association is thought to support predictive processes (Kang, Eglington, & Yap, 2018). Interestingly, they found that RC ability was negatively correlated with the N400 effect during backward association (i.e. stronger comprehenders had less of an N400 effect), and had no significant relationship with forward association in a text context. The authors suggest that stronger readers receive less benefit from lexical priming effects in a sentence context—an interpretation consistent with behavioral suggestions that stronger readers operate at the “message-level” while reading, and only rely on specific lexical information when difficulties arise (Stanovich, 1980). Consistent with this interpretation, Mossbridge et al. (2013) also failed to find an N400 effect during text reading, but instead found a significant role for a P600-like positivity in stronger comprehenders. The authors compared good and poor comprehenders as they read texts and scrambled words. They found that stronger comprehenders had a greater frontal-midline positivity around 400-500 ms after the target word onset, and this effect was stronger in text comprehension than word reading. These results provide a compelling contrast to word-level ERP relationships with RC ability, which emphasize a positive association between RC ability and the size of the N400 effect. They instead suggest that the P600 plays a more important role at the discourse level of processing.

In the final ERP study examined, Broadway et al. (2015) tested the effects of mind-wandering and attention on RC during passage reading. They found that signatures of attention, including pre-stimulus alpha, as well as P1 and N1 amplitudes, predicted 82% of variance in online RC performance. Similar to Aboud et al. (2019), these findings emphasize the importance of online executive functions, such as attention, in RC performance/ability.

Summary of ERP studies of discourse comprehension

While word-level ERP findings point to RC ability having a strong association to language and memory circuits related to the N400 effect, discourse-level findings show a diminished and potential negative relationship between RC ability and the N400 effect. Conversely, greater P600 effects were associated with higher RC ability for both word and discourse tasks. There is also some evidence that RC ability may also correspond with amplitude of earlier components (P1, N1) that are sensitive to attention.

Structural MRI studies on RC ability

In our last section, we briefly review several studies that have examined how RC ability correlates with gray matter in the brain. Interestingly, this structural work has a high degree of consensus, finding that discrepant RC ability (independent of decoding) is related to medial and lateral frontal areas. Bailey et al. (2016) used multivariate pattern analysis (MVPA) to predict gray matter volume (GMV) patterns in children in TD, DYS, or S-RCD subgroups. They found that S-RCD had lower GMV primarily in the right prefrontal cortex compared to both TD and DYS. Patael et al. (2018) examined children in the same age range as Bailey et al. (2016), who were in TD or general reading disability (RD) subgroups. They found that RC ability (partialling out decoding ability) positively correlated with GMV in the left dlPFC, dmPFC, hippocampus, and right TP. Additionally, the discrepancy between decoding ability and comprehension corresponded with GMV specifically in the left dlPFC, and that the dlPFC GMV was predictive of discrepancy score 3 years later. These findings emphasize the role of the left dlPFC in resilient/recovery processes for reading. Lastly, Welcome et al. (2011) measured radial expansion, cortical thickness, and thickness asymmetry in TD, resilient poor readers (low decoding, high comprehension), and poor readers (low decoding, low comprehension). Both TD and resilient readers showed greater radial expansion (i.e. local brain size) in the right frontal cortex (IFG/dlPFC) and right lateral partial regions compared to poor readers.

The structural findings share some interesting overlap with functional MRI results. In particular, both sets of studies find differences in the IFG, dlPFC, and hippocampus. Interestingly, the structural studies did not find any association between RC ability and the temporal lobes, echoing the inconsistent role of temporal regions in fMRI studies on RC ability (see below for Discussion).

Discussion

To date, neurobiological literature points to wide-spread associations between individual differences in RC ability and semantic, memory, and executive systems in the brain (see Figure 1.2), and these systems are distinct from ortho-phonological processes associated with dyslexia (Cutting et al., 2013a; Richlan et al., 2011). Across MRI tasks, the most consistent findings were RC-related differences in frontal areas (bilateral IFG and MFG/SFG) for both passage and word comprehension, and the left IPL in passage comprehension (see Figure 1.2). Interestingly, while temporal areas were implicated across several studies, findings were less consistent than frontal areas, and qualitative comparisons suggest that associations with portions of the temporal lobe may be driven by decoding ability. This finding is surprising given the temporal lobes' prominent roles in RC processes, and specifically vocabulary (Hagoort, 2013; Visser et al., 2012). The strong link between RC ability and frontal areas across reading processes parallels behavioral findings that RC ability is significantly related to executive functions beyond the impact of vocabulary and decoding (Locascio, Mahone, Eason, & Cutting, 2010). RC ability may consequently be determined by complex interactions across semantic and executive networks, rather than stemming from modular difficulty with vocabulary alone. On the temporal side, ERP findings suggest that both the N400 and P600 are important to RC ability, but that the N400 may be less important in sentence comprehension and beyond. These findings suggest that there may be a temporal trade-off between the N400 and P600 in strong comprehenders, depending on the task. Additional study is needed to piece apart the complex interactions of these processes, including more refined spatiotemporal understandings of network and ERP component interactions that support RC in general.

Limitations and Future Directions

Current neurobiological findings are highly confirmatory of behavioral research showing language and executive predictors of RC ability. However, the literature provides little consensus regarding a fundamental neural mechanism that drives RC ability, in part due to several methodological limitations. First, decoding ability is rarely accounted for in the current studies, raising questions about the distinction between orthographic-phonological versus higher-order contributions to RC ability findings. Second, a lack of examination at the pure discourse level of reading (i.e. passages versus word comparisons) or multi-tiered semantic processing tasks limits interpretations on how

RC ability plays out across multiple levels of reading. The latter limitation is of particular interest, given that language areas are known to provide flexible support for a diverse range of behaviors, so decreased activation in a single area could result in diverse aberrant behaviors depending on task-demand (see below). Lastly, to identify these complex neural behaviors, studies also need to utilize imaging modalities/methodologies that increase spatial and temporal resolution, including functional connectivity analyses in fMRI rather than activations alone, as well as the use of combined MRI and EEG analyses.

On a theoretical front, examinations of RC ability in the present literature are often aligned with behavioral models of reading, or psycholinguistic models of language. While these frameworks are valuable, no studies to date test competing hypotheses on RC ability within a *primarily* neurobiologically-driven framework. Neurobiologically-driven hypotheses based on known properties of brain networks provide compelling possibilities for how, when, and where processing difficulties arise in weaker comprehenders. In particular, there are three primary neural patterns that may account for the diverse array of behaviors related to both the typical or atypical range of RC ability:

1.) Bottleneck hypothesis: A primary, early deficit in region/network X results in insufficient information being passed to region/network Y, which results in poor behavioral outcomes for functions supported by X and Y (as discussed in the context of general language processes in Vagharchakian, Dehaene-Lambertz, Pallier, & Dehaene, 2012).
    a. Example: Poor/inefficient semantic retrieval circuits may result in low resolution or slow semantic information getting passed into semantic integration circuits, causing damaged or inefficient semantic retrieval *and* integration processes, as well as impacting any other later dependent processes (such as RC).

2.) Hub hypothesis: Region/network X flexibly supports multiple cognitive functions depending on task demand (and related input from external systems). A deficit in region/network X consequently results in poor behavioral outcomes across the range of functions the region/network supports (as discussed in the context of brain injury in Warren et al., 2014).

    a. Example: Left ventral IFG has been associated with semantic retrieval and semantic integration. It has been proposed to serve a generalized function in unifying semantic information; consequently, damage to this area could result in a wide range of semantic deficits leading to downstream RC difficulties.

3.) Primary or secondary executive dysregulation hypothesis: A deficit in region/network X as well as deficit in executive region/network Y results in a primary deficit related to X, as well as failure of Y to rescue X (as discussed for a wide range of disorders in Cole, Repov, & Anticevic, 2014).

    a. Example: A primary semantic deficit (either through bottleneck or hub mechanisms) can be relieved by executive processes that help recover part of the lost efficiency/function in the semantic pipeline. Executive processes can consequently act as a "gateway" for whether semantic difficulty at the neural level results in semantic difficulty at the behavioral level. Notably, the secondary executive deficit hypothesis can operate alongside either the Bottleneck or Hub hypotheses.

In order to build towards a mechanistic understanding of RC ability in the brain, future studies need to interrogate these competing neurobiological hypotheses. In particular, the relationship of brain areas and RC ability need to utilize (1.) network approaches that can capture a wider array of brain region characteristics, including executive interactions (see Chapters 2-4), (2.) multiple reading tasks to identify potential multifunctionality of brain areas, particularly filling in the gap of RC ability and discourse-level processes (see Chapter 2), and (3.) refined spatiotemporal neuroimaging techniques to identify when and where RC ability interfaces with language processes (see Chapters 3-4).

Current Dissertation

In the current series of studies, we address the gaps in the literature by using neuroimaging approaches to examine RC ability (independent of decoding) at the word-, sentence-, and discourse-levels of reading with both spatial and temporal sensitivity.

1.) Chapter 2 uses functional connectivity analysis in MRI to broadly ascertain the neural systems related to RC ability during word- and discourse-level processing (independent of word decoding) with a particular focus on semantic and executive hub areas.
2.) Chapter 3 uses a joint analysis of MRI and ERP data to identify where and when different semantic cognition occurs during sentence reading.
3.) Chapter 4 applies the framework from Chapter 3 to examine how the spatiotemporal progression of semantic cognition is impacted by RC ability.

Through this series of experiments, our goal is to create a preliminary spatiotemporal model of where and when RC ability impacts reading processes in the progression from word to text reading.

Chapter 2

Reading comprehension ability during word and discourse processing

Motivation

In Chapter 2, we seek to test the Hub and Executive Dysregulation hypotheses of RC ability proposed in the Introduction. For the Hub hypothesis, we are interested in 1.) examining whether areas of shared activation for word and passage reading have different connectivity patterns depending on task demand (i.e. whether they exhibit multifunctional "hub" characteristics), and 2.) testing if these flexible network patterns are important for RC ability. To test the Executive Dysregulation hypothesis, we also examine connectivity/ hub patterns in an executive seed area, and see whether these patterns are predictive of RC ability.

Neurocognitive Requirements for Skilled RC

Skilled reading comprehension (RC) requires the integration of word-level (WL) and discourse-level (DL) processing of a text. Early adolescence (~10-14 years old) is a period of reading development marked by a transition in the classroom from a focus on WL reading ("learning to read") to cohesive integration of WL and DL processes ("reading to learn"). Readers with RC deficits have been found to show correlated but separable difficulties in both word and text reading processes, including vocabulary skills (Cain & Oakhill, 2006; Kate Nation, Snowling, & Clarke, 2007; Spencer, Quinn, & Wagner, 2014), integration of semantic information within and across sentences (Oakhill et al., 2003; Oakhill & Cain, 2012), and working memory and other executive functions (WM; Locascio, Mahone, Eason, & Cutting, 2010.; Nation, Adams, Bowyer-Crane, &

Snowling, 1999; Stothard, 1992). These findings suggest that RC deficits may involve unique and interactive deficits in WL and DL processes, particularly semantic processing and WM. Nevertheless, despite the estimated prevalence rate of approximately 30% of adolescent readers struggling with RC (U.S. Department of Education: *National Assessment of Educational Progress*, 2013), the neurobiological underpinnings of WL and DL functions, and how they are appropriately integrated during reading, is poorly understood. Surprisingly, no neuroimaging studies to date have examined the interaction between WL and DL processes in adolescents. The current study aimed to address this significant gap in the literature by using a naturalistic reading paradigm in order to investigate the relationship between these tiers of reading in adolescent readers who ranged in reading ability.

Surveying the literature for individual WL and DL studies reveals consistent neural networks identified across both levels of reading. The literature has clearly established that WL reading recruits a widespread network of left-lateralized language regions (Price, 2012). These include activation of the left occipitotemporal area (OT; for full abbreviations list see Abbreviations), particularly the putative visual word form area (pVWFA), which is thought to support orthographic processing, including rapid visual word recognition (McCandliss, Cohen, & Dehaene, 2003; Schlaggar & McCandliss, 2007). Additionally, WL processing recruits phonological support regions, including subregions of the inferior frontal gyrus (IFG; BA 44 in particular), with additional associations with the supramarginal gyrus (SMG; Richlan, 2012;C. J. Price, 2012; Vandermosten, Boets, Wouters, & Ghesquière, 2012). Finally, the middle temporal gyrus (MTG) and temporal pole (TP), and other subcomponents of the IFG (BA 45 and 47 especially) are thought to support WL semantic functions (i.e. the connection of word stimuli to meaning; Price, 2012). In the context of these findings, WL neuroimaging work appears to map reasonably well onto behavioral models of reading, which suggest that skilled reading requires adequate formation and integration of the orthographic, phonological, and semantic representations of words (Perfetti, 2007). In addition to these language-specific functions, behavioral and neuroimaging studies have also suggested that the integration of word representations is supported by top-down or executive processes such as WM (Christopher et al., 2012)—cognitive abilities which are largely associated with the dorsolateral prefrontal cortex (dlPFC; Coelho, Lê, Mozeiko, Krueger, & Grafman, 2012; Fedorenko, 2014). Consequently, the dlPFC could also play an important role in WL processes (Kovelman et al., 2012).

Previous literature has revealed that DL processing involves a complex integration of multiple skill sets spanning different cognitive domains, including those required for WL reading. In addition to the WL processing requirements mentioned above (Kendeou, van den Broek, Helder, & Karlsson, 2014; Perfetti, 2007), in order to comprehend a text meaning must be integrated across multi-word units through combinatorial semantic and syntactic unification (i.e. DL processes; Friederici, 2011; Hagoort & Indefrey, 2014; Humphries, Binder, Medler, & Liebenthal, 2007). This act of building meaning is supported by domain-general executive functions, including WM, inferencing, planning/organization, and social cognition, which work to appropriately maintain, organize, and contextualize the incoming information (Cutting, Materek, Cole, Levine, & Mahone, 2009; Ferstl, Neumann, Bogler, & von Cramon, 2008; Kendeou et al., 2014; Sesma, Mahone, Levine, Eason, & Cutting, 2009). Through these convergent functions, meaning is integrated into an evolving internal representation of the text known as the “situation model” (Dijk & Kintsch, 1983; Whitney et al., 2009). Because reading connected texts requires integration of WL processes, not surprisingly, neuroimaging studies find large areas of overlap between word and passage reading, including left IFG, TP, and MTG (Friederici, 2011; Hagoort & Indefrey, 2014; Price, 2012); the dlPFC has also been implicated (Christopher et al., 2012; Coelho, Lê, Mozeiko, Krueger, & Grafman, 2012; Fedorenko, 2014). Discourse-specific areas include domain-general nodes within the default mode network (DMN) including the dorsal medial prefrontal cortex (dmPFC), bilateral angular gyri (AG), posterior midline regions, and in some cases, the hippocampus and bilateral anterior superior temporal sulcus (Buckner, Andrews-Hanna, & Schacter, 2008). This dispersed network is implicated in numerous cognitive tasks, but in the context of discourse processing, appears to support inferential and contextualization functions, including social cognition (Ferstl et al., 2008; Mar, 2011).

Central to the current study, regions of overlap between WL and DL processing are implicitly interpreted in discourse processing studies as primarily supporting “lower-level” WL processes, (i.e. they are subtracted out using WL baseline tasks). However, studies examining these left-lateralized language and WM areas suggest that these regions are potentially multi-functional, with flexible network properties depending on task demand, or, perhaps due to smaller functionally specific subregions. Indeed, subregions of the IFG form a complex functional gradient potentially supporting a broader role of the IFG in the unification of information (Hagoort, 2005): BA 44 and BA 45 are both implicated in syntactic unification; BA 44 additionally is related to phonological functions; and BA 45 (along with BA 47) is also thought to support semantic processes (Cappa, 2012; Hagoort & Indefrey, 2014; Hagoort, 2005; Price, 2012; Pugh et al., 2001). More generally, IFG, MTG, and TP have been associated with multiple functions including WL reading (Cappa, 2012; Jefferies, 2013; Pugh et al., 2001; Tsapkini et al., 2011), combinatorial semantics (Hagoort & Indefrey, 2014; Humphries et al., 2007), syntax (IFG, MTG, TP; Cappa, 2012; Hagoort & Indefrey, 2014; Hagoort, 2005), semantic storage (MTG; Jefferies, 2013; Price, 2012), and executive semantic functions (Whitney, Kirk, O’Sullivan, Lambon Ralph, & Jefferies, 2011).

Whether these regions are truly multifunctional, or reflect smaller, functionally-specific subregions is an open question. For example, the canonical Broca's area has been divided into multiple subdivisions based on connectivity, cytoarchitecture, and transmitter receptor distribution (Amunts & Zilles, 2012), some of which map onto proposed, distinct functions (Friederici, 2011). Consequently, areas which appear to exhibit flexible network properties could be comprised of different neuronal subpopulations. To determine whether hub regions exhibit flexible connections due to true multifunctionality or proximal, heterogeneous subdivisions, the dynamic network and functional characteristics of these regions requires close interrogation in the context of reading and reading deficits. From this context, heretofore when we refer to the term multifunctionality, we acknowledge that it may reflect either "true" multifunctionality or further subregions that are proximal but perhaps heterogeneous in function.

In addition to language regions common to WL and DL processing, neuroimaging and behavioral studies suggest that the dlPFC-based top-down, executive control and WM functions may play critical, independent and integrative roles in WL and DL cognition (Christopher et al., 2012; Coelho et al., 2012; Fedorenko, 2014; Locascio, Mahone, Eason, & Cutting, 2010; Newman, Malaia, Seo, & Cheng, 2013; Petten, Weckerly, Mclsaac, & Kutas, 1997). A traditional cognitive model of reading, the simple view of reading (Hoover & Gough, 1990), hypothesizes that skilled RC ability requires appropriate integration of WL and oral DL (listening or language comprehension) processes. An expanded version of this model suggests that this integration is potentially facilitated by executive functions (Cutting et al., 2015). Practically, this integration seems to involve semantic processing, particularly connecting orthographic representations to meaning, and integrating this meaning across units of text. Behavioral studies of RC deficits have suggested that struggling readers could have deficits in this integration process, rather than the component skills of word reading and oral language (Locascio, Mahone, Eason, & Cutting, 2010.; Sesma, Mahone, Levine, Eason, & Cutting, 2009). In this context, the dlPFC may play a role in top-down maintenance of WL and DL integration, specifically by managing semantic-orthographic representations and combinatorial semantic processing.

Thus, previous literature on word and discourse processes indicates that semantic (including orthographic-semantic networks) and executive overlap regions described above may be multi-functional in the context of reading at multiple levels. Due to the dynamic activity of these areas, some studies have suggested that these overlapping language and executive regions are cognitive "hubs" (TP, Patterson, Nestor, & Rogers, 2007; IFG, Bitan et al., 2005; Hagoort & Indefrey, 2014; MTG, Visser, Jefferies, Embleton, & Lambon Ralph, 2012); i.e. they exhibit flexible network activity by communicating with a greater number of disparate networks ,and "support and/or integrate multiple types of information" (Power, Schlaggar, Lessov-Schlaggar, & Petersen, 2013). Importantly, a recent study by Power et al. (2013) suggests that damage to hub regions has a significant impact on clinical outcomes across different cognitive domains. Consequently, examination of multifunctional regions has potentially significant implications both within and beyond the context of reading (Cole et al., 2013). By examining network properties of multifunctional passage and word overlap regions, we expected not only to identify patterns predictive of reading ability, but also sought to better identify potentially flexible network characteristics of hub areas within the traditionally identified language network.

Current Study

In the current study, we used an expository text reading paradigm to examine reading networks in adolescents with a range of word reading and RC abilities. In addition to the inclusion of both WL and DL processing tasks in our paradigm, we also purposely utilized expository text for our DL task. Expository text is distinct from narrative text because it conveys information on subject matter without reliance on narrative structure or characters. Key for this study, it is a genre that is increasingly relied upon during the fourth grade transition from “learning to read” to “reading to learn” and has been shown to have distinct and increased cognitive burden from narrative texts, including increased demand on processes involved in vocabulary, semantic coherence, WM, and other executive functions (Berman & Nir-sagiv, 2007; Eason, Goldberg, Young, Geist, & Cutting, 2012). Additionally, expository comprehension has been found to be more difficult for young readers, due to less global coherence markers and decreased subject background knowledge (Baretta, Tomitch, MacNair, Lim, & Waldie, 2009; Berman & Nir-sagiv, 2007). Because expository texts places increased demand on skill sets that correlate with poor RC ability, and due to its central pragmatic importance, this genre provides an ideal environment in which to examine the neural underpinnings of adolescent RC ability, and how WL and DL processes integrate. Since young readers with RC deficits struggle with overlapping but separable difficulties in both word and passage reading, we were particularly interested in the activity patterns of regions recruited for both of these tasks.

Through this paradigmatic approach, we aimed to address the following questions: 1.) What are the neural correlates of expository text comprehension, particularly in relation to WL processing regions in adolescents? and 2.) Are regions that support both word and passage reading differentiated by task-specific network connectivity patterns? For each question, we additionally sought to address how these findings might be modulated with RC ability, independent of decoding. From previous literature, we hypothesized that, as examined through GLM mean activation analyses, adolescent word and passage reading would each recruit a shared, left-lateralized processing network, including those that support orthographic (OT area), semantic functions (IFG, MTG, and TP), and potentially WM (left dlPFC). We also expected constrained recruitment of regions within the DMN specifically for DL processing. However, given the evidence that 1.) Multi-functional regions show unique predictions of a myriad of clinical outcomes, 2.) Specific language and WM regions are reported to be multi-functional across different reading demands, and 3.) Struggling readers behaviorally demonstrate multi-tier semantic and WM/executive deficits, we additionally hypothesized that semantic/WM regions activated for both passage- and word-reading were likely to underlay critical network differences (as examined through functional connectivity analyses). Importantly, we further expected that hypothesized mean activation and connectivity findings would be modulated by reading skill thus revealing novel information about reading development. Given the behavioral, theoretical, and neural implications of executive functions in RC ability, we particularly anticipated that dlPFC activation and connectivity to the language network would be associated with RC ability.

Methods

Participants and inclusion criteria

Out of an original cohort of 131 subjects who were scanned as part of a larger ongoing project of reading comprehension, we selected individuals for participation in the current study who had greater than 85 standard score IQ, and between 85-115 standard scores on basic reading tests (n = 98; see Behavioral Testing section for rationale and mean values). From these 98 subjects, subjects were excluded based on the following exclusion parameters: motion (n = 29 excluded for average motion outliers > 10%), in-scanner task performance (n = 12 excluded for poor in-scanner task performance, see below), and inadequate head coverage (n = 19). The final analysis included 38 adolescents, aged 9-14 years old (mean age = 12.1 +/- 1.5; 24 female). All participants were native English speakers with normal hearing and vision, and no history of major psychiatric illness or traumatic brain injury/epilepsy. All subjects had no history of a developmental disability or contraindication to MRI. Each participant gave written consent at the beginning of the study, with procedures carried out in accordance with Vanderbilt University's Institutional Review Board. Participants received $150 for behavioral and neuroimaging testing.

Behavioral testing

Participants who met pre-screening eligibility requirements completed a comprehensive test battery (measures relevant to the current study reported in Table 2.1). All participants had typical IQ (standard score > 85 on Full Scale, Performance, and Verbal IQ of the Wechsler Abbreviated Scale of Intelligence; mean IQ = 107.6 +/- 8.1; Wechsler, 2011). Additionally, to ensure that participants had at least the entry level word recognition/decoding ability to complete the paradigm, participants had to have a standard score of 85-115 on the basic reading composite score and subtests of the Woodcock Mastery Test-Revised (Woodcock, 1998). Subtests of the basic reading composite score included Letter-Word Identification and Word Attack, which measure word recognition and decoding ability, respectively. As one primary question in this paper is how the full range of RC ability influences neural networks of reading, RC ability, as measured by the Gates MacGinitie (MacGinitie, 2000), was allowed to vary (mean percentile = 61.7 +/- 23.6; see Table 2.1 for demographic information). One subject did not complete the Gates MacGinitie, and subject's score was replaced with the group mean for all related analyses. For the Supplemental Analysis, Sentence Span (Swanson, Cochran, & Ewers, 1989) was used to assess working memory capacity.

Measure	Mean (SD)	Range
Age	12.1 (1.5)	9-14
WA %ile	47.0 (17.8)	18-90
LWID %ile	56.2 (18.8)	20-92
Gates %ile	61.7 (23.6)	14-98
WASI ss	107.6 (8.1)	89-123

Table 2.1: Demographic data for n = 38 subjects.

fMRI tasks

Passages condition (see Figure 2.1a)**.** Eight expository passages were constructed in-lab and equated across measures of word concreteness, syntactic simplicity, referential cohesion, causal cohesion, and narrativity (i.e., the degree to which the text uses everyday oral conversation and tells a story with familiar characters, events, places, and things) using Coh-Metrix 2.0 (McNamara et al., 2005). Passages were additionally matched on descriptive factors, including: number of words, average sentence length, and Flesch-Kincaid grade-level (range from 4.0-4.9), ultimately matching across 23 discourse measures. To ensure equivalence of all measures across passages, measures for each of the 8 passages were individually compared to the mean of the remaining 7 passages. Passages were considered equivalent when measures were within a 90% confidence interval of the mean of the remaining passages. Four of these passages were used for the Passages condition and four were used for the Words condition (see below), which included words from the passages in randomized order. All passages were 150 words in length. Each sentence was no longer than 13 words. The passages were all expository and included the following topics: Hang Gliding, Wrasses, Velvet Worms, and Hydroponics. Each passage consisted of two paragraphs, the first of which served to introduce the topic while the second elaborated on a particular detail of the subject matter.

Words condition (see Figure 2.1b). The words condition consisted of scrambled words presented in “phrases”, which were exactly matched in length, word type, and presentation time to the phrases in the passages (see Figure 2.1b).

Symbolic baseline (see Figure 2.1c). The baseline condition included three non-alphanumeric symbols (two symbol types) displayed horizontally on a slide (see Figure 2.1c), and was matched in presentation time to the word and passage phrases.

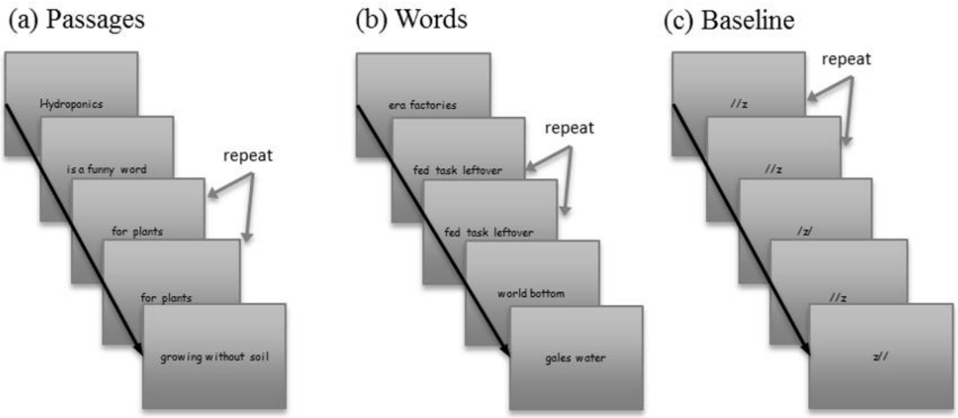


Figure 2.1: Sample stimuli from each of the three conditions.

Stimulus procedure

Single word presentations in sentential context have been reported to create an uncomfortable, artificial reading experience (Rayner, 1986). In the current study, passages were consequently divided into syntactic phrases (verb, noun, and propositional), ranging from 1-6 words in length. Each phrase was presented on a separate trial. We allowed 550 ms for each content word and 275 ms for each function word. For timing purposes, we presented no more than three content words per slide. The interval between phrase stimuli was randomized to allow for event-related analyses (not included in this study; jitter ranging from 550 ms-4000 ms). The baseline condition was presented between paragraph 1 and paragraph 2 of both the Passages and Words conditions. The purpose of this design was to allow participants' activation to return to baseline after reading each block (paragraph). A typical presentation sequence was: 1) Passage condition, Paragraph 1; 2) Baseline condition; 3) Passage condition, Paragraph 2; 4) Baseline condition; 5) Words condition; 6) Baseline condition. In half of the runs per subject, the Words condition was presented first. Two lists were used, which randomly alternated whether the first run of the scanning session was Words or Passages. The mean time for the Passages block was 78.54 s (SD = 22.94); Words mean = 82.45 s (SD = 3.29); and Baseline mean = 47.69 s (SD = 1.48).

To monitor whether participants attended to all stimuli, 8% of the stimuli within each task block were randomly repeated on two consecutive screens. Participants pressed a button with their right thumb when they detected a phrase repetition or a symbol configuration repetition. Only subjects who responded to greater than 75% repetitions correctly per block and had less than 95% sporadic buttons pushes (button pushes during non-repeated stimuli), were included in the analysis.

fMRI data acquisition, preprocessing and first-level analyses

Imaging was performed on a Philips Achieva 3T MR scanner with an 8-channel head coil. Functional images were acquired using a gradient echo planar imaging sequence with 40 (3mm thick) slices with no gap and consisted of 4 runs, each 7 minutes (190 dynamics per run). Additional imaging parameters for functional images included TE=30 msec (for optimal BOLD contrast at 3T), FOV 240 x 240 x 120 mm, slice thickness=3 mm with 0 mm gaps, 75 degree flip angle, TR=2200 msec, and a matrix size 80×80 (interpolated), yielding 3mm^3 isotropic voxels.

All functional data were analyzed using MATLAB (Mathworks, Natick MA) and SPM8 (Frackowiak, Friston, Frith, Dolan, & Mazziotta, 1997). The functional data for each participant were slice-timing corrected, aligned to the mean functional image, normalized to MNI space and spatially smoothed with an 8 mm FWHM Gaussian filter. All subject masks underwent dual-rater quality assessment checks. Due to differences in subject masks, the cerebellum was not included in our analysis. In our first-level analysis, standard regression models were created using an estimated HRF for each condition; the size motion parameters (x, y, z translational; x, y, z rotational) and outlying volumes as determined by ART (Whitfield-Gabrieli; http://www.nitrc.org/projects/artifact_detect/) were included in the design matrix as regressors of no interest. Subjects with greater than 10% average motion outliers and greater than 20% motion outliers in any individual run were not included in the final analysis. For the standard GLM analyses three sets of contrasts for each participant were created: Words vs. Symbols, Passages vs. Symbols, and Passages vs. Words.

Group-level imaging analysis

SPM8 and MATLAB (Mathworks, Nattick MA) were used to create whole brain activation maps. Individual contrast maps were brought up to a group level, one-sample t-test to analyze Passages and Words. The conjunction of *Passages* > *Symbols* and *Words* > *Symbols* was performed using SPM's minimum t-value conjunction algorithm. AFNI's 3dClustSim algorithm was used to determine the probability of false positive clusters (and appropriate correction for multiple comparisons) through iterative Monte Carlo simulations (n = 10,000). All group-level analyses were subjected to an uncorrected statistical threshold of $p < 0.005$ and a cluster size of 118 voxels, which was determined by 3dClustSim to be equivalent to p-corrected < .05 (2-sided).

Connectivity analysis

Connectivity analysis was performed using the CONN toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012). The toolbox uses the CompCor method (Behzadi, Restom, Liau, & Liu, 2007) to estimate confounding signals. White matter and CSF signal (derived from T1 images; characterized by 5 dimensions), movement artifacts, six movement parameters (as determined by ART), and the first temporal derivative of the movement parameters were regressed out of the signal. To remove correlations driven by general, task-related co-activations, task effects and their first temporal derivative were also removed from the signal (Whitfield-Gabrieli & Nieto-Castanon, 2012). Analysis was run across the whole duration of the concatenated blocks per task. High-pass filtration with a cut-off value of .008 Hz was applied to remove slow oscillations driven by physiological noise. One subject was excluded from connectivity analysis due to excessive motion specifically during the T1 scan.

For subject-level analysis, the corrected voxel time-series was extracted for each pre-defined ROI (defined below), then averaged to produce one time series per ROI. Whole-brain bivariate correlation maps were then generated for each ROI and converted to Fischer’s z scores. For group-level analyses, ANCOVA models were run to identify whole-brain task-related difference with and without additional covariates of interest. For all connectivity results, only positive correlations were investigated.

Seed regions

For the connectivity analyses, we were specifically interested in isolating semantic, orthographic, and executive function regions that were active in both *Words > Symbols* and *Passages > Symbols* (see Table 2.2). Specifically, we were interested in overlap nodes previously identified as part of the primary frontal-temporal semantic network, namely the left IFG (BA 44, 45, and 47), left MTG (BA 21), and left TP (BA 38), which have been found to support word and text-level semantic processes (Friederici, 2011; Hagoort & Indefrey, 2014; Jefferies, 2013; Price, 2012; Binder, Desai, Graves, & Conant, 2009). Additionally, we examined the pVWFA and dlPFC overlap areas, since their associated functions of orthographic-semantic and WM processes, respectively, have been implicated in unique word and text-level functions (Christopher et al., 2012; Rimrodt et al., 2009). To isolate these specific overlap regions, the Words > Symbols and Passages > Symbols conjunction (described above) was masked by Brodmann Area (BA) using the WFU PickAtlas Talairach Daemon atlas regions (WFU Pickatlas, version 2.5.2; Maldjian et al., 2003, Lancaster et al., 2000; Lancaster et al., 1997), with dilation = 3. Seeds were closely evaluated to ensure there were no overlapping voxels. As the pVWFA does not have an associated BA, the Passage and Word conjunction map was masked with a spherical ROI (radius = 10) centered at [-43, -55, -17], which was implicated as the central pVWFA point in a meta-analysis (converted to MNI; Richlan, Kronbichler, & Wimmer, 2009). Consequently, the following seeds from the Passage/Word conjunction map were run in a whole-brain connectivity analysis: IFG (comprised of BA 44, 45, and 47), MTG (BA 21), TP (BA 38), dlPFC (BA 46 and 9), and pVWFA (ROI centered at -43, -55, -17 with a radius of 10). With BA masking, the resulting dlPFC seed localized to the frontal border of BA 46/9 at the inferior frontal sulcus. In order to examine a more constrained, centralized dlPFC seed, we masked the Passage/Word conjunction map with a dlPFC map defined in the Neurosynth cortical dlPFC meta-analysis (Yarkoni et al., 2011). This seed overlapped with our original BA 46/9 seed. For all subsequent analyses of the BA 46/9 seed, we performed supplemental analysis on this secondary seed to examine the regional specificity of results.

For each seed, hierarchical contrasts were run for *Words* > *Symbols* and *Passages* > *Words*. For comparison purposes, *Passages* > *Symbols*, *Passages alone* (without baseline), and *Words alone* were additionally run to assess whether patterns were only due to relative differences to the baseline tasks. See Appendix for result coordinates and statistics.

Anatomical Region	**CM MNI Coordinates**			**Peak MNI Coordinates**			**k**	**BA**
	x	**y**	**z**	**x**	**y**	**z**		
L dlPFC	-52	18	28	-44	16	26	116	46, 9
L IFG	-48	25	5	-46	28	2	1841	47, 45, 44
L TP	-48	15	-21	-54	18	-8	210	38
L MTG	-58	-25	-8	-58	-34	-2	1195	21
L pVWFA	-43	-55	-18	-44	-48	-14	489	37

Table 2.2: Center of mass (CM) and peak coordinates for five connectivity seeds. Seeds were pulled from the Passages > Symbols and Words > Symbols GLM conjunction analysis in language and executive areas.

Results

GLM results

Words > Symbols (Figure 2.2)**.** Compared to Symbols, Word reading elicited greater activation in language areas and language homologues including left fusiform gyrus (including pVWFA), bilateral/left dominant IFG (BA 47, 44, 45) extending bilaterally into dlPFC (BA 46/9), bilateral MTG, left STG extending to left ventral SMG, and bilateral temporal poles. Additional activations included motor regions (SMA and left precentral), bilateral hippocampus, left putamen, bilateral anterior insula, and bilateral occipital regions extending into ITG and MTG.

Passages > Symbols (Figure 2.2)**.** Compared to Symbols, Passage reading exhibited greater activation in traditional perisylvian language areas and their right hemisphere homologues. These included pVWFA, bilateral/left dominant IFG (BA 47, 44, 45), bilateral MTG, and bilateral TP. Left and right IFG additionally extended upwards into the dlPFC (BA 46/9). Regions associated with the DMN were also seen, including bilateral/left dmPFC/SFG extending to SMA, bilateral AG, PCU, bilateral STS, and bilateral hippocampus. Additional activations were seen in left putamen, bilateral dorsal insula/rolandic operculum, bilateral occipital regions extending into ITG and MTG, and bilateral precentral gyrus.

Passages > Words (Figure 2.2)**.** In a direct contrast of Passages vs. Words, Passages showed greater activation in heteromodal regions, including bilateral/left dominant TP extending to left MTG, bilateral anterior superior temporal sulcus (STS), bilateral AG, and dorsal PCU. Except for dorsal PCU, all of these activations were also greater in Passage-Baseline.

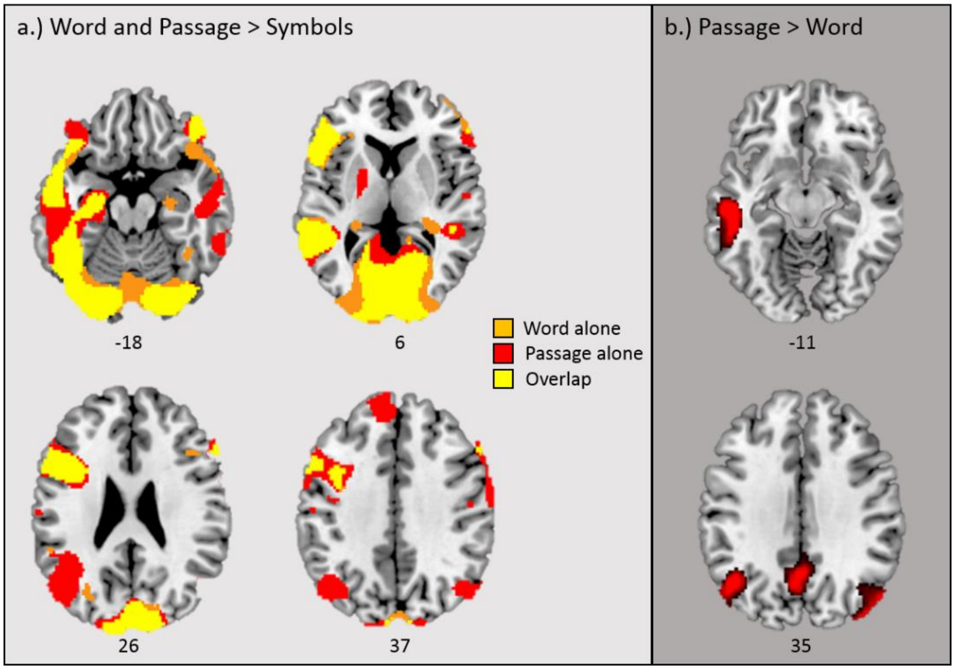


Figure 2.2: Activations for Passages, Words, and Passages > Words. a.) A Boolean rendering of Passages > Symbols and Words > Symbols shows that both Passage reading (red) and Word reading (orange) activate a dispersed overlapping language and WM network (yellow). B.) Passage reading compared to WL reading uniquely recruits regions in the DMN, including bilateral AG, PCC, and bilateral anterior STS. Results displayed at p-corrected < 0.05. Adapted from Aboud et al. (2016).

Seed-to-whole-brain connectivity of overlap regions (positive correlations only)

We ran whole-brain analysis on the 3 language seeds (L IFG, L MTG, and L TP), pVWFA, and dlPFC GLM conjunction areas (activations seen in both Passages > Symbols and Words > Symbols). All results are reported at $p < .05$ as determined by 3dClustSim (p-uncorr < .005, k = 118). To identify shared correlations across seeds, seed-to-whole-brain analyses were run separately for each seed region, and additional Boolean overlap maps were generated across seed correlation maps to identify areas of convergent correlations. Results that fall within the language and WM network are in bold. Seed region characteristics are reported in Table 2.2. See Appendix for result coordinates and statistics.

Words > Symbols (Figure 2.3). *Three language seeds (L IFG, L MTG, L TP):* In Words compared to Symbols, all language seeds correlated with left OT area extending into pVWFA. Regions also correlated with bilateral middle occipital areas (IFG and MTG), right IFG (IFG and TP), left frontal operculum/RO (IFG and TP), primary motor and somatosensory cortices (IFG, TP, and MTG), and right ITG (TP). Supplemental analysis indicated that IFG correlations with the left pVWFA were driven by BA 44 and BA 47.

pVWFA: The pVWFA was more strongly correlated with left MTG in Words than Symbols, as well as with bilateral occipital regions, left insula, bilateral precentral gyrus, right postcentral, and right middle frontal gyri.

dlPFC: In Words compared to Symbols, dlPFC correlated with left MTG, along with right dlPFC (BA 9/46), left MFG (BA 9, 6), bilateral middle occipital regions, and left RO in Words compared to Symbols. The more constrained dlPFC seed did not replicate BA 46/9 word-level findings, instead showing connectivity to bilateral precentral, bilateral RO, right orbitofrontal, and right dlPFC.

Passages > Words (Figure 2.3). *Three language seeds (L IFG, L MTG, L TP):* All language seeds correlated with left AG more strongly in Passages compared to Words. Additionally, during Passages, language seeds showed correlation with other language areas including left ventral MTG (MTG and TP) and left TP/anterior MTG (IFG), along with bilateral caudate (IFG and TP), SFG (IFG, TP, MTG; different subdivisions), occipital regions (IFG, TP, and MTG), bilateral thalamus

(IFG), PCC/PCU (IFG and TP), and ACC (TP). Supplemental analysis indicated that IFG correlations with the left AG were driven by BA 45 and BA 47.

pVWFA: In Passages greater than Words, the pVWFA correlated with left AG, bilateral TP, left SMG, left thalamus, left middle cingulate, right MTG, left/bilateral fusiform, and left dlPFC/MFG.

dlPFC: In Passages greater than Words, the left dlPFC correlated more strongly with left AG (which overlapped with the AG seen in the 3 language seeds and pVWFA connectivity results), extending into more dorsal AG and regions of the left lateralized DMN, specifically showing greater connectivity to left-lateralized PCC, SFG, and temporal pole. Additionally, dlPFC correlated with right ventral fusiform/parahippocampal regions. With the exception of left PCC, findings were replicated with the constrained dlPFC seed, which additionally showed connectivity to dorsal PCU.

Of note, the 3 language seeds, pVWFA, and left dlPFC all showed convergent correlation with the left AG in Passages compared to Words.

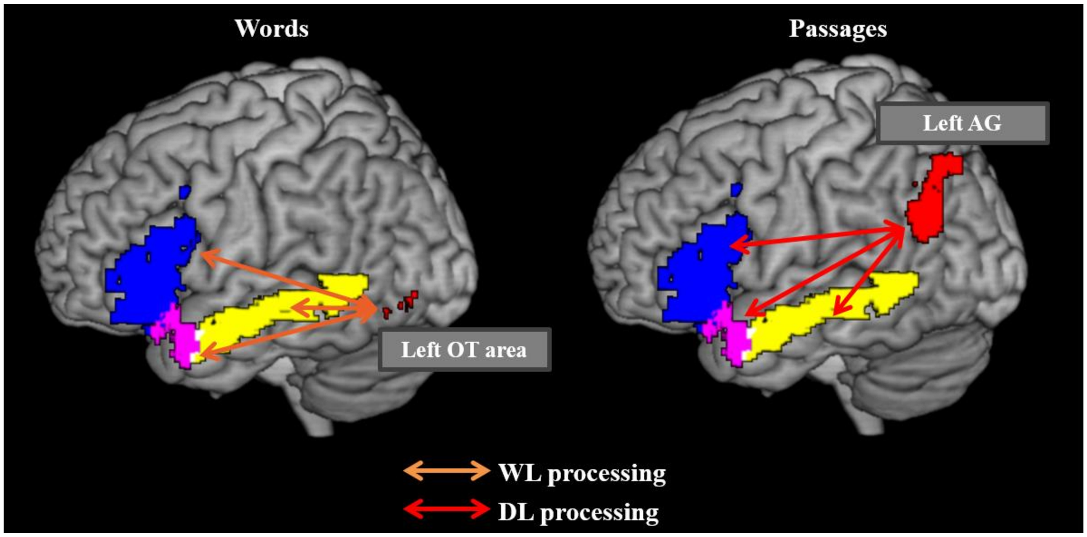


Figure 2.3: Left-lateralized language regions of mean overlap activity in Passage and Word reading show differential connectivity patterns in WL (Words > Symbols; orange arrow) and DL (Passages > Words; red arrow) processes. Specifically, the three seeds show convergent correlation with the left OT area during WL reading, and additively shows correlation with the left AG during Passage reading. Results displayed at p-corrected < 0.05.

Seed-to-whole-brain connectivity analysis of overlap regions with reading metrics

To assess how out-of-scanner behavioral measures of RC ability predicted correlations among the regions of interest (independent from decoding ability), we ran whole-brain connectivity from each the original seeds (3 language seeds, VWFA, and left dlPFC).

Words > Symbols connectivity modulated by RC ability (Figure 2.4)**.** We found that during WL reading higher RC predicted widespread connectivity patterns from our seeds of interest to classic semantic retrieval and memory areas (see Figure 2.4). (Note: as this analysis was included as an ancillary examination of data in Aboud et al. (2016), we examined whole-brain findings rather than examining within-mask results as done in Aboud et al. (2016)). With increased RC ability, our seeds showed the following:

Left dlPFC: Increased correlations with the left hippocampus, frontal pole (FP), and left TP.

Left IFG: Increased correlations with the FP.

Left MTG: Increased correlations with the dmPFC, FP, left TP, and SMA.

Left TP: Increased correlations with R TP, dmPFC, bilateral SMG, bilateral precentral gyrus, bilateral Heschl's gyrus, and Insula.

pVWFA: Increased correlations with right ventral IFG and cerebellum.

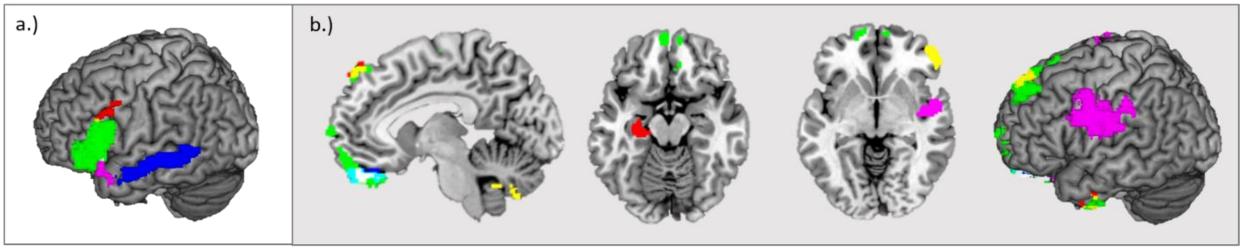


Figure 2.4: Higher RC ability corresponded with increased functional connectivity patterns of language and executive hub regions during word reading. We found that RC positively correlated with greater connectivity between (a.) our seed regions (b.) and frontal, language, memory, and motor areas, with convergent connectivity from multiple seeds to the orbitofrontal cortex, dorsomedial prefrontal cortex, and ventral TP. Seed regions include: left dlPFC (red); left IFG (green); L TP (purple); left MTG (blue); and left pVWFA (yellow; not shown). Connectivity patterns for each seed are matched in color. Cyan indicates that two seeds have overlapping connectivity to that area. White indicates that three seeds have overlapping connectivity to that area.

Passages > Words connectivity modulated by RC ability (Figure 2.5)**.** *Gates:* In Passages compared to Words, reading comprehension ability was positively correlated with connectivity between the left dlPFC and left ventral AG. No other seed regions showed significant correlations predicted by Gates percentile within the defined mask, including the more constrained, supplemental dlPFC seed**.**

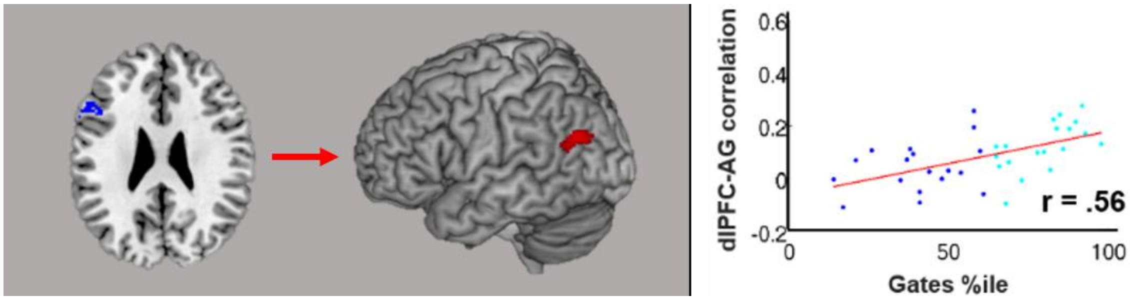


Figure 2.5: RC ability positively predicts correlations between the left dlPFC and the left AG in DL processing. Low and high RC ability (as determined by median split of behavioral metric) represented in dark blue and light blue, respectively). Results displayed at p-corrected < 0.05. Adapted from Aboud et al. (2016).

Supplemental physio-physiological results

To assess how increased activation in dlPFC predicted whole-brain left AG results during Passage reading, the time series for the convergent left AG (from all 5 seeds) was extracted and entered into a first-level, whole-brain connectivity analysis in which each voxel-level time series was predicted by the interaction of the left AG and left dlPFC time series. Second-level t-test was run to compare the interaction term for Passages versus Symbols.

We found that a one unit increase in dlPFC activation predicted increased correlation between the left AG and the left VWFA, as well as the left parahippocampal gyrus. Findings were replicated in Passages alone. Preliminary analysis indicates that dlPFC prediction of left AG to the left OT area is positively correlated with WM span. Findings were replicated for the constrained dlPFC seed.

Discussion

The goal of this study was to identify the neural networks that support adolescent discourse processing, and how these networks may be modulated by level of RC skill. We had two main questions: 1.) What are the neural correlates of expository passage reading, and, more centrally, how are these networks related to WL processing in adolescents? 2.) Do brain areas that are active for both word and passage reading, particularly language and WM processing regions, show separable, task-specific connectivity patterns? With each question, we also sought to understand how behavioral indices of RC ability modulated findings.

Neural correlates of expository text comprehension in adolescent readers

Consistent with previous work, our GLM results showed that during both word and passage reading adolescents recruited left-lateralized language areas traditionally associated with reading (see Figure 2.2). These include regions thought to support rapid visual word recognition (left OT areas and pVWFA) and areas associated with semantic processing (left IFG, MTG, and TP). This overlap network also included the dlPFC, a critical region in WM processes for both WL and DL processes. Additionally, there were areas uniquely associated with DL processing. As compared to WL processing, adolescent readers activated portions of the DMN, which has previously been seen in other DL analyses and is thought to support integration of world knowledge (see Figure 2.2; Ferstl et al., 2008; Mar, 2011).

One plausible hypothesis for the function of overlap regions between word and passage reading could be that they perform common functions (e.g., primarily underpin processes important for WL reading, since passage reading includes word processing). However, the overlapping activations across both tasks could obscure complex, task-specific processes. Previous fMRI studies suggest that these regions seen in both word and passage reading are “multi-functional” within and outside of the language domain, either through as-of-yet undefined functional subdivisions (Friederici, 2011) or functionally flexible neuronal populations (Hagoort, 2005). For instance, areas in left IFG have been found to support multiple cognitive processes: BA

45 is associated with both semantic and syntactic unification (Hagoort & Indefrey, 2014; Hagoort, 2005; Price, 2012), and BA 44 has been found to support phonological, syntactic, and speech-motor mapping functions (Fadiga et al., 2006; Friederici, 2011; Amunts, 2012). TP is implicated in semantic memory and domain-general meaning associations across stimulus modalities (Tsapkini et al., 2011), and the pVWFA has been proposed to be involved in general visual processes which include but are not limited to a role in word identification (Vogel, Petersen, & Schlaggar, 2014). While MTG is primarily studied in the context of language, within this domain it is associated with word and text-level processes, including syntax (Hagoort, 2014), semantic storage (Price, 2012), and semantic control (Jefferies, 2013; Whitney, Kirk, O'Sullivan, Lambon Ralph, & Jefferies, 2011). In this context, the literature therefore encourages an exploration of these regions in the context of their flexible "information processing characteristics" (Vogel et al., 2014) rather than restrictive cognitive properties.

This movement towards identifying regions based on information processing characteristics has been more successfully accomplished in domain-general areas, such as our final overlap region of interest, the left dlPFC. The dlPFC has been found to support a range of higher-level functions, including working memory (WM) and top-down executive control (Ptak, 2012), which is necessarily adaptive to support changing external goals (Smallwood, Brown, Baird, & Schooler, 2012). While the specific role of the dlPFC in RC is unclear, neuroimaging work and behavioral studies on WM suggest that the dlPFC may play a role in both WL and DL reading processes, including support of word-to-text integration (Stafura & Perfetti, 2014a; Van Petten et al., 1997) and discourse construction/coherence (Coelho et al., 2012).

Differential functional connectivity networks during word- and discourse processing

To examine networks that might underlie multi-tier RC deficits, we isolated regions whose mean activation overlapped during word and passage reading, and which have been implicated in WL and DL reading processes: (a) the pVWFA, a region previously found to critically contribute to reading through support of both orthographic and orthographic-semantic linking (b) IFG, MTG, and TP, all implicated in the frontal-temporal semantic network (henceforth referred to as *language overlap regions*; (Binder et al., 2009), and (c) the dlPFC, as prior studies suggest that WM, which is supported by the dlPFC, may play a role in both WL and DL functions. Our findings indicate that key language and WM regions that show shared activation in word and passage reading have different network correlations for these respective tasks. Importantly, this differentiation was predicted by reading ability.

Word-level connectivity patterns and dissociable influences of decoding and RC ability

WL connectivity was characterized by coordination between semantic and orthographic processing regions. All three language overlap regions showed convergent correlations with a key region in visual word recognition, the left occipitotemporal area (extending to the pVWFA). Similarly, the pVWFA seed showed coordination with the left MTG (overlapping with the left MTG seed), a region consistently implicated in word-level semantic storage and vocabulary processes. In Supplemental Analyses, this pVWFA-to-MTG coupling as well as pVWFA, MTG, and dorsal IFG activations were associated with WL reading ability (see Appendix). This is consistent with previous studies that typically developed readers show greater bottom-up communication from the fusiform gyrus to left MTG as compared to children with reading deficits during single word reading (Liu et al., 2010), and readers with dyslexia have reduced structure and function of the IFG and pVWFA (Richlan, 2012; Richlan, Kronbichler, & Wimmer, 2013). Our findings consequently suggest that WL processing and WL reading ability are characterized by activation of semantic and orthographic regions, as well as greater coupling between semantic and orthographic processing networks. These findings are consistent with behavioral models of reading. According to the Lexical Quality Hypothesis, adequate word recognition requires building appropriate semantic, orthographic, and phonological representations of the words, and for these representations to appropriately converge into a unified understanding of the word (Perfetti, 2007).

Interestingly, RC ability at the word level was not marked by increased connectivity of these systems. Rather, readers with higher RC, independent of decoding ability, had greater convergent connectivity from language *and* executive areas to the left ventral TP and medial prefrontal (mPFC) areas, which are consistently implicated in passive and controlled semantic retrieval processes (Davey et al., 2016). Supplemental examinations of RC ability and WL activations (not connectivity) also showed a relationship with the left TP, in addition to the left ventral IFG and left temporoparietal junction (TPJ; see Appendix). These activations and connectivity are consistent with previous literature on RC ability and word reading that emphasize a role for frontal areas, including the IFG (see Introduction). However, we provide the additional discrimination that 1.) the left TP appears to be a critical hub area for RC ability independent of decoding, 2.) connectivity of an executive area, the left dlPFC, is a distinguishing characteristic of higher RC ability at the word level, and 2.) the left MTG appears to be more closely related to decoding ability that RC ability. Overall, our findings provide evidence that at the word-level, RC ability is characterized by separate neural patterns than decoding ability, and specifically involves differences in frontotemporal semantic retrieval circuits centered around the left TP.

Overall, connectivity findings for WL processing were highly consistent with the central role of the pVWFA in word recognition, and suggest that stronger basic readers not only have greater activation of word recognition areas (as found in our GLM results), but also have greater communication between these areas and other semantic and orthographic processing regions. Conversely, higher RC ability was associated with increased activation of and connectivity to semantic retrieval areas.

Discourse-level processing networks and effects of RC ability

DL processing was characterized by independent, convergent positive correlations between all seed regions and the left AG. The left AG is a heteromodal region that is implicated in a wide range of cognitive functions, including spatial cognition, the DMN, math processing, and semantics (Seghier, 2013). Within the context of language, the left AG has been extensively studied and consistently found to support global semantic/conceptual integration processes, including the integration of local semantic information into larger meaningful textual representations (Price, Bonner, Peelle, & Grossman, 2015; Seghier, 2013). As DL processing requires the coordinated effort to combinatorically integrate word-pair-, sentence-, and discourse-level units of meaning, in addition to maintaining previous units of information in WM, it is theoretically consistent that DL processing involves tighter coupling between the whole overlap network and the left AG.

In addition to coupling with the left AG, DL processing was marked by greater coupling within the traditional left-hemisphere language network. Specifically, the left IFG, TP, and posterior MTG were correlated with each other in DL processing. These three regions are thought to form an executive semantic control network (Whitney et al., 2011), which processes local combinatorial semantic information and semantic inferences, as opposed to the more global processes of the left AG. Consequently, compared to the orthographic-semantic network found in WL processing, our results characterize DL processing with local-global semantic network interactions. This is consistent with neural models of language processing (Friederici, 2011), in which sub-sentence information is necessarily passed to (and informed by; Stafura & Perfetti, 2014) higher-level processing centers (left AG) in order to be integrated into a cohesive internal model (Whitney et al., 2009). Interestingly, compared to WL reading, the pVWFA was also found to be tightly coupled with both local (left TP and left MTG) and global (left AG) semantic processing nodes, as well as with the left SMG, a region associated with phonological processing (Price, 2012). In the context of the Lexical Quality Hypothesis, this could suggest that DL processing requires more rigorous coordination between the phonological-orthographic-semantic nodes, as represented by pVWFA, left SMG, and local/global semantic regions (left MTG, left TP, left AG), respectively. However, these network connections were not found to be mediated by basic reading ability or RC ability, and further study is needed to tease apart the specific functional roles of this network.

Our results for the influence of RC ability on DL processes show that higher RC ability was marked by increased correlations between the left dlPFC and the left AG. In the context of the WL findings on RC ability, these results suggest that lower RC ability involves (1.) decreased semantic retrieval activation/connectivity during WL reading, (2.) decreased semantic integration processes during DL reading, and (3.) decreased executive oversight of semantic cognition across reading tasks.

The dlPFC may be a flexible hub that supports and integrates WL and DL processes

Interestingly, a comparison of word- and discourse-level associations with RC ability show that stronger comprehenders have greater flexible connectivity to semantic retrieval and integration circuits for word- and discourse-level processes, respectively. Consequently, in addition to properties of the semantic network, adequate RC appears to require flexible, task-dependent coupling of this executive area.

The dlPFC and its associated cognitive functions are hypothesized to support the integration, prediction, and organization of different types of incoming text information (Christopher et al., 2012; Fedorenko, 2014). Consequently, the WM and executive control behaviors associated with the dlPFC are of particular interest in the context of RC deficits. Executive functions related to dlPFC are independently associated with success in word reading and RC (Cain & Oakhill, 2006; Locascio et al., 2010; Oakhill & Cain, 2012). Additionally, readers with lower WM ability have shown decreased efficiency in local-global contextual dependence (Van Petten et al., 1997). These findings have led to behavioral models of reading in which executive functions not only independently supports fluency and maintenance of conceptual information for WL and DL processing, respectively, but also supports the appropriate integration of WL and DL information (Cutting et. al, 2015). Within this framework, we would expect the dlPFC to mediate the relationship between WL and DL networks, and thus facilitate phonological, semantic, combinatorial semantic, and conceptual integration.

While the methods used in this paper do not allow for causal interpretations, our supplemental analysis does suggest an additional role of the dlPFC in WL and DL integration (see Appendix). Specifically, examination of the interaction of dlPFC activation and left AG whole-brain connectivity (in Passage vs. Baseline) showed that one unit increase of dlPFC activation positively predicted coupling between the left AG and the left pVWFA—the two primary convergent nodes for DL and WL processing, respectively. Further, the relationship between left AG and OT areas is positively predicted by WM capacity. This suggests that the WM capabilities of dlPFC potentially facilitate greater communication between WL and DL networks. Future studies should explicitly examine WM and other executive function measurements and their predictions of network interactions, as well as apply causal modelling to examine directional relationships between the dlPFC, AG, and the language network.

Conclusion

Our findings indicate that word and passage reading recruit activation in overlapping regions, but these areas form task-specific networks within and beyond the language network. Specifically, our functional connectivity analyses indicate that overlap areas in the language network exhibit multi-functional, task-specific correlations, and that these correlations are predicted by WL reading and RC ability. Word reading is characterized by connections between lexico-semantic regions and orthographic processing regions, and these orthographic-semantic connections are predicted by word decoding ability. Conversely, RC ability predicts increased activation and convergent connectivity to semantic retrieval areas, particularly in the left TP. Passage reading not only involves these WL processing networks, but additional communication between the same overlap areas and the global integration processes in the left AG to support DL processes. RC ability is predictive of coupling between higher-order information maintenance and meaning coherence regions. Consequently, stronger comprehenders appears to be characterized by greater communication between semantic retrieval and integration hub areas during WL and DL reading.

The interaction between these flexible networks and RC ability encourage additional exploration of overlap regions in naturalistic reading environments. More generally, our findings highlight the fact that shared regional activity is not necessarily indicative of shared functions, even within the same cognitive domain. While it has long been known that brain regions perform multiple cognitive functions, our results suggest that connectivity may be critical for truly dissecting differences, even within similar tasks where one is presumed to be controlling for some aspect of the other.

Limitations and Future Directions

The current study has a few limitations as well as areas that should be more extensively examined in future studies. First, as there is some evidence that OT regions respond to visual properties, it is possible that Words vs. Symbols pVWFA connectivity results were confounded by lower-level visual processes driven by visual discrepancies between the two stimuli types. However, the fact that all reported WL connectivity findings are replicated in Words alone, and are also consistent with functional and structural associations from other literature, suggests that the effect of visual characteristic differences on the current results is likely minimal. Secondly, regions of interest in the current study were limited to large brain areas; to further the current exploration of multifunctionality in reading, future studies should examine network patterns from smaller subdivisions of overlap regions. The current study also encourages further investigation of network properties in young readers, including the use of interventional paradigms to examine how RC interventions mediate connectivity patterns in struggling reader populations. The directional roles of these nodes can also be explored with causal modeling of connectivity data. Additional work should examine how these network connections are influenced by text genre, as expository text specifically places increased demand on WM capacity and semantic processing, and decreased demand on social cognition. Through these examinations, neuroimaging techniques can be used to set the groundwork for neurobiologically-informed RC interventions. Such knowledge not only has the potential to improve clinical and educational approaches to developmental reading processes, but also to contribute to our general understanding of basic language processes.

Chapter 3

Spatiotemporal progression of semantic cognition in the brain

Motivation

In Chapter 2 we were able to provide some evidence that RC ability is related to semantic retrieval and integration circuits centered around multi-functional language and executive hub regions (i.e. the Hub and Executive Mediation Hypotheses; see Chapter 1). However, there are several limitations that prevent mechanistic insight into the interface between the brain and RC ability: 1.) restrictions to region of interest analysis may overlook key whole-brain network properties that contribute to RC ability, 2.) temporal limitations of fMRI prevent examination of rapid neural processes, and 3.) the broad paradigm used in Aboud et al. (2016) requires reverse inference. Chapter 2 consequently does not allow us to test the Bottleneck Hypothesis (which requires temporal specificity), or determine with certainty the complex and timely network trade-offs associated with individual differences in RC ability. A more in-depth and methodologically precise approach is needed to piece apart the relationship between RC ability and semantic processing networks in the brain.

The next study aims to provide spatiotemporal characterization of semantic cognition during sentence reading. Specifically, we use joint analysis of fMRI and EEG to identify where and when semantic processes occur. The joint ICA approach allows us to sub-divide cognitive processes into different interactive brain networks over time. This, combined with a rigorous stimulus design meant to capture different dimensions of semantic cognition, will provide the methodological power to disentangle the networks that support RC ability over time during text comprehension (Chapter 4), and specifically test the Language Bottleneck hypothesis proposed in the Introduction.

Neurocognitive Correlates of Semantic Cognition

The ability to extract meaningful information from a text is a key predictor of educational and occupational outcomes (Ricketts et al., 2014; Ritchie & Bates, 2013). Yet, 20% of adults in the U.S. are unable to identify basic information when reading (U.S. Department of Education, 2019). While the ability to sound out words (i.e. "decoding" ability) accounts for a degree of comprehension performance, approximately 10% of readers with typical decoding ability still struggle to comprehend texts due to difficulties in accessing and utilizing meaning during reading (i.e. "semantic cognition") (Spencer et al., 2014; Stothard & Hulme, 1995). Neurobiological studies have made significant progress in identifying brain regions that support semantic cognition; however, there is currently no consensus on the spatiotemporal progression of meaning processes during real-time comprehension. These limitations are due, in part, to methodological restrictions in neuroimaging techniques that prevent a full spatiotemporal picture of cognitive processes (as discussed in Osterhout et al., 2012). Here we use a fused analysis of fMRI and ERP data as subjects perform a novel paradigm to track where and when semantic cognition occurs during sentence comprehension.

Psycholinguistic literature highlights that semantic cognition is not a one-dimensional construct. Rather, adequate comprehension of a written sentence requires accessing word meaning (semantic retrieval), and unifying retrieved word meaning based on the ongoing "message level" context of the sentence (semantic integration) (Davey et al., 2016; Peter Hagoort, 2005). Here, we briefly review the definitions and neurobiological findings for where and when these two semantic sub-processes occur.

Where semantic cognition occurs in the brain: Evidence from MRI and Lesion studies

In the context of a written sentence, semantic retrieval is the process of connecting the orthographic-phonological dimensions of a written word to its meaning stored in long-term memory. Semantic retrieval is not an isolated process: the local context of a word (including the other individual words in the sentence, syntax, other lexical qualities, and world knowledge) influences the ease of retrieval through bottom-up priming effects (Kutas & Federmeier, 2011). Semantic retrieval has traditionally been studied through the manipulation of these priming effects. In the context of a sentence, word pairs that are either semantically related (e.g. “bird” and “wings”) or unrelated (e.g. “bird” and “finger”) are embedded into a sentence, so that the local relationship between words are either strongly or weakly related in meaning. For example, in the sentence “A bird spread its wings”, neural access to the concept of “wings” is made easier by the preceding activation of the highly related word “bird”. Conversely, in the sentence “The bird landed on Mary’s finger”, retrieval of the word “finger” is more taxing due to a lack of a lexical prime. Notably, in both of these sentences, the word pairs are related to each other by the context (i.e. the sentences “make sense”); however, studies have shown that manipulation at the local level in sentences, regardless of context, does impact the difficulty level of semantic retrieval (Van Petten, Coulson, Rubin, Plante, & Parks, 1999; Van Petten & Luka, 2006). While distinct from single-word reading processes (as described in Chapter 2), semantic retrieval priming paradigms are still thought to capture variability in bottom-up spreading activations (Kutas & Federmeier, 2011). The neural correlates of semantic retrieval processes, within and outside of a sentence context, are still heavily debated. Some researchers argue for a localized semantic retrieval area in the left middle temporal gyrus (MTG) (Hagoort, 2013; Lau et al., 2008). However, work in patients with semantic dementia and semantic aphasia (with lesions in the temporal poles and MTG, respectively) suggest that semantic retrieval involves wide-scale, bottom-up reactivation of multiple semantic dimensions of a word that converge onto a semantic "hub" region in the temporal poles (TP) (Davey et al., 2015; Rogers, Patterson, Jefferies, & Ralph, 2015). Resolution of these debates is made difficult by the spatial and temporal restrictions of commonly used neuroimaging approaches.

When reading connected texts, readers must also engage in regions that support the top-down, ongoing unification of retrieved word meanings into the evolving mental representation of the text. One canonical way to examine semantic integration is to manipulate the semantic plausibility of sentences, and consequently impede/support semantic integration (e.g. sentence "The cat licked the airplane" versus "The cat licked the bowl"). Studies have identified a consistent association between semantic integration and frontal areas, including bilateral/left IFG (BA 47 and 45) and dorsolateral prefrontal cortex (dlPFC). Davey et al (2015) suggests that the MTG acts as a communication point between frontal integration areas and the semantic retrieval processes in the temporal poles, while Hagoort (2013) suggest the retrieval-integration circuit primarily occurs through iterative communication between MTG and IFG, respectively. Of note, some research separates the unification of word meanings from the control of accessing upcoming word meanings; however, for the purposes of the present study, we identify these processes under the umbrella term of "semantic integration".

When semantic cognition occurs in the brain: evidence from ERP studies

MRI studies reveal that adequate semantic cognition requires dynamic interactions between temporal and frontal language areas that support semantic retrieval and integration, respectively. However, these processes occur on the scale of milliseconds; consequently, the poor temporal resolution of MRI only allows for a limited understanding of semantic cognition. Event-related potentials (ERPs) provide insight into the rapid neural responses related to semantic cognition. ERP semantic studies have primarily focused on two temporal components: the N400 and, more recently, the P600. Here, we briefly describe the characteristics of these neural responses.

The N400 component is a negative waveform that occurs between 300-500 ms after stimulus onset, and which has increased negative amplitude for semantically incongruent (e.g. semantically "difficult") stimuli. This component is thought to reflect the effort of integrating a critical word into the preceding context. Interestingly, studies have demonstrated that incongruent word pairs, sentences, and discourse all show greater negativity of the N400 component's amplitude—a phenomenon referred to as the "N400 effect". Consequently, the N400 appears to reflect both semantic retrieval and integration. While many studies have attempted to localize the N400 effect to a specific brain area/network, there is currently no consensus on the primary neural source. While some argue for localization of the N400 to the MTG (Lau, Almeida, Hines, & Poeppel, 2009), Kutas & Federmeier (2011) suggests that the N400 is not reflective of a single neural source, but instead results from a "wave" of activations across diverse areas in the brain. This interpretation accounts for seemingly contradictory findings in the N400 literature, namely that the N400 appears to be associated with both automatic ("bottom-up") and controlled ("top-down") processes, and localizes to different sources depending on task. For instance, some evidence suggests that the N400 passive spreading and prediction effects both traces to left anterior temporal cortex (Lau, Weber, Gramfort, Hämäläinen, & Kuperberg, 2016), while other work emphasizes a role for posterior temporal structures and potentially frontal regions (Lau et al., 2008). This array of findings has led some to suggest the N400 reflects diverse, "reverberating activity" within the full fronto-temporal semantic loop described in the section above. However, the localization of the N400 for semantic retrieval and integration in a sentence context has not been quantitatively examined through a unified paradigm, or using joint fMRI or ERP approaches.

The second ERP component shown to have a relationship with semantic manipulations is the P600. The P600 is a positive waveform measured at central parietal electrodes that occurs 500-800 ms post-stimulus, which has traditionally been used as an index of syntactic difficulty/anomaly, and more broadly, the structural coherence of a sentence (Osterhout, 1997). In recent work, the P600 has been found by a number of studies to index semantic plausibility in sentences (Brouwer & Hoeks, 2013; DeLong, Quante, & Kutas, 2014; Hoeks, Stowe, & Doedens, 2004; Kuperberg, Sitnikova, Caplan, & Holcomb, 2003). These findings have led to multiple competing proposals for the functionality of the P600, including that the P600 supports syntactic-only re-appraisal (Osterhout & Holcomb, 1992), semantic-syntactic re-appraisal (Kuperberg, 2007), semantic integration (Brouwer et al., 2012), and/or domain-general processes (Burkhardt, 2007; Shen, Fiori-Duharcourt, & Isel, 2016). Localization studies of the P600 have also produced varied results, with some localizing the effect to frontal areas (as discussed in Brouwer & Hoeks, 2013), temporal lobes (Service et al., 2007), and others to wide spread activations in frontal and temporo-parietal regions (Kielar et al., 2015). Similar to the N400, diverse findings related to the P600 has led some researchers to propose that this component contains multiple cognitive substrates involved in combinatorial semantic-syntactic processes (Kuperberg, 2007). However, greater spatiotemporal resolution is needed to identify the nature of the P600 (Friederici, 2002a), in particular whether the P600 is linked to semantic, syntactic, and/or domain-general regions during sentence comprehension.

Current Study

MRI and ERP studies have found that semantic cognition is supported by dispersed, rapidly interactive brain networks. However, the limited spatial and temporal resolution of each modality prevents consensus on a neurocognitive model of semantic cognition. In particular, it is unclear 1.) how specific fronto-temporal language areas interact on the millisecond time-scale to support semantic cognition, and 2.) how these patterns map onto the N400 and P600 effects described in the literature. To address these questions, studies need to have real-time, high-resolution observations paired with task manipulations that ground findings in defined cognitive processes (Osterhout, McLaughlin, Kim, Greenwald, & Inoue, 2004). In the present study, we use joint independent component analysis (jICA) of fMRI and ERP to map the time course of brain activations during semantic cognition. In order to piece apart the cognitive processes associated with the spatiotemporal progression, we use a novel sentence reading paradigm that manipulated semantic retrieval and integration processes. Through the combined sensitivity of joint imaging modalities and a refined cognitive task, we seek to bridge the gap between MRI and ERP semantic cognition literature, and provide evidence for a neurocognitive model of semantic cognition.

Methods

Participants

Thirty right-handed participants were recruited from Vanderbilt University. All participants were native English speakers with normal or corrected-to-normal vision, no history of major psychiatric illness, and no contraindication to magnetic resonance imaging (MRI). To ensure that subjects had typical IQ and did not have dyslexia, we administered the Kaufman Brief Intelligence Test—matrices subtest and Woodcock Johnson Reading Mastery Test III—letter word identification (LWID) and word attack (WA) subtests (McGrew, Schrank, & Woodcock, 2007). Behavioral metrics confirmed that subjects had typical IQ (minimum > 85 ss; mean = 111.52 +/- 8.48) and basic reading ability (minimum > 85 ss; mean = 105.94 +/- 7.9). Out of the original subject pool, n = 4 were excluded due to motion artifacts (n = 3) and inability to complete the two sessions (n = 1). The final analysis included 26 adults (mean age= 25.36 +/- 3.69). Participants gave informed consent at the beginning of the study, with procedures carried out in accordance with Vanderbilt University's Institutional Review Board (IRB). Participants received compensation for behavioral and neuroimaging testing as per the study's IRB

Stimulus construction

In order to isolate semantic retrieval and integration processes, we followed an approach by (Van Petten et al., 1997) and employed a novel 2x2 sentence reading design that manipulated lexical priming (i.e. whether or not embedded word pairs were semantically related to one another) and sentence congruence (i.e. whether or not the sentence "made sense"). The paradigm resulted in four conditions: 1.) Congruent word pairs, congruent sentence (CWCS), 2.) Incongruent word pairs, congruent sentence (IWCS), 3.) Congruent word pairs, incongruent sentence (CWIS), and 3.) Incongruent word pairs, incongruent sentence (IWIS; see Figure 3.1 for example). From these conditions, we could capture semantic retrieval the comparison of unprimed vs. primed embedded word pairs, with and without message-level congruence support (IWCS vs. CWCS; IWIS vs. CWIS). Similarly, we could capture semantic integration through the comparison of silly versus non-silly sentences, with and without lexical priming support (CWIS vs. CWCS; IWIS vs. IWCS; see Figure 3.1).

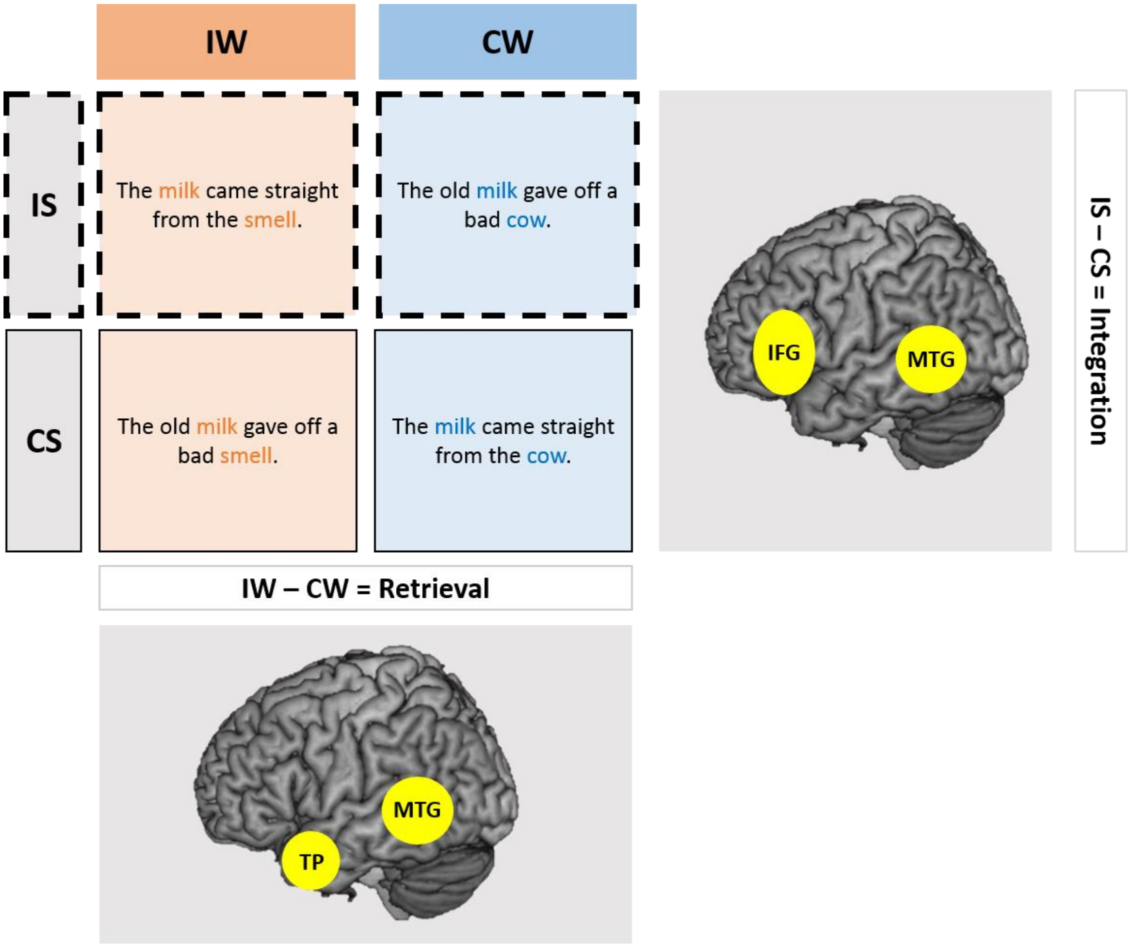


Figure 3.1: Example Stimulus for the 2 x 2 congruency design, in which word pairs embedded in a sentence were not primed (first column; orange; incongruent words; IW) or primed (second column; blue; congruent words; CW), and sentence pairs were implausible (top row; dashed lines; incongruent sentences; IS) or plausible (bottom row; solid lines; congruent sentences; CS). The comparisons of IW-CW and IS-CS provide insight into semantic retrieval and integration, respectively. Highlighted brain areas reflect areas highlighted in the literature as supporting retrieval (temporal poles and middle temporal gyri; TP and MTG) and integration (inferior frontal gyri and MTG; IFG).

Over two sessions (see below), participants read 192 sentences that had an expected sentence-final critical word (48 sentences/condition). Stimuli was constructed in sets of two sentence frames, each containing a matched prime word. Sentences ranged from 4-11 words. The South Florida Association Norms were then used to identify two critical word lists that had strong association strength with the prime word ($\geq$ 0.07) or weak association with the prime word (< 0.07; only 4 sentences across both lists had non-zero association strength). Due to previous findings that typical adult readers are more sensitive to backward association strength in the context of sentence reading (Stafura et al., 2015), backwards association strength was manipulated to be higher than forward association strength (mean of backward strength = 0.32; mean of forward strength = 0.10). Nevertheless, both backward and forward strength was significantly greater in congruent vs. incongruent word-pairs ($p < 0.0001$). In the incongruent words condition, sentence stimuli was constructed such that the critical word was not primed by any preceding words in the sentence, including the matched prime word. Notably < 0.05% of the incongruent word conditions had any non-zero priming relationships with other words in the sentence. The CC condition was allowed to have multiple priming effects in addition to the matched prime word. The two critical word lists (strong and weak association) were matched on word length, word type (noun, adjective, verb), syllable number, concreteness, and orthographic neighborhood size. Word pairs were embedded in the sentence frame sets to create predictable (“congruent”) and implausible (“incongruent”) sentences. Implausible sentences either contained information contradictory to known world properties (e.g. *The bird spread its fingers*) or to world experience (e.g. *Amy got in trouble for getting dirt on her mud*), or contained internally contradictory information (e.g. *The glasses did not work and made her eyes see*). A task-probe on whether the sentence made sense (see below) revealed that subjects were able to distinguish incongruent sentences from congruent sentences with a high degree of accuracy.

Stimulus presentation

Two separate lists of stimuli were constructed. Each list contained a total of 192 sentences (48 sentences/condition) presented across 4 runs (duration = ~ 6 minutes/run). In order to minimize repetition effects related to repeated sentence frames, sentence presentation order was randomized within the list. Lists were counterbalanced across fMRI and EEG per subject. Additionally, fMRI and EEG administration order was counterbalanced across subjects (see below). During each session, sentences were presented one word at a time (see Appendix). Each word was presented for 500 ms, with a 100 ms pause between words. To ensure task attention and sentence comprehension, subjects were probed after the end of each sentence about whether the sentence did or did not make sense (i.e. sentence congruency measure). The sentence's terminal word was followed by a 500 ms break (indicated by a plus sign), then a probe of "yes/no", during which the subject had 1250 ms to respond on a button box. All subjects had high accuracy (> 90%) for the sentence probe task, confirming that incongruent sentences were highly identifiable, and that subjects stayed on task. Due to high performance on the probe, all sentences were included in the final analysis.

fMRI/EEG acquisition

In order to counteract any learning effects related to the task, the fMRI and EEG sessions were separated by an average of 6.1 +/- 3.5 months, and fMRI/EEG administration order was counterbalanced across subjects (n = 13 subjects performed the EEG session first). Subjects were additionally counterbalanced on which of the two stimuli lists they received for their first session, as well as response hand.

fMRI data acquisition and preprocessing

All fMRI scans were acquired at Vanderbilt University Institute of Imaging Sciences on one of two Philips Achieva 3T MR scanners with a 32-channel head coil. Scanner was regressed out from all analysis. Functional images were acquired using a gradient echo planar imaging sequence with 40 (3 mm thick) slices with no gap and consisted of 4 runs (single run duration (TA) = 6 minutes; 160 dynamics per run). Slices were parallel to the anterior-posterior commissure plane. Additional imaging parameters for functional images included echo time (TE) = 30 msec, FOV 240 x 240 x 120 mm, 75 degree flip angle, and repetition time (TR) = 2200 msec, and 3 mm^3 voxels. Image processing was completed using Matlab R2018b and SPM12 (Friston et al., 1994). Experiment design was event-related, with the events timed to the sentence-final critical word. Preprocessing included slice timing correction, realignment of volumes, normalization of functional images to a standardized space, and motion correction using ART. Subjects with > %20 motion outliers were excluded from the analysis (n = 1). For each subject, contrast maps were generated per condition (CWCS, IWCS, CWIS, IWIS) versus a plus-sign baseline. These subject-level contrasts were input into the joint ICA pipeline.

EEG data acquisition and preprocessing

All EEG data was acquired at the Vanderbilt Kennedy Center, using a 128 channel geodesic net (EGI, Inc., Eugene, OR). Data was sampled at 250 Hz with filters set to .1-100 Hz. The vertex was used as the reference during data acquisition. Data processing was completed using NetStation and Matlab. EEG was segmented into epochs of 1000 ms, starting 100 ms before the onset of the target word. For all conditions, the target word was the sentence-final word. Trials contaminated with ocular or muscle artifacts were excluded from analysis. Recordings were re-referenced to an average reference. To be included in the statistical analysis, individual condition ERPs were based on a minimum of 20 trials; n = 2 subjects were excluded due to excessive motion artifacts. The N400 was defined as the mean voltages in a 300-600 ms latency window when compared to the 100 ms prestimulus baseline, pulled from centroparietal electrodes (Electrodes: 54, 55, 62, 80, 81, 32, 7, 107; Kutas & Federmeier, 2011). Pre-processed time signals for each condition were averaged across subjects, then entered into a grand average across subjects per condition. These grand averages were input into the joint ICA pipeline. Confirmatory analysis of the waveforms revealed expected N400 effects across incongruent conditions. Difference waves were generated for Incongruent – Congruent Words, and Incongruent – Congruent Sentences, and the maximum negative peak within the N400 time window (300-600 ms) per subject was input into a one-sample t-test. The N400 effect was significant for word congruence ($t = -4.19$; $p < 0.001$) and sentence congruence ($t = -12.12$; $p < 0.001$) manipulations. These findings confirm that our paradigm captured expected EEG patterns (see Appendix).

fMRI-ERP joint ICA (jICA) analysis

Fusion analysis was performed using the Fusion ICA Toolbox (FIT) in Matlab, and followed processing protocols established by Calhoun et al. (2006) and Mijović et al. (2012) (see also Edwards, Calhoun, & Kiehl, 2012; Ouyang et al., 2015), which were developed for parallel fMRI/EEG acquisition (notably, parallel acquisition has been found to be more ideal for this approach than simultaneous acquisition; see (Mijović et al., 2012). In JICA, independent components for fMRI and EEG are simultaneously estimated. Compared to other multimodal analysis approaches, jICA allows for the spatial and temporal components of EEG and fMRI, respectively, to influence each other, and is consequently considered to truly be a “fused” data analysis approach (Mijović et al., 2012). In jICA, the spatial fMRI maps and the ERP component timecourse are concatenated into a subject x data input matrix (the ERP timecourse is upsampled using a cubic spline interpolation so that it is the same dimensionality as the spatial fMRI vector; Mijović et al., 2012). The fMRI and ERP data are first-level contrast map and grand average timecourse, respectively, for one condition. Consequently, the only within-subject data in the pipeline is condition. The model consequently assumes that ERP peaks and BOLD responses change in a similar way across subjects. This approach has notably been found to provide robust, high-quality data decompositions (Mijović et al., 2012) which have been validated across a number of cognitive substrates and populations (Calhoun et al., 2006; Calhoun, Liu, & Adali, 2009; Edwards, Calhoun, & Kiehl, 2012; Ouyang et al., 2015). The jICA algorithm outputs group-level, joint independent components that includes information for each modality (i.e. one component includes both an ERP time course and a spatial map). Condition-specific maps and time-courses are back-reconstructed to allow identification of how each condition contributes to the cross-condition components. The strength of this contribution is reflected by a subject- and condition-specific parameter weighting (i.e. a measure of how "strong" the component signal is within that subject and condition), which can be used to statistically identify condition differences per component.

A limitation of this ICA stacking method is that it assumes each condition has a similar underlying signal that only differs in magnitude. However, in the present study, a measurement of spatial divergence (Renyi divergence) revealed that the average divergence across conditions was very low (divergence < 2). To further address this concern, for each component we supplementally examined the conjunctions of back-reconstructed spatial maps per condition to determine if each condition showed convergent findings on the primary spatial component. If conditions did not show convergence, back-reconstructed maps are reported and discussed. Throughout, spatial maps are thresholded at $p < 0.005$. Multiple comparison correction was not necessary because ICA is a multivariate, not univariate, analysis.

ICA parameters

The Infomax algorithm was used to identify joint components. To determine the ideal number of components, we followed protocols established by Artoni et al. (2014) and Himberg et al. (2004). First, we used ICASSO to identify the number of stable components. ICASSO iteratively runs ICA to determine the stability of generated components. As recommended by Himberg et al. (2004), we set the component number to the subject number ($n = 26$), and performed 50 ICASSO iterations. There were $n = 15$ components with a liberal but reasonable r-index ($> .25$), which reflects the component's internal correlation across iterations. We then ran the final analysis using $n = 15$ components. The stability index (Iq) for all generated components was > 90.

Component selection

As done in Calhoun et al. (2006), we took advantage of the ERP signals to identify components that reflected noise versus true brain signals. We applied the following criteria: 1.) Components had to contribute > 1 standard deviation (SD) of variance to the grand mean of the EEG signal ($n = 5$ components removed) (Edwards et al., 2012). 2.) We used the findpeaks Matlab function to identify any components with an excessive number of peaks (outliers defined as > 30 peaks; $n = 1$ component removed). 3.) After non-noisy components were identified, the remaining components were screened to determine whether they met N400 or P600 criteria (a negative peak between 300-600 ms, or a positive peak between 500 and 800 ms).

Once peaks were identified, condition differences were examined by running paired t-tests between subject parameter weights for the following condition comparisons: IWCS vs. CWCS (retrieval with contextual support), IWIS versus CWIS (retrieval without contextual support), CWCS versus CWIS (integration with lexical support), IWCS versus IWIS (integration without lexical support), and IWCS versus CWIS (retrieval versus integration).

Results

Our joint ICA approach resulted in one spatiotemporal component whose time course reflected N400 characteristics, and three spatiotemporal components whose time course reflected P600 characteristics (see Figure 3.3 and Appendix). Below, we describe the characteristics of each spatiotemporal component, including peak latency, spatial localization, and condition sensitivity.

Joint Component 1 (JC1)

Latency. The first joint component temporally mapped onto a classic N400. The negative peak latency occurred at 400 ms post-stimulus, which fell into the N400 effect time-window for our average ERP results (see Appendix).

Localization. The N400 component corresponded with a widespread spatial network in canonical language regions, which have previously been associated with N400 localization studies (Kutas & Federmeier, 2011; Lau et al., 2008, 2016). The regions included bilateral STG, left MTG extending into TP, bilateral IFG/dlPFC (BA’s 45, 46, 47), Cingulate Gyrus, PCU, and the motor/cerebellar regions.

Condition differences. Condition comparisons revealed that only incongruent sentences showed significant loadings onto this component. Additionally, the weighting differences for incongruent versus congruent sentences were significant, including: CWIS > CWCS ($t = 5.93$; $p < 0.001$); IWIS > IWCS ($t = 3.80$; $p < 0.001$); CWIS > IWCS ($t = 6.14$; $p < 0.001$). The significant finding of CWIS > IWCS revealed that this component was significantly more related to integration than retrieval processes. Comparisons of back-reconstructed spatial images for each condition revealed no common overlapping areas. Because of this, we ran an exploratory supplemental analysis to examine qualitative network differences comparing the spatial maps for IW versus CW (semantic retrieval) and IS versus CS (semantic integration). Conjunctions were generated from minimum t-value of the subconditions. Comparisons revealed that IW had unique associations with the left MTG, as well as more expansive activation of the bilateral TP than CW. Comparisons of IS versus CS revealed that while IS mapped primarily onto language areas seen in the general component, CS mapped onto areas within the DMN (see Appendix). Mappings onto the DMN for congruent sentences support the idea that, in the absence of increased processing demands, automated spreading activations occur during this time window.

Joint Component 2 (JC2)

Latency. The first joint component within the P600 range (P600a) had a positive peak latency at 500 ms post-stimulus, which fell into the early P600 effects window in the average ERP findings, specifically for the IWIS condition.

Localization. P600a corresponded with co-activation of bilateral STG, parahippocampal areas, right SMG, ACC, PCU, premotor and sensory areas, insula, and the cerebellum.

Condition differences. Condition examinations revealed that all conditions significantly mapped onto JC2. Supplemental examinations of back-reconstructed condition maps demonstrated that all conditions spatially converged on the general component. Still, the joint weightings were significantly stronger in the completely incongruent condition (IWIS) than all other conditions: IWIS > IWCS ($t = 4.54$; $p < 0.001$); IWIS > CWIS ($t = 4.12$; $p < 0.001$). Comparisons additionally revealed a significant interaction effect between word-level and sentence-level incongruence: the effect of IWIS > IWCS was significantly greater than the effect of CWIS > CWCS ($t = 3.14$; $p = 0.003$). This result suggests that the component is specifically sensitive to sentence congruence in the absence of word-level semantic support. This component's early latency and sensitivity to novelty reveals similarities with previously described properties of P300b (see Discussion and Leckey & Federmeier (2019).

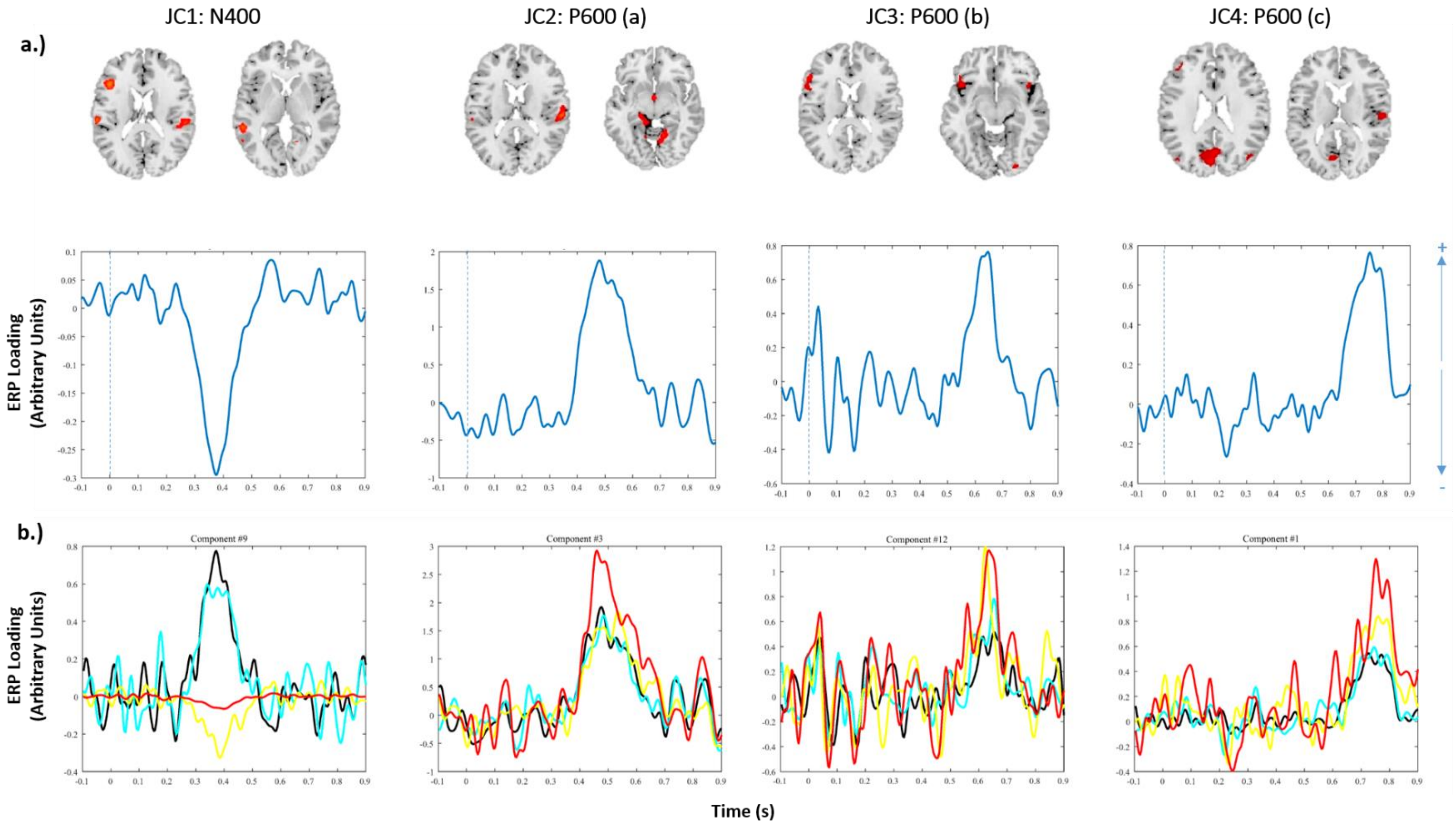


Figure 3.2 (a.) Joint ICA analysis resulted in four spatiotemporal components (JC1-JC4) that mapped onto language, memory, and domain-general processing areas (top panel); spatial network changes corresponded with one negative component in the N400 time-window, and three positive components in the P600 time window (bottom panel). (b.) Comparisons of ERP weightings for each condition revealed that components were sensitive to different cognitive demands, particularly semantic integration skills required in incongruent sentence processing: CWCS (black), IWCS (blue), CWIS (yellow), IWIS (red). All results reported at $p < 0.005$.

Joint Component 3 (JC3)

Latency. The second joint component within the P600 range (P600b) exhibited classic spatiotemporal properties of the "syntactic" P600, with a positive peak latency at 600 ms post-stimulus.

Localization. P600b corresponded with the largest co-activated clusters in bilateral ventral IFG and left dorsal IFG, as well as activation in bilateral STG, parahippocampal and fusiform gyri, PCC, SPL, sensory areas, and the cerebellum.

Condition differences. Condition examinations revealed that all conditions significantly mapped onto JC3. Supplemental examinations of back-reconstructed condition maps demonstrated that all conditions spatially converged on the general component. However, incongruent sentences had significantly stronger mappings in the absence of lexical support, including: IWIS > IWCS ($t = 2.59$; $p = 0.02$). There were no significant interaction effects.

Joint Component 4 (JC4)

Latency. The third joint component within the P600 range (P600c) had a late positive peak latency at 800 ms post-stimulus.

Localization. P600c corresponded with co-activation of regions within the DMN, including PCU, mPFC, left AG, and PCC. Additional co-activations could also be seen in bilateral STG, sensory areas, the insula, and the cerebellum.

Condition differences. Condition examinations revealed that all conditions significantly mapped onto JC4. Supplemental examinations of back-reconstructed condition maps demonstrated that all conditions spatially converged on the general component. As in JC3, the only significant condition comparison was for IWIS > IWCS ($t = 3.08$; $p = 0.006$), and there were no significant interaction effects. This findings suggest that this component is particularly sensitive to sentence congruence in the absence of a supportive word-level semantic context.

Discussion

In the present study, we used joint ICA of fMRI and ERP to identify the spatiotemporal progression of semantic cognition during sentence reading. Instead of finding a clear delineation between semantic retrieval and integration processes, our results instead revealed four spatiotemporal components within the typical range of semantic cognition that were primarily sensitive to semantic integration difficulty. These components included: a language component with temporal characteristics mapping onto the canonical N400; a memory component similar to characteristics of the P3b within the range of the P600 (P600a); a semantic and syntactic network mapping onto the canonical P600 (called here P600b); and a default mode network (DMN) component mapping onto a late positive potential (called here P600c).

The N400 maps onto previously identified sources for incongruent sentences.

The first joint component reflected a canonical N400 component that mapped onto a broad network of fronto-temporal language areas, including bilateral STG, IFG, left MTG, and bilateral TP. This mapping is largely in line with previous MRI studies on semantic cognition (Kutas & Federmeier, 2011; Lau, Gramfort, Hämäläinen, & Kuperberg, 2013; Lau et al., 2008; see Figure 3.1), as well as N400 localization studies, and consequently provides a proof-of-concept for the JICA framework in the context of language. Interestingly, however, supplemental examinations of the condition-specific spatial maps revealed that the N400 component had no spatial convergence across the four conditions. Qualitative comparisons of semantic retrieval revealed that sentences with incongruent words recruited the MTG and more expansive recruitment of the bilateral TP than sentences with congruent words. This finding is directly in line with previous literature on semantic retrieval (Davey et al., 2015; Hagoort, 2013; Price, 2012). Novel to the present study is the finding that while harder semantic integration recruited greater language areas, easier integration recruited areas in the default mode network (DMN), a network associated with bottom-up spreading activations (see Appendix). These seemingly contradictory findings actually provide preliminary insight into a long-standing debate within the N400 literature of whether the N400 is an automated or controlled component. In particular, the results suggest that in typical adult readers, for which congruent sentences should be largely automated, the N400 time-window (though in our findings, not an N400 component) reflects bottom-up spreading activation in the default mode, thought to assist with meaning resonance (Davey et al., 2016), while incongruent sentences prompt potentially costly activation in frontal areas and the larger language network that result in a robust N400 effect.

Notably, the JICA framework failed to identify an N400 component that significantly distinguished semantic retrieval difficulty, despite a significant (but small) N400 effect in the average ERP results. This may reflect a methodological limitation, in which smaller waveform effects are divided into multiple components, and consequently are unidentifiable. The absence of a word-level N400 effect does, however, coincide with previous observations that word priming effects are less observable when they are embedded in a sentence for typical adult readers (Stafura & Perfetti, 2014b; Stafura et al., 2015). We would anticipate, however, that these findings would be different for younger populations or those with language difficulties, and future studies should apply similar methodologies to examine these differences (see Future Directions).

The P600 effect includes spatially and functionally distinct memory, re-appraisal, and consolidation effects.

The P600 time window contained three distinct sub-components, which were each sensitive to some form of sentence incongruence, and whose characteristics corresponded with memory, reappraisal and situation model processes, respectively.

JC2 (Memory schema and the P600a). The first subcomponent, JC2, included activations of the hippocampus and bilateral STG. The STG is an area previously associated with the binding of semantic-syntactic information (Skeide, Brauer, & Friederici, 2014). These activations corresponded with an early window of the P600 effect observed in the mean EEG results (P600a). Though JC2 was observable across all conditions, it was particularly sensitive to the fully incongruent condition (IWIS), and had a word-by-sentence congruency interaction effect; i.e. the JC2 effect was larger for incongruent sentences without local word priming, than incongruent sentences with local priming. The combination of latency, localization, and condition effects suggest that this component shares similarities with the P3b in the literature. While typically studied in the context of oddball tasks, the P3b can have a latency as late as 500 ms depending on cognitive demand, but is typically not discussed in the field of semantic cognition (Leckey & Federmeier, 2019). The P3b has been posited to localize to the hippocampus and temporal lobes, but source localization restrictions have made it difficult to confirm (Polich, 2007). The current study consequently provides evidence that the P3b (1.) plays a role in RC in general, (2.) is sensitive to sentence novelty, and (3.) localizes to the hippocampus and bilateral/right STG in a sentence context. The P3b literature provides a few potential interpretations of JC2's role in sentence processing. One possible interpretation could be that JC2 reflects a post-hoc memory-schema update of the sentence structure/semantics (i.e. the context updating model) (Donchin & Coles, 1988). The observed network patterns are similar to those seen in memory schema encoding in language (Milivojevic, Varadinov, Vicente Grabovetsky, Collin, & Doeller, 2016) and semantic-syntactic interactions (Skeide et al., 2014), and the component's specific sensitivity to the fully incongruent sentence condition (IWIS), suggests an interaction with stimulus novelty, with any congruency (at word or sentence level) mitigating the novelty effect. A second interpretation is that JC2 reflects the transition from sentence re-analysis to the initiation of a behavioral response (Verleger, Jaśkowski, & Wascher, 2005). However, this does model does not explain the increased weighting for the fully incongruent paradigm. Our findings consequently strongly support the idea that, in the context of sentence reading, the P3b exhibits a delayed latency that contributes to the earliest portions of the P600 effect for highly incongruent stimuli, and this component may support a memory schema check that is sensitive to novelty and related to syntactic and semantic information. However, more study is needed to verify the functional role of this component.

JC3 (Re-appraisal and the P600b). The second subcomponent, P600b, maps onto well-described semantic (bilateral ventral IFG) and syntactic (left dorsal IFG) processing areas. In terms of ERP waveform properties, the P600b is the P600 subcomponent that most closely aligns with the P600 reappraisal effect (Osterhout & Holcomb, 1992). This effect is classically associated with reassessment in the face of syntactic violations. However, the effect is heavily debated, in part due to findings that syntactically allowable sentences with semantic incongruities result in P600 effects (i.e. the "Semantic Illusion Effect"; see Brouwer et al. (2012) for review). In particular, the P600 effect has been proposed to reflect syntactic-only re-appraisal (Osterhout & Holcomb, 1992), semantic-syntactic re-appraisal (Kuperberg, 2007), semantic integration (Brouwer et al., 2012), and/or domain-general processes (Burkhardt, 2007; Shen et al., 2016), among others. In the present study, several convergent findings support the conclusion that P600b effect is driven by both semantic and syntactic re-appraisal processes during sentence comprehension. First, the P600b component maps onto well-known semantic and syntactic frontal areas (ventral and dorsal IFG, respectively; Price et al. (2012). Second, the P600b is most strongly associated with the fully incongruent sentence condition (IWIS), beyond incongruent sentences with primed word pairs (CWIS); this finding is inconsistent with previous suggestions that the P600 is a syntactic component that is tricked into activation by lexico-semantic associations (i.e. the semantic attraction theory; as discussed in Kuperberg (2007). Additionally, the pairwise design in the current study ensures that congruent and incongruent sentences had identical sentence frames in which only the final word determined congruency, decreasing the chance that results were driven by differences in syntactic complexity. Our findings consequently support previous suggests that reassessment in the context of sentence comprehension (in typical adults) is a dynamic process that involves both syntactic and semantic systems at ~600 ms post-stimulus (Kuperberg, 2007).

JC4 (Consolidation and the P600c). The final component within the P600 range had a late peak latency at ~800 ms and corresponded with activations within the DMN. The primary cluster in the activation map was in the dorsal, posterior portion of the PCU. Interestingly, this area directly overlaps with several studies on narrative processing, which have found that the PCU is specifically sensitive to event boundaries within stories (Baldassano et al., 2017b; Whitney et al., 2009). Whitney et al. (2009) has proposed that this portion of the PCU acts to update situation models at key narrative moments (i.e. “narrative shifts”), which corresponds with the region’s more general association with episodic memory (Zhang & Li, 2012). More specifically, previous work has shown that incongruent information within a story elicits stronger responses in the PCU. Additionally, recent ERP work found strong evidence for a relationship between a P600 at similar latency and situation model updating (Burkhardt, 2007). Our finding that JC4 is sensitive to incongruent sentences is the first to consolidate MRI and ERP literature findings to provide joint evidence that situation model updating occurs at the tail-end of the P600 effect in sentence processing.

Conclusion

The present study reveals a spatiotemporal progression of activations in domain-specific and domain-general areas that support language processing during sentence reading. Out findings converge with prominent psycholinguistic theories of language progression, including identification of neural processes that support (in succession): semantic integration, syntactic-semantic schema checks, sentence re-appraisal, and (at the highest level) information consolidation (Friederici, 2002b). Within each of these processes, we provide additional evidence that (1.) the N400 time window does indeed reflect task-specific processes that can be bottom-up or top-down, (2.) the P3b (referred to here as P600a) plays a critical role in language-memory interface during sentence reading, (3.) the canonical P600 (referred to here as P600b) localizes to both syntactic and semantic regions, and (4.) later positive potentials (referred to here as P600c) may reflect situation model processes. These results consequently contribute to several debates within the neurolinguistics literature, and through refined spatiotemporal information, reveal specific attributes of known, highly-utilized ERP phenomenon.

Limitations and Future Directions

This study has several limitations. First, the embedded word pair stimuli had higher backward strength relationships than forward strength. This was purposefully manipulated in the present study due to previous findings that typical adult readers show greater sensitivity to backward strength than forward (Stafura et al., 2015). However, we would anticipate that this decision may contribute to some of the memory processes observed in the JICA progression, while forward strength word primes may result in less memory-heavy processing at the word-level. Future studies should examine these nuanced differences. Secondly, the current findings should be replicated in simultaneous fMRI-EEG; while previous studies have shown high replicability of joint ICA in simultaneous and parallel methodologies, a simultaneous study is still needed to confirm the real-time correspondence of these complex signals. Third, the use of word pairs embedded in sentences and a typical adult reader population resulted in low N400 effects for semantic retrieval processes. Future studies should utilize high spatiotemporal methods to examine single word reading, word-pair priming effects, and sentence congruency effects in a range of populations, particularly in younger readers and readers with language and reading deficits.

Through joint analysis of multimodal neuroimaging, our results provide insight into the online evolution of language during natural reading. These contributions provide a mechanistic understanding of semantic cognition in the brain, and reveal previously unidentified relationships between MRI and ERP signals that have the potential to impact multiple areas of study. In particular, we hope that these findings can assist in the increased understanding and identification of language-related disorders, including those who struggle with reading-related behaviors.

Chapter 4

The spatiotemporal progression of reading comprehension ability in the brain

Motivation

In Chapter 2, I found that RC ability is associated with hub properties of semantic and executive areas during reading, providing support for the Hub Hypothesis and Executive Dysregulation Hypothesis outlined in the Introduction. In my final section, I use the fused fMRI/ERP framework from Chapter 3 to test whether lower RC ability can be traced to a language bottleneck. Here, we define bottleneck as one process resulting in a delayed and diminished proceeding process. Consequently, the current study aims to examine whether the spatiotemporal components and/or inter-component relationships predict RC ability.

Previous Evidence for a Language Bottleneck

While not studied in the context of RC ability, previous ERP and MRI studies have identified certain spatial and temporal signatures of a language bottleneck. In the ERP literature, Kuperberg et al. (2007) proposes that typical language processing involves competing language streams, in which there can either be semantic or structural re-appraisal of a sentence, particularly in the face of integration difficulties. This proposal was extended by Kim et al. (2018) who found that in the context of sentence reading, lower verbal working memory was associated with a greater N400 and diminished P600 response. This could potentially reflect a “competitive” relationship between the N400 and P600, in which a heightened N400 suppresses an adaptive P600 response. Less work on language bottleneck processes has been performed in the MRI literature due to temporal constraints. However, the left IFG and portions of the anterior temporal lobe have been identified as particularly sensitive to language bottleneck effects during speeded reading (Vagharchakian et al., 2012). These findings may have important implications for struggling readers. However, the temporal progression of language processes and their interactions have not yet been examined in relation to RC ability. In the present study, we first look at the relationship between RC ability and all components generated from the joint ICA analysis from Chapter 3. Because brain activations in the P300 temporal range have been associated with word recognition (Dien & O'Hare, 2008), semantic cognition (Leckey & Federmeier, 2019; Polich, 2007), and language/reading ability (Molfese, Fletcher, & Denton, 2013; Shaheen, Shohdy, Abd Al Raouf et al., 2011), we also perform a secondary analysis probing the relationship of RC ability to a P300 component generated by the same joint ICA pipeline. This analysis is used to ensure that we are capturing the full temporal progression of RC ability as it interfaces with the language stream. For each of the components of interest, we then examine whether the relationships across components are predictive of RC ability, beyond the component predictions alone. For each of these questions, we additionally examine whether the difficulty of semantic cognition (i.e. semantic retrieval and integration) interacts with these relationships.

Given that the P600 and IFG appear to be sensitive to language bottleneck effects, and also are both the most consistent markers of RC ability in the literature (see Introduction), we hypothesize that RC ability will be positively related to the joint component P600b that maps onto the IFG. We also anticipate that an increased N400 will result in a lower P600b, and this will have negative impacts on RC ability.

Methods

Participants

Participants included n = 23 healthy adults with typical IQ and basic reading ability. For additional descriptions of subject-inclusion criteria, please see Chapter 3.

Behavioral metrics

In order to assess subject RC ability, we administered two RC batteries: Woodcock Johnson IV (WJ-IV)— Passage Comprehension subtest and the Nelson Denny Reading Test (NDRT) (Brown, 1960; Schrank, Mather, & McGrew, 2014). The WJ-IV requires subjects to read a sentence and fill in a missing word, while the NDRT asks subjects to read passages and answer a series of comprehension questions. Scores were converted to z-scores and averaged to form an RC ability component. To control for basic reading (BR) ability, scores on the WJ-IV Letter Word Identification (LWID) and Word Attack (WA) subtests were averaged and converted to z-scores.

Analysis

Imaging collection and pre-processing protocols are described in Chapter 3. We examined the N400/P600 components generated by the joint ICA pipeline. In a secondary analysis, we also examined a P300 component that met peak criteria that was generated from the same joint ICA output. The P300 is an ERP response classically studied in the context of oddball stimulus. However, a long history of work has also found this component to support semantic memory processes, in which higher P300 amplitude is predictive of greater recall, particularly when stimulus contains semantic information (Polich, 2007, 2012). This has led to proposals that the P300 is the earliest candidate for automatic spreading activations in the semantic system during language processing, and may in fact be conflated with the earliest portions of the N400 effect (Hill, Strube, Roesch-Ely, & Weisbrod, 2002; Lau, Holcomb, & Kuperberg, 2013). In the present study, we consequently include the P300 as a secondary component of interest to determine whether RC ability traces to the earliest stages of semantic processing during sentence reading.

Component weightings were utilized to identify significant relationships to RC ability. These weightings reflect the degree to which a component contributes to a subject's overall neural signal within a specific condition. Thus, for all ANOVA's, subjects had four weightings per component (reflecting the four conditions), which were treated as repeated measures. In order to ascertain components with a significant relationship to RC ability, we followed a two-step process. First, we ran individual ANOVA's for each component, in which Condition, BR ability, and Component Weighting were entered as predictors for RC ability. There were no significant Condition x Component interactions in predicting RC ability, so the interaction effect was removed from the model. The first analysis step identified four components related to RC ability (P300, N400, P600a, and P600b). We then ran an ANOVA to test whether components identified in step one independently predicted variance in RC ability. This resulted in 3 final components (P300, N400, and P600b; see Results). N400 and P600b characteristics are described in Chapter 3, and P300 characteristics are described in the section "Role for the P300 in RC ability" below.

In a final analysis, we were interested in testing whether inter-component relationships were predictive of RC ability. To examine this effect, we calculated the pairwise weighting differences across the 3 significant components (i.e. Component 2 weightings – Component 1 weightings). We then ran three additional ANOVA's, which included Condition, BR ability, Component 1 weighting, Component 2 weighting, and Component Weighting Difference as predictors of RC ability. All significant results are reported at $p < 0.05$.

Results

The individual ANOVA's revealed four components with a significant relationship to RC ability, including: 1.) the N400 component that mapped to activation in the language network (negative relationship with RC ability), 2.) the P600a component that mapped to parahippocampal gyrus and STG (positive relationship with RC ability), and 3.) the P600b component that mapped to bilateral ventral and left dorsal IFG (positive relationship with RC ability; for full descriptions of components 2-4 see Chapter 3).

Secondary examination of the P300 component and RC ability

As described in the Methods, in addition to the N400 and P600 components, we wanted to perform an exploratory examination of the P300 component due to its described but less-discussed relationship with early semantic cognition, and more specifically automated spreading activations of meaning from long-term memory (Dorjee, Devenney, & Thierry, 2010; Hill et al., 2002; Lau, Holcomb, et al., 2013; Polich, 2012). Here, we briefly describe the characteristics of the P300 from the joint ICA output. Our findings revealed that the P300 waveform peaked at ~300 ms, and mapped onto the following areas: bilateral superior temporal poles (BA 38/22), orbitofrontal cortex, cingulate, right SMG, basal ganglia, left parahippocampal gyrus, cerebellum, and primary sensory areas. Condition comparisons (paired t-tests across conditions) revealed that this component was significantly more positive for congruent than incongruent sentences: CWCS > CWIS ($t = 4.26$; $p < 0.001$); IWCS > CWIS ($t = 3.93$; $p < 0.001$); IWCS > IWIS ($t = 4.74$; $p < 0.001$). These findings parallel previous work identifying a positive relationship between P300 amplitude and semantic congruency (Dorjee et al., 2010) which likely reflect semantic memory processes in the TP and parahippocampal gyrus. The lack of a significant effect for semantic retrieval in the P300 parallels our N400/P600 findings, again suggesting that semantic retrieval difficulty manipulations are not sensitive enough in a sentence context to reach significance in typical adult comprehenders. We next tested whether the P300/temporal pole component weightings were significantly predictive of RC ability beyond word decoding. We found that this component was significantly positively associated with RC ability (3.70; $p < 0.001$). As such, we included the P300/temporal pole component in the remaining analyses.

Inter-component relationships and RC ability

After identifying four significant components related to RC ability, we were next interested in determining (1.) which components independently contributed to RC ability, and (2.) whether inter-component interactions were related to RC ability. To determine independent contributions, the four significant components were input as dependent measures in a single model predicting RC ability (controlling for condition and basic reading ability). The model was significant ($F = 10.5$; $p < 0.0001$), and t-tests revealed that only the P300, N400 and P600b components significantly predicted RC ability. The P300 was positively predictive of RC ability ($t = 2.14$; $p = 0.04$); the N400 was negatively predictive of RC ability ($t = -1.99$; $p = 0.049$); and the P600b was positively predictive of RC ability ($t = 3.81$; $p < 0.001$). The P600a did not significantly predict RC ability when the other components were included in the model ($t = -1.57$; $p = 0.12$). There were no significant interactions between component and condition in predicting RC ability.

In the next set of analyses, we were interested in identifying whether inter-component relationships were predictive of RC ability, beyond the components themselves. To test this, we pulled the three components that significantly independently contributed to RC ability, and ran two ANOVA’s comparing temporally adjacent components, in which Condition, BR ability, Component A, Component B, and Component A – Component B were input as predictors of RC ability. We found that the difference between the P300 and N400 components was significantly positively associated with RC ability beyond P300 and N400 main effects ($t = 2.24$; $p = 0.03$). We additionally found that the difference between the N400 and P600 components was significantly negatively predictive of RC ability beyond N400 and P600b main effects ($t = -3.76$; $p < 0.001$). These findings suggest that less efficient comprehension is predicted by a greater language-related activations in the N400 time-window relative to anterior temporal and inferior frontal activations in the P300 and P600b, respectively (see Figure 4.1).

In a final analysis, we were interested in seeing whether the apparently detrimental effect of a large N400 also resulted in a sluggish P600b response. To examine this, we used the grand average ERP data, and ran an ANOVA to examine whether the lowest peak in the N400 range (300-600 ms) was predictive of P600 latency (defined as where the maximum peak in the P600 range occurred, 500-600 ms; of note, the average maximum P600 peak in the raw ERP data fell within the peak range of the P600b joint component). In the model, condition was used as a repeated measure. We found that greater N400 amplitude did indeed predict a slower P600 ($t = -2.35$; $p = 0.02$), and the difference between N400 amplitude and P600 latency (z-scaled) was significantly negatively predictive of RC ability, beyond N400 amplitude and P600 latency alone ($t = 3.44$; $p < 0.001$).

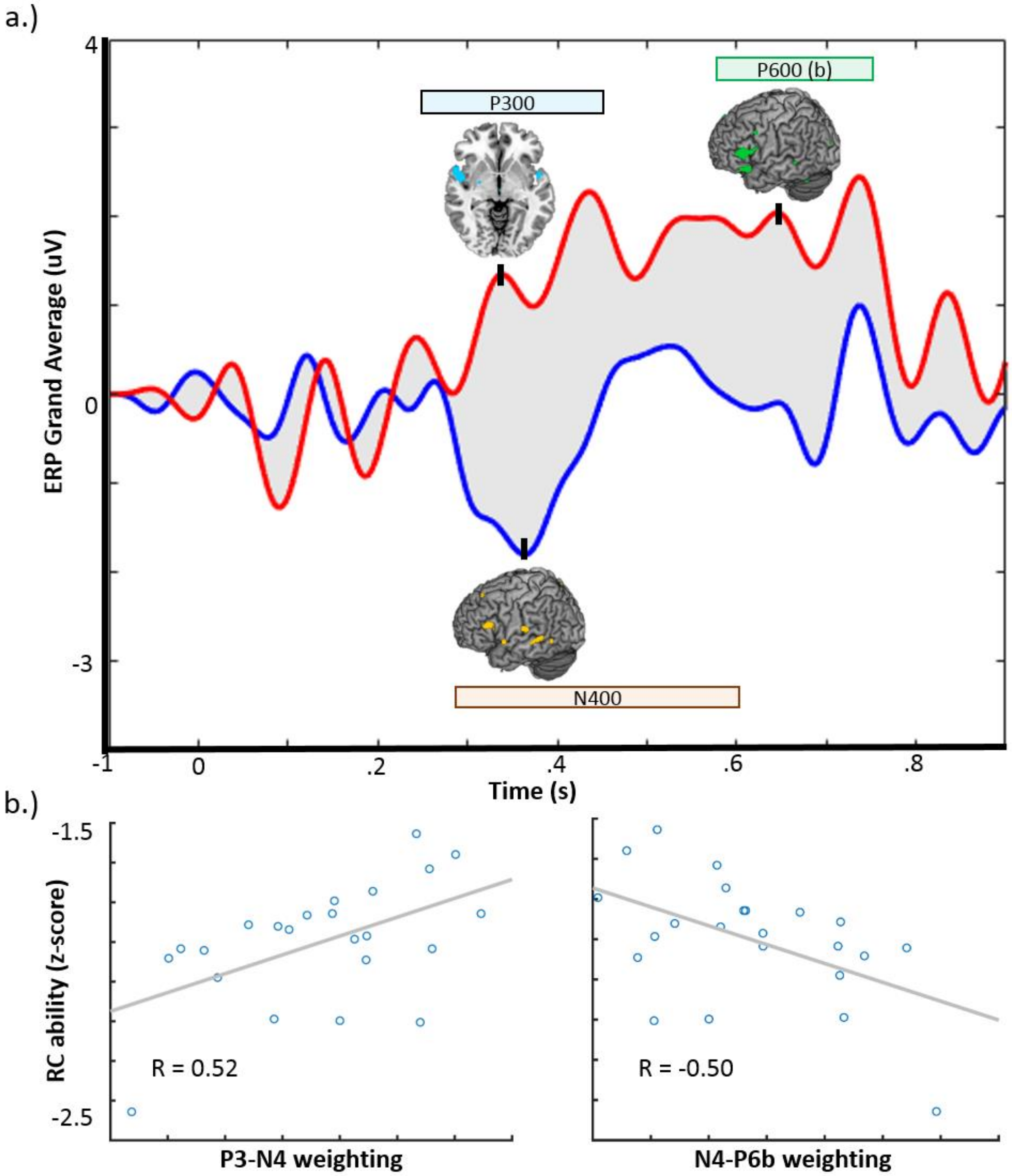


Figure 4.1 a.) A comparison of single subject grand averages of ERP data for the two subjects with the highest (red) and lowest (blue) comprehension scores. The group spatial components and related time windows (indicated by box length) for P300 (light blue), N400 (orange), and P600b (green) are overlaid onto the subject ERP responses, demonstrating the dynamic relationship between the significant components, and how those dynamics contribute to RC ability (the P300, N400, and P600). In particular, low P300 amplitude in the poor comprehenders leads to a large N400 effect, which is followed by a severely diminished P600b response. These relationships can also be captured through (b.) the weighting differences of temporally adjacent components, which are significantly predictive of RC ability.

Discussion

In the current study, we were interested in examining where and when RC ability interfaces with the language processing stream during sentence reading. Our findings suggest that lower (but still typical) RC ability is related to a less efficient trade-off of language-related networks over the course of milliseconds, regardless of semantic task demand. We found that RC ability (independent of word decoding) first impacts the language processes in a network centered on the bilateral temporal poles (TP) and parahippocampal gyrus at ~300 ms post-stimulus. The specific activation area in the TP/parahippocampus and P300 response have each previously been associated with the accessing and encoding semantic information from/into long-term memory (Dorjee et al., 2010; Jefferies, 2013; Price, 2012), and was more strongly related to retrieval than integration processes in the current study. This interpretation is consistent with our findings that this component was stronger for congruent versus incongruent sentences, which would be a preferred stimulus to encode for typical adult readers. These findings parallel RC ability literature that has also found that TP structure and function is positively related to RC ability (Cutting et al., 2013b; Ryherd et al., 2018; Shankweiler et al., 2008), though this is the first study to link this activation to a time-window (and the P300 specifically) during sentence reading. For lower RC, diminished semantic activation in the TP resulted in the same TP region coupling with a broader (and potentially higher-cost; see Chapter 2) fronto-temporal language and executive network at ~400 ms. Examinations of the N400's subsequent interactions with the P600b-IFG component revealed that this greater N400 weighting/amplitude predicted a lower and more sluggish P600b response, and this inverse relationship was highly predictive of RC ability. These findings provide strong evidence that low TP activation triggers increased (and inefficient) language activation in the N400 time-window, which then results in an adverse processing bottleneck in the left/bilateral IFG at ~600 ms.

The current results are consistent with the literature in several ways. First, previous work in typical adults has found positive associations between RC ability and the TP, the IFG, and frontal areas (Cutting et al., 2013b; Patael et al., 2018; Ryherd et al., 2018), including our single word findings in Chapter 2 (see Discussion for synthesis across chapters). As highlighted in the Introduction, the N400 effect has also been found to be less predictive or negatively predictive of RC ability in sentence reading tasks as compared to word reading, while the P600 effect remains positively predictive. The results presented here are consequently consistent with the literature to date, and in fact reflect all of the primary areas currently highlighted in the MRI literature on RC ability (see Figure 5.1 in Discussion). However, the temporal specificity of the current analysis has allowed for a more granular understanding of network mechanisms related to RC ability.

Limitations and Future Directions

The current findings are restricted to adult readers who fall within the typical range of decoding ability and RC. On one hand, this demonstrates the sensitivity of the current findings; still, it cannot be assumed that readers with RC deficits would show similar patterns. Future studies need to use spatially and temporally sensitive neuroimaging metrics to identify where and when RC deficits impact the language processing stream. We would also anticipate that these findings would significantly differ in developing readers. In particularly, it is likely that in populations with less automatized word-reading ability, lexical priming effects would be more important. Future studies should also perform regional examinations, particularly in executive areas, to determine when/how EF regions mediate language processes across a range of readers. Lastly, the current study was restricted to parietal electrodes in the EEG, and consequently was unable to examine potentially earlier contributions to RC ability (for instance in the N200 or LAN). Future studies should examine additional ERP’s at different time points in a sentence, in order to get a full picture of word-by-word neural signals related to RC ability.

This is the first study to propose a neurobiological model of RC ability with both spatial and temporal sensitivity. We hope the proposed evidence can support additional use of multi-modal imaging analysis in studies on RC ability, reading disorders, and intervention studies.

Chapter 5

Discussion: A preliminary neurobiological model of reading comprehension ability

Motivation

Reading comprehension (RC) is a tremendously complex neural task that requires timely coordination of multiple brain networks. The present dissertation aimed to identify where and when RC ability interfaces with the language processing stream during reading, independent from word decoding ability. Across three studies, I examined RC ability in the context of word-, sentence-, and discourse-level processes, and attempted to isolate specific dimensions of meaning processes through the manipulation of semantic retrieval and integration. Here I briefly summarize my global findings, discuss the limitations in my interpretation of the findings, and then address whether these combined results provide evidence for the Bottleneck, Hub, or Executive Dysregulation hypotheses posed in the Introduction.

Findings on Word Reading Processes

We examined the relationship between RC ability and word-level processes in two ways: 1.) In Chapter 2 we examined functional connectivity from language and executive hub areas during word reading, and 2.) in Chapter 4, we examined semantic retrieval of word meaning in the context of sentence comprehension. Chapter 3 revealed that lower RC ability corresponded decreased convergent connectivity between fronto-temporal language areas and the left ventral TP and mPFC. The TP has largely been overlooked in the RC literature, despite known contributions to semantic cognition, including differential roles in automatic spreading activations and combinatorial semantics (Lau, Gramfort, et al., 2013). A long history of findings has led to proposals that the TP is the "semantic epicenter" during retrieval processes from long-term memory (Jefferies, 2013). Frontal areas along with the TP have been specifically associated with bottom-up semantic retrieval processes, in which the TP acts as an amodal semantic hub that communicates with areas within the DMN (including the prefrontal cortex) in order to consolidate widespread cortical activations associated with reactivation from long-term memory (Davey et al., 2015, 2016). These findings are somewhat convergent with previous literature that has found associations between RC ability and the TP during word reading (Cutting et al., 2013b; Horowitz-Kraus, Buck, & Dorrmann, 2016; Ryherd et al., 2018). However, our activation findings as well as previous studies also identify a potential role for the left IFG and hippocampus in RC ability during single-word processes (Cutting et al., 2013b; Malins et al., 2016). Thus, while the current evidence suggests a central, early roles for semantic retrieval processes in the TP and frontal cortex in RC ability during word reading, important questions remain in terms of the specific functionality of regions within this retrieval network. Our findings do, however, confirm that the left MTG is not as important for RC ability. Instead, left MTG activation and connectivity was key to decoding ability; this result emphasizes the need to control for decoding ability in studies on RC ability.

In Chapters 3 and 4, we attempted to more specifically isolate memory-based meaning retrieval from the sensory, orthographic, and phonological networks associate with word reading in general. However, a primary finding in Chapters 3 and 4 was that our manipulation of semantic retrieval did not significantly interact with any of our identified spatiotemporal components, and our manipulations of semantic cognition sub-types (i.e. semantic retrieval and integration) did not show expected interactions with RC ability. Our approach was consequently unable to successfully identify semantic retrieval processes in the context of a sentence, or how semantic retrieval relates to RC ability. One possibility for this finding is that the joint ICA approach was unable to identify an N400 effect specific to semantic retrieval. However, supplemental examinations of the ERP N400 and P600 effects revealed no significant correlations with RC ability for semantic retrieval. An examination of the literature reveals that several studies have failed to find an interaction between priming effects (e.g. hard versus easy semantic retrieval) in the N400/P600 and RC skill level (Balass et al., 2010; Stafura & Perfetti, 2014b). However, Balass et al. (2010) did find mean amplitude differences in the P600 component (not effect) for newly learned words in skilled versus unskilled comprehenders, providing support for a role of general component amplitude in RC ability. More broadly, a lack of interaction with semantic difficulty may indicate that weaker comprehenders have globally reduced efficiency even in language processes that should be automated (e.g. fully congruent sentences). Consequently, our findings may reflect a general pattern that should be examined in future studies.

Overall, our findings from Chapter 2 provide some evidence for a central role of the left TP, specifically, and a role for classic semantic retrieval areas, generally, in RC ability during single word reading. However, the way in which retrieval processes play out during sentence reading is still unclear.

Findings on Sentence Processes

In Chapters 3 and 4 we found a progression of spatiotemporal components that support sentence comprehension, and identified four components that contribute to RC ability. Based on the timing and spatial mapping of each component, we propose that these three components map onto semantic memory, semantic integration, and semantic-syntactis re-appraisal networks. Each of these components was strongly characterized by semantic integration demand (Chapter 3), but integration demand did not interact with RC ability (Chapter 4). Rather, in typical adult comprehenders, N400 and P600 *effects* and related activations were preserved, but the *components* were the only significant markers for RC ability. Consequently, our findings suggest that typical RC ability is characterized by differences in semantic integration processes during sentence comprehension, but that in typical adult readers, the effect of semantic integration *difficulty* is not significant. Within this context we found that RC ability was marked by a progression of related and potentially competing activation patterns over the course of milliseconds. After the sentence final word, early decreased activation in a semantic memory system centered on bilateral TP triggered the TP to connect outwards to a larger network of language areas within the N400 time window. Findings in Chapter 3 revealed that, independent from RC ability, this larger network was related to semantic integration difficulty, while easier integration mapped on to the DMN. This could suggest that in a sentence context, a language network response in the N400 range is a costly activation related to reduced automation of language processes. The fact that readers with lower RC rely on this network regardless of integration or retrieval difficulty suggests that the pattern of their language-network trade-off is generally less efficient. Comparisons of N400/P600 relationships revealed that greater activation of the N400 resulted in a stunted P600 response in bilateral IFG appraisal system (see Chapter 3). Our sentence-level findings consequently point to a dynamic progression of language-networks, which in poor comprehenders results in a processing bottleneck between the N400 language network and a P600 semantic-syntactic re-appraisal network. Consistent with behavioral findings, this progression appears to be related to semantic integration in the context of sentence reading (Landi & Ryherd, 2017). While the TP again appears to play a central early role in RC ability, it is unclear how the activations from single word reading feed into the spatiotemporal progression described here for sentence reading. Future studies will need to explicitly examine the relationship between RC ability and single word, word pairs, sentences, and discourse in order to capture how network dynamics change based on hierarchical context.

Findings on Discourse Processes

Lastly, at the discourse-level of comprehension we found that readers with lower RC had decreased correlations between the left dlPFC and the left AG. This finding parallels results from Aboud et al. (2019) which show that poorer comprehension corresponds with decreased correlations between the executive fronto-parietal control network (FPN) and the default mode network (DMN). Of note, Aboud et al. (2019) found that this effect was specific to science passages, which were also examined in Chapter 2. This decreased interaction could reflect either lower involvement of the FPN in supporting content integration into background knowledge (which is in greater demand for science texts), or decreased use of the FPN to keep the DMN "on-track" (Aboud, Bailey, Del Tufo, Barquero, & Cutting, 2019b; Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010). The findings in Chapter 2 add an additional dimension: the left dlPFC is required to support word-level processes differently than discourse-level processes, and this flexibility predicts RC ability. The dlPFC consequently appears to support and integrate multiple levels of reading in the strongest comprehenders (see Larger Implications below).

Summary

Across studies, my results suggest that rapid semantic processes in the TP, mPFC, and other semantic retrieval areas may be the earliest interface between RC ability and the language processing stream during reading (Chapters 2 and 4; see Figure 5.1 and Limitations), and inefficiencies in this network may result in a cascade of downstream negative effects during text reading.

At the single word level of reading (Chapter 2), we found that lower RC ability corresponds with reduced connectivity to the TP and mPFC from multiple language and executive hub regions (Chapter 2). In sentence comprehension (Chapter 4), lower RC ability corresponded with early lower activation of the TP, mPFC, and parahippocampal gyrus (at ~300 ms post-sentence-final word). This decreased activation then resulted in the TP coupling with a more extensive network of language processing areas, and this process appeared to reduce and delay important re-appraisal functions in the IFG. Additionally, we found evidence that the left dlPFC interfaces with multiple networks throughout this progression, and a reduction of this multi-tiered interface contributes to lower RC ability. Notably, the proposed model includes all major brain regions found in the systematic review of RC ability in the brain (see Figure 5.1 and Introduction), but allows for differentiation of systems across reading levels and time.

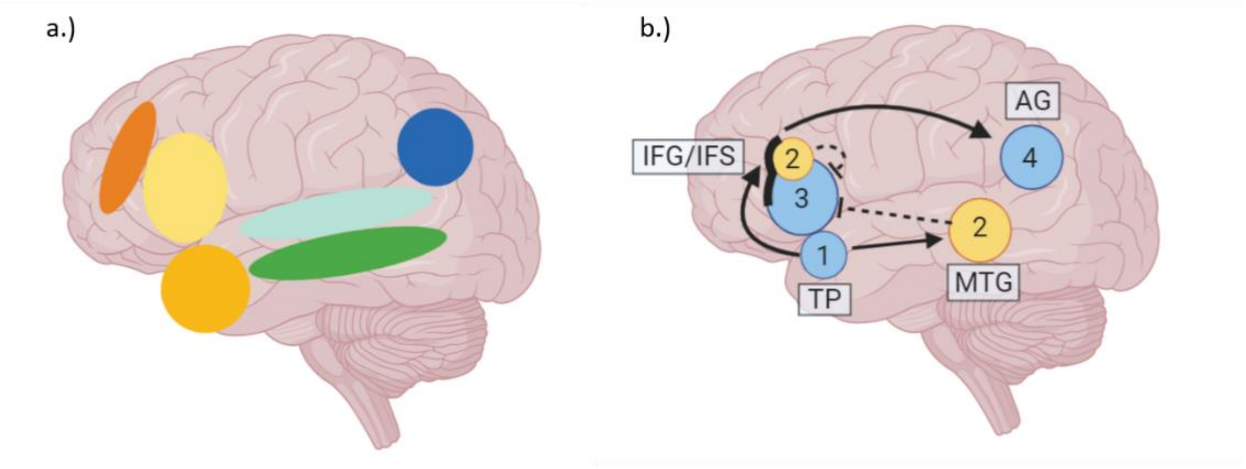


Figure 5.1 (a.) The current proposal identified a wide range of brain areas associated with RC ability in the literature, and (b.) through functional connectivity and joint MRI/ERP analyses found convergent evidence for a preliminary neurobiological model of RC ability during sentence and discourse reading (progression indicated by numbering). Lower RC corresponds with reduced activations (blue areas) of TP/parahippocampal gyrus, which triggers a costly activation (orange) in fronto-temporal language areas, including the left dlPFC. This activation delays re-appraisal processes in the left IFG/dlPFC (language bottleneck indicated by dashed line; dlPFC indicated by thick black line). Poorer comprehenders additionally show reduced connectivity between the dlPFC and the left AG during discourse-level processing.

Larger Implications for Neurobiological Patterns Contributing to RC Ability

In this final section, I will discuss the evidence from the current project that relates RC ability to the different neurobiological hypotheses presented in the Introduction. Namely, a larger goal of the present project was to determine whether lower RC ability traces to (1.) hub dysregulation, (2.) executive dysregulation, and/or (3.) a language bottleneck. Across the two studies, we found evidence for all three hypotheses, and a refined look at the spatiotemporal properties of language provided evidence for a preliminary neurocognitive model of RC ability (see Figure 5.1).

Characteristics of the TP's involvement in RC ability provide evidence for both bottleneck and hub theories. Lower activation in the TP appears to result in a processing bottleneck in the N400/P600 time-window. However, the overlap of the TP (and frontal areas) across multiple time-points (i.e. the P300 and N400 joint components; Chapter 3), as well as their flexible task-dependent functional connectivity with other brain areas (Chapter 2), suggests that the TP contributes to multiple important processes along the language pipeline. Dysregulation of these regions may consequently result in (1.) a causal bottleneck in non-deficit areas, as well as (2.) compounded cognitive inefficiencies during RC due to iterative reliance on the TP at different stages of language. This interpretation also helps explain the diverse array of behaviors related to RC ability/disability, spanning from single-word difficulties to semantic integration, to syntax. In the proposed model, all of these behaviors are threatened by (1.) hub dysregulation that results in (2.) a linguistic bottleneck.

Our findings that the left dlPFC is required to flexibly couple with the language network provides additional support for the Hub Hypothesis, as well as evidence for the Executive Dysregulation hypothesis. First, RC ability was predicted by the left dlPFC’s flexible coupling with the left TP and the left AG for word- and discourse-level reading processes, respectively. Second, with increased working memory ability, the left dlPFC mediated the relationship between canonical word reading and discourse processing areas (see Chapter 2). Lastly, examination of the N400 and P600b components in Chapters 3 and 4 reveals that the spatial mappings for both of these components overlap with the left dlPFC seed from Chapter 2. Consequently, the left dlPFC appears to play a critical role in supporting *individual* reading behaviors as well as integrating *across* different reading behaviors (Chapter 2). These findings encourage a non-modular view of RC ability in the brain. Future studies on RC ability should examine executive and language areas through the lens of multi-functionality, as well as utilize methodologies with high spatiotemporal resolution to capture dynamic network exchanges over time.

Ongoing Questions

In this dissertation I have provided preliminary evidence for the neural mechanisms that underlay typical variability in RC ability. However, many questions remain. Future studies will need to use convergent methodologies to test the spatiotemporal progression presented here, including examination of ERP signals outside of centroparietal electrodes. As done in Li et al. (2019), it would be fruitful to track spatiotemporal patterns across words in a discourse context to identify the dynamic local and global interactions that comprise adequate comprehension, including predictive processes early on in sentences that likely determine the nature of the interactions presented here. Additionally, future studies should examine a range of reader subgroups. In general, we would anticipate that the effects of semantic retrieval/integration difficulty would be more likely to impact vulnerable populations of readers, such as developing readers and those with reading disabilities. I hope that the current findings can lay a preliminary groundwork for more granular examinations of RC ability in the brain, with the long-term goal of assisting struggling readers through neurobiologically-driven intervention approaches.

APPENDIX

Chapter 1 Supplemental Material

Study #	**Reference**	**Modality**	**Task**	**Child/ Adult**	**Groups**	**Metric of Interest**	**Findings (positive)**	**Findings (negative)**
1	Cutting et al. (2013)	fMRI	Word	Child	TD, SRCD, DYS	S-RCD versus TD, Low vs. High frequency words	R IFG	L IFG, Hipp
2	Welcome et al. (2011)	fMRI	Word	Adult	TD, DYS, RR	Visual Word Semantic Judgment		L MTG, ACC
3	Malins et al. (2016)	fMRI	Passage and Word	Adult	TD	Incongruent vs. Congruent Words	L IFG, L Precentral, L Fusiform	
4	Ryherd et al. (2018)	fMRI	Passage and Word	Child	TD	(1.) Auditory and Visual Text; (2.) Visual Word and Text	(1.) L IFG, B MFG, B TP; R Occipital, L Fusiform, B SFG, B MTG; (2.) B MTG, B TP, R STG,	(1.) B ACC, B PCC, B Parahipp, B Insula, B IPL, R MFG, R PCU, R Insula, L Caudate; (2.)

							R Occipital, R SFG, L IFG, B MFG, B PCU, L Thalamus, L Precentral	B Postcentral, R STG, R Transverse Temporal, R Insula
5	Aboud et al. (2019)	fMRI	Passage	Child	TD	Expository versus Narrative Visual Texts	FPN-DMN	-
6	Horowitz-Kraus et al. (2013)	fMRI	Passage	Child	TD	(1.) Auditory Narrative in Adolescents; (2.) Auditory Narrative in 6 yo Predicting RC in Adolescence	(1.) B STG, R Cingulate, B IPL, L Precentral, L Fusiform, L MTG, L TP, L Lingual (2.) B MFG, R AG, L IFG, L SMG;	
7	Horowitz-Kraus et al. (2015)	fMRI	Passage	Child, Adult	TD	Auditory Narrative in 6 yo Predicting RC in Adulthood	B STG, L ACC, Cuneus, Precentral	
8	Smallwood et al. (2013)	fMRI	Passage	Adult	TD	Visual Passage	PCC-R IFG/Insula	PCC-Striatum

9	Shankweiler et al. (2008	fMRI	Sentence	Adult	TD	(1.) Incongruent vs. Congruent Visual Sentences; (2.) Incongruent vs. Congruent Auditory Sentences	(1.) B IFG, B MFG, B SFG, L Occipital, L IPL, L Precentral, R Fusiform, L PCU; (2.) L MTG, L MFG, R ITG, L Insula, R Precentral	
10	Bailey et al. (2016)*	MRI	-	Child	TD, SRCD, DYS	GMV	R dlPFC, L STG	L MTG, L SMG, R Hipp
11	Patael et al. (2018)	MRI	-	Child	TD, RR	GMV	L dlPFC, B IFG, B SFG, R ACC, LTP	-
12	Welcome et al. (2012)	MRI	-	Adult	TD	Radial expansion	R IFG	
13	Balass et al. (2010)	ERP	Word	Adult	TD	(1.) Learned Words vs. Unlearned; (2.)	(1.) P600; (2.) N400	-

						Related vs. Unrelated		
14	Landi et al. (2007)	ERP	Word	Adult	TD	Word Semantic Judgment	N400 and Late Positivity	-
15	Perfetti et al. (2005)	ERP	Word	Adult	TD	(1.) Learned words vs. Unlearned; (2.) Related vs. Unrelated	(1.) P600; (2.) N400	-
16	Mossbridge et al. (2013)	ERP	Passage and Word	Adult	TD	Visual Text Comprehension vs. Scrambled Words	Late positivity	-
17	Stafura et al. (2014)	ERP	Passage and Word	Adult	TD	Visual Text Comprehension	N400 (trending)	-
18	Stafura et al. (2015)	ERP	Passage	Adult	TD	(1.) Visual Word Semantic Judgment with Forward Association; (2.) Text Comprehension with Backward Association	(1.) N400	(2.) N400

19	Broadway et al. (2016)	ERP	Passage	Adult	TD	Visual Passage	P1, N1	

Supplemental Table 1.1. Final studies included in the systematic review and their significant findings specific to positive and/or negative associations with higher RC ability (in the case of a negative ERP component, a positive association means more negative with higher RC). Null findings not included; cerebellum excluded. A dash ("-") indicates a connectivity finding. Multiple analyses in a single study are separated by semicolons. Abbreviations: typically developing (TD), dyslexia (DYS), specific reading comprehension deficits (S-RCD), resiliant readers (RR), gray matter volume (GMV), right (R), left (L), bilateral (B). For brain region abbreviations see Table 1. *Only primary findings included; for full list of regions see reference.

Chapter 2 Supplemental Material

Word > Symbols Modulated by Word Reading Ability

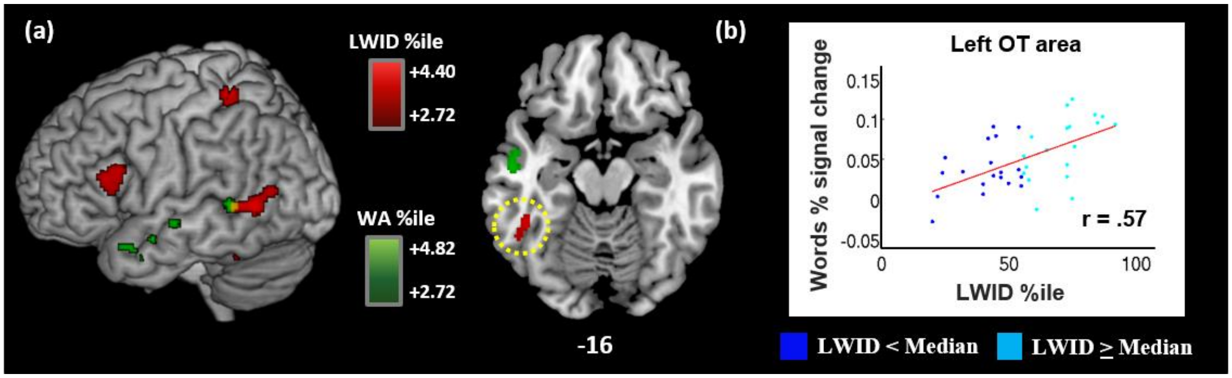
In Word reading greater than Symbols, both Word Attack (WA) and Letter Word ID (LWID) show positive correlation with activation of the left MTG. Each measurement also predicted activation in unique regions:

Word > Symbols modulated by Word Attack (WA)

WA percentile showed unique positive correlations with activation in the left anterior STS, extending into left TP.

Word > Symbols modulated by Letter Word Identification (LWID)

LWID percentile showed unique positive correlations with activation in the left OT area (including pVWFA), left IFG, and left superior parietal lobule.



Supplemental Figure 0.1: Correlations between word readin ability and activations during word reading. (a) During word reading only, word reading ability, as measured by Word Attack (green) and Letter Word Identification (red) measures, predicts activation in language regions, including the orthographic processing regions in the left OT area. Both measurements of word reading predicted activation in the left MTG (yellow). (b) Plot of LWID Percentile score by Words percent signal change in the left OT area. Low and high word reading ability (as determined by median split of LWID percentile) represented in dark blue and light blue, respectively. Results displayed at p-corrected < 0.05.

Word > Symbols Modulated by Gates Percentile

In Word greater than Symbols, Gates percentile was positively correlated with activation in the left ventral IFG, left TP, and left temporoparietal junction (TPJ). These mappings were qualitatively different from those of word reading ability (above).

Passages > Symbols modulated by Gates Percentile

In Passages greater than Symbols, Gates percentile was positively correlated with activation in left IFG (BA 47, 45, and 44) extending into left insula, left dlPFC (BA 46 and BA 9), bilateral TP extending into right ventral IFG and ventral insula, and pVWFA. Additional results included positive correlation between Gates and activation in regions associated with the DMN, including dmPFC, bilateral AG, dorsal PCU, PCC, anterior cingulate cortex (ACC), left hippocampus extending to the amygdala, and bilateral anterior STS. Additional correlations were seen in bilateral postcentral, right caudate, left thalamus, right SPL, and bilateral lingual gyrus. No findings survived the discourse-level comparisons of Passages > Words.

GLM Contrast	**Anatomical Region**		**MNI Coordinates**		**k**	**Max T**	**BA**
		x	**y**	**z**			
Words > Symbols							
Language and WM	L Middle Occipital	-24	-100	-4	26997	17.99	18
	R Middle Occipital	22	-100	-6	[ ]	15.63	18
	L Inferior Occipital	-38	-86	-12	[ ]	10.05	19
	L Fusiform	-40	-44	-26	[ ]	9.71	37
	L pVWFA	-46	-48	-12	[ ]	9.41	37
	R Cuneus	2	-86	26	[ ]	8.18	17
	L IFG	-46	30	-4	[ ]	8.08	45, 47, 44
	L MTG/STG	-52	-42	4	[ ]	7.83	22
	L Hippocampus	-24	-30	-4	[ ]	7.77	35
	L Cuneus	-2	-92	22	[ ]	7.31	17
	L MTG	-50	-34	0	[ ]	6.86	21
	L Precentral Gyrus	-52	-2	50	[ ]	6.3	6
	L anterior MTG: TP	-58	-12	-14	[ ]	6.28	21/38
	L ventral IFG	-52	20	2	[ ]	6.12	47
	L dorsal IFG: dlPFC	-46	12	24	[ ]	5.69	45, 46, 9
	L TP	-44	20	-18	[ ]	5	38
	R Fusiform Gyrus	38	-50	-22	[ ]	4.59	37
	R ventral IFG: TP	54	40	-10	1302	5.39	47
	R IFG	40	24	22	156	3.64	45
Memory and Motor	R Hippocampus: Thalamus	24	-28	-4	1186	7.27	35
	L SMA	-2	2	68	142	4.46	6

Passages > Symbols							
Language, Memory, and Executive	L IFG	-48	30	2	29810	11.61	45, 47
	L ventral IFG	-48	28	-10	[ ]	11.28	47
	L Middle Occipital	-22	-102	-4	[ ]	11.03	18, 17
	L MTG	-58	-34	-2	[ ]	10.48	21
	R Calcarine	12	-90	4	[ ]	10.39	17
	L Fusiform: Hipp.	-42	-46	-26	[ ]	9.49	37
	L pVWFA	-50	-46	-10	[ ]	9.33	37
	L IFG	-46	16	22	[ ]	9.24	44, 45
	L STG: AG	-64	-42	2	[ ]	9.06	22, 39
	L Precentral	-48	4	48	[ ]	8.48	6
	L dorsal IFG: dlPFC	-38	8	28	[ ]	7.96	45, 9
	L TP	-50	10	-28	[ ]	7.24	38, 21
	L MFG/SFG	-10	50	48	[ ]	6.78	8, 9
	R STG/MTG	46	-34	0	2605	6.52	21
	R ITG	66	-44	-16	[ ]	5.8	21, 20
	R TP	48	18	-30	[ ]	5.33	38
	R IFG	60	30	12	2732	8.19	46, 45
	R Precentral Gyrus	62	-8	42	[ ]	6.19	6
	R MFG	56	22	38	[ ]	4.83	9
	R MFG	42	38	-16	[ ]	4.8	11
	R Insula	48	-14	18	[ ]	4.73	43
	R ventral IFG	54	32	-12	[ ]	4.06	47
	R AG: MTG	54	-70	30	515	5.42	39
	R Parahipp/Hipp	26	-26	-8	165	7.22	35

Passages > Words							
DMN	L AG	-44	-60	30	1286	4.92	39
	L MTG/anterior STS	-50	-24	-10	1045	5.4	21, 20
	R MTG: AG	52	-76	16	884	5.14	39, 19
	R Superior Occipital	40	-86	26	[ ]	4.45	19
	L/R PCU	0	-56	34	380	4.29	7, 31
	R MTG/anterior STS	54	-2	-26	251	4.49	21, 20
	L SFG	-20	26	52	180	3.41	6

Supplemental Table 2.1: GLM analyses for Words > Symbols, Passages > Symbols, and Passages > Words. Cluster size (k) in mm^3. BA, Brodmann Area. All T-values are significant at p = 0.05. For large clusters, brackets indicate sub-cluster peaks in BA or functional regions distinct from primary peak, extracted using a decreased peak search space of 4 mm within the main cluster. Clusters are identified by general cognitive domains based on the majority of sub-peak locations within the cluster.

Covariate	**Anatomical Region**		**MNI Coordinates**		**k**	**Max T**	**BA**
		x	**y**	**z**			
Words > Symbols							
LWID							
Language	L Fusiform/OT area	-44	-46	-12	140	3.89	37
	L MTG/STG	-46	-50	4	452	4.4	21, 22
	L IFG	-52	22	20	173	3.35	45, 44
	L IPL/SPL	-28	-50	46	175	3.79	40
WA							
Language	L anterior MTG/STG	-54	-16	-8	255	4.83	21, 22, 38
	L posterior MTG/STG	-44	-52	8	156	3.69	21, 22, 39
Passages > Symbols							
Gates McGinitie							
Language and WM	L IFG: dlPFC	-56	22	14	2308	6.36	45, 47, 44, 9
	R TP: ventral IFG	30	22	-26	2050	5.31	47, 38
	L TP	-44	6	-42	[ ]	4.98	38
	L anterior MTG	-56	-18	-20	810	4.39	21
	L fusiform	-58	-50	-12	[ ]	4.15	37
DMN	L SFG	-10	40	50	3875	6.08	8
	L SFG	-8	26	54	[ ]	5.07	6
	L PCU	-6	-52	40	561	5.32	7
	L PCC	-8	-54	24	[ ]	3.06	31

	L AG	-46	-64	32	1538	4.96	39
	R AG	54	-66	38	119	3.34	39
	L Hippocampus	-20	-6	-18	865	6.48	34
Motor and Visual	R Lingual /Cuneus	2	-86	0	471	4.55	18, 17
	R Postcentral	38	-30	48	394	4.06	40, 3, 2
	L Thalamus	-6	-14	8	185	4.03	NA
	R Caudate	14	10	14	164	3.85	NA
	R SPL	18	-68	64	192	3.77	7

Supplemental Table 2.2: GLM covariate for word recognition (LWID) and decoding (WA) ability (in Words > Symbols) and RC ability (Gates percentile; Passages > Symbols). Cluster size (k) in mm^3. BA, Brodmann Area. All T-values are significant at p = 0.05. For large clusters, brackets indicate sub-cluster peaks in BA or functional regions distinct from primary peak, extracted using a decreased peak search space of 4 mm within the main cluster. Clusters are identified by general cognitive domains based on the majority of sub-peak locations within the cluster.

Seed region	**Whole-Brain Correlation Regions**		**MNI Coordinates**		**k**	**Max T**	**BA**
		x	**y**	**z**			
Words > Symbols							
L IFG	R IFG	50	20	30	1456	5.86	44, 45, 46, 9, 8
	R/L Middle Occipital L OT area	42	-84	-4	4106	5.46	18, 37
	L Insula	-34	10	20	366	5.11	13, 44
	R Postcentral	12	-44	70	420	4.45	3, 7
	R Orbitofrontal/IFG	42	40	-12	284	4.44	11, 47
	L Postcentral	-60	-6	40	238	4.31	6, 9
	L Postcentral	-56	-6	16	140	3.97	43, 4
L TP	L Insula/RO	-36	8	20	180	5.24	13, 44
	R OT area	52	-50	-24	259	4.43	37
	L OT area	-42	-72	-10	276	4.30	37
	R Precentral	14	-32	72	208	4.10	3
	R IFG	46	18	14	224	3.79	44
L MTG	L Postcentral	-64	-6	20	471	5.13	4, 43, 44
	R Middle Occipital	44	-84	-10	775	5.12	18, 19
	L Middle Occipital: L OT area	-34	-86	-4	620	4.68	18, 19
	L Paracentral Lobule	-14	-30	70	173	4.39	4
	R Paracentral Lobule	14	-38	64	434	4.20	4
pVWFA	L MTG	-46	-40	2	566	4.82	21, 22
	L Middle Occipital	-26	-84	6	457	4.36	18
	L MFG	-46	4	52	294	4.33	6
	R Middle Occipital	30	-96	2	187	4.05	18

	L Insula	-36	10	20	126	4.03	13, 44
	R Postcentral	20	-24	52	221	3.89	4
L dlPFC	L MTG	-48	-38	4	138	4.52	21
	L Middle Occipital	-20	-106	-2	150	4.23	18
	R Middle Occipital	14	-102	16	531	4.17	18
	L MFG	-58	12	34	154	4.12	9, 6
	R MFG/Precentral	46	8	30	461	3.97	9, 46
	L Rolandic Operculum	-44	-6	16	250	3.89	13
Overlap Regions							
pVWFA		-41	-55	-16	190	-	37
L MTG		-49	-40	3	121	-	21, 22

Supplemental Table 2.3: Seed-to-whole-brain connectivity analyses for Words > Symbols. Overlap center of mass coordinates are reported in final rows. Cluster size (k) in mm^3. BA, Brodmann Area. All T-values are significant at $p < 0.05$.

Seed Region	**Regions**		**MNI Coordinates**		**k**	**Max T**	**BA**
		x	**y**	**z**			
Passages > Words							
L IFG	L AG	-44	-62	24	1065	6.00	39
	L TP	-54	0	-38	312	4.55	38, 21, 20
	L Thalamus	-10	-4	12	169	4.39	NA
	L SFG	-12	40	52	139	4.35	8
	R PCC: Cuneus	24	-66	8	499	4.17	30, 31, 18
	R Thalamus	8	-6	-2	255	4.13	NA
L TP	L PCU	-4	-68	34	970	5.82	7, 31
	R Caudate Head	8	2	4	1102	5.32	NA
	L AG	-40	-62	38	1417	5.26	39
	L SFG: ACC	-18	62	6	860	4.72	10, 32
	L MTG	-64	-26	-6	260	4.62	21, 20
	L PCC/Calcarine	-26	-66	6	143	4.50	30
	R SFG	12	36	40	465	4.50	6
	L Lingual Gyrus	-12	-46	2	190	4.15	30
L MTG	L AG	-44	-58	22	1050	6.51	39
	L SFG: SMA	-10	40	52	139	5.26	8, 6
	L MTG	-64	-44	2	225	4.14	21
	L/R Lingual Gyrus	-14	-92	-14	278	3.99	17
	R Calcarine	24	-58	6	126	3.88	18
pVWFA	L SMG	-56	-30	38	744	5.25	40
	L dlPFC	-30	18	42	133	4.59	8, 9
	L TP	-54	4	-30	189	4.51	21, 38, 20
	R TP	48	-2	-32	126	4.50	21, 38, 20
	L AG	-38	-64	22	571	4.45	39

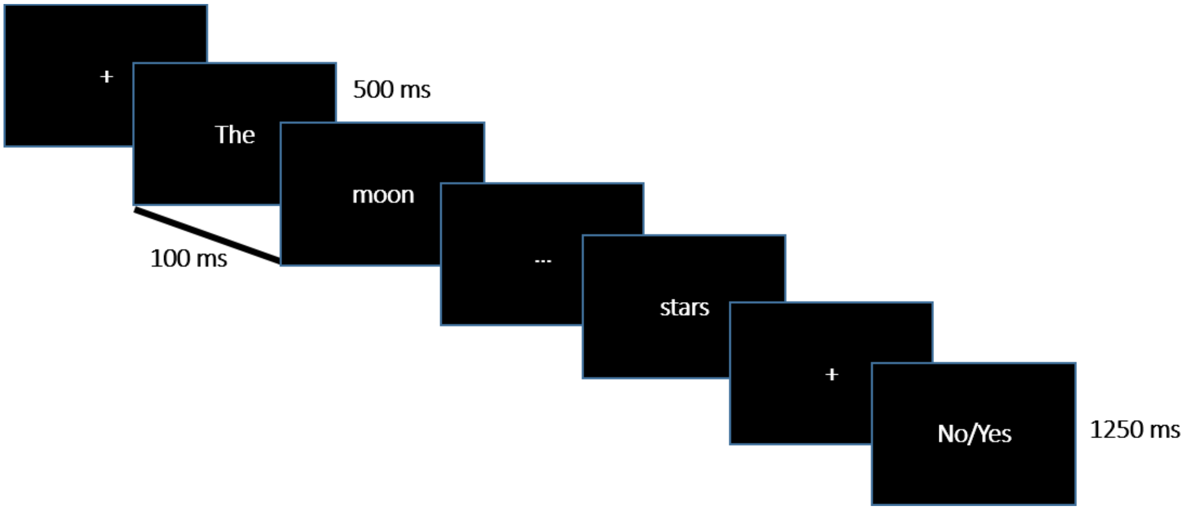
	R Fusiform/ Parahippocampal	38	-38	-26	342	4.42	37, 20
	L Cingulate	-10	-32	40	282	4.40	31
	L ITG	-58	-46	-18	227	4.38	20
	L Thalamus	-6	-26	12	127	4.13	NA
L dlPFC	L AG	-40	-62	26	1222	6.77	39
	L SFG	-14	24	62	1118	5.44	9, 8, 6
	R Parahippocampal	28	-24	-28	319	4.85	36
	L TP	-50	4	-22	392	4.54	38, 21, 20
	R ITG	26	-4	-38	126	4.44	20, 36
	L Thalamus	-12	-26	-8	151	3.49	NA
	L PCC	-6	-56	6	184	3.46	29
Overlap Regions							
L AG		-41	-62	30	159	-	39

Supplemental Table 2.4. Seed-to-whole-brain connectivity analyses for Passages > Words. Overlap center of mass coordinates are reported in final row. Cluster size (k) in mm^3. BA, Brodmann Area. All T-values are significant at $p < 0.05$.

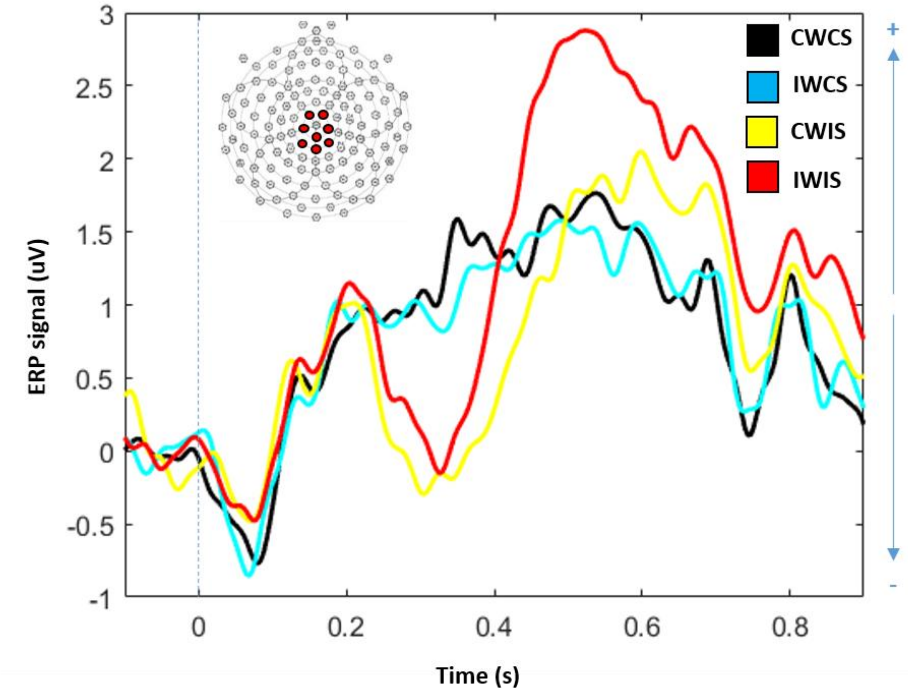
Seed Region	**Whole-Brain Correlation Regions**		**MNI Coordinates**		**k**	**Max T**	**BA**
		x	**y**	**z**			
Passages > Symbols predicted by dlPFC activation							
L AG	L OT area	-44	-38	-22	129	3.74	37
Passages > Symbols predicted by dlPFC activation * Sentence Span							
L AG	L OT area	-44	-26	-22	133	4.74	20, 36

Supplemental Table 2.5. Physio-physiological results in Passages compared to Symbols. One unit increase in dlPFC mean activation predicts increased correlation between L AG and L OT area. The relationship between L AG and L OT (as predicted by dlPFC activation) is correlated with WM ability (measured by Sentence Span). Cluster size (k) in mm^3. BA, Brodmann Area. All T-values are significant at $p < 0.05$.

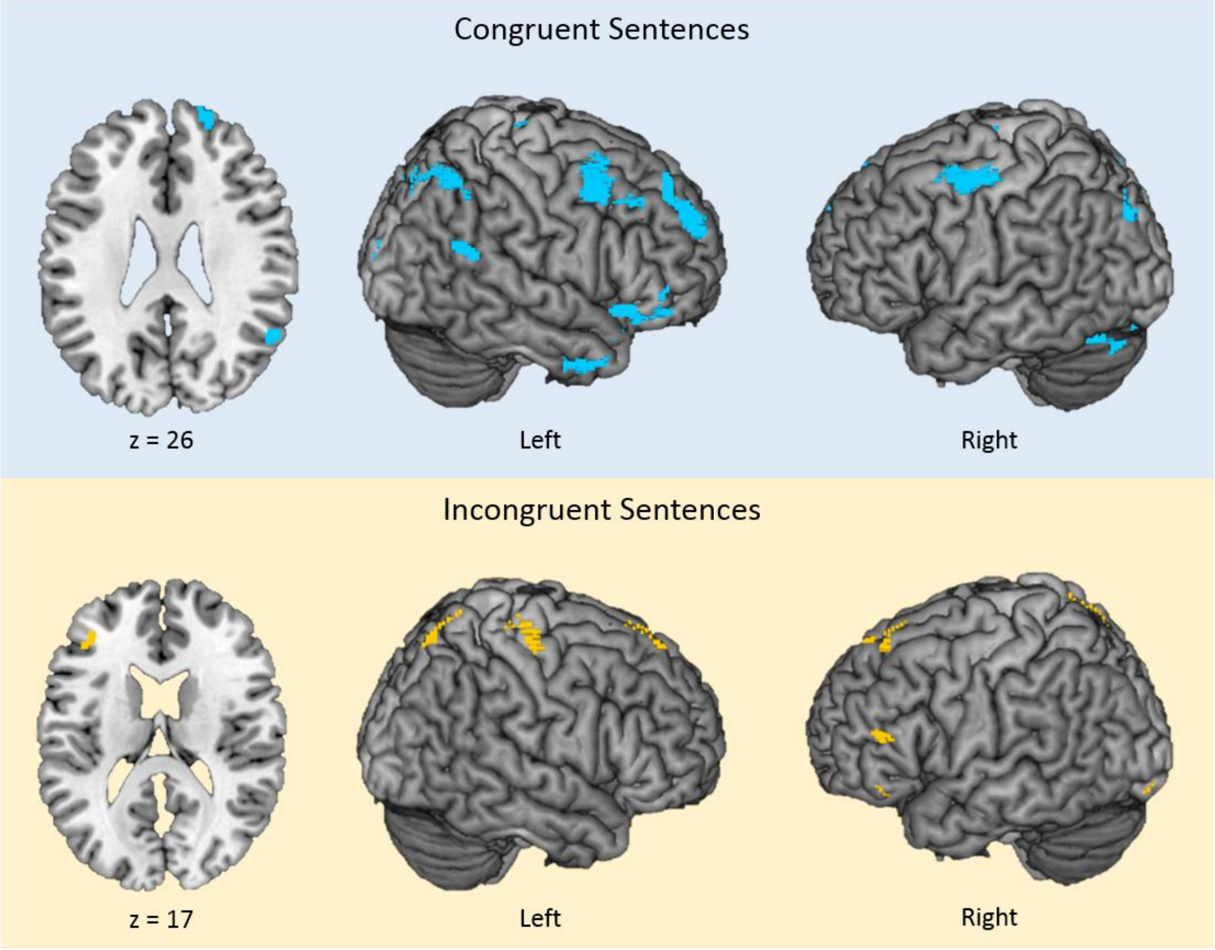
Chapter 3 Supplemental Material



Supplemental Figure 3.1. Timing parameters for the sentence stimuli. Each stimulus screen was presented for 500 ms, with 100 ms between screens. After the sentence was finished, subjects saw a plus sign, then a prompt of “No/Yes” for 1250 ms, during which time they had to press a button for whether the sentence did or did not make sense.



Supplemental Figure 3.2. ERP waveforms for the four primary conditions: Congruent Word, Congruent Sentence (CWCS; black); Incongruent Word, Congruent Sentence (IWCS; blue); Congruent Word, Incongruent Sentence (CWIS; yellow); Incongruent Word, Incongruent Sentence (IWIS; red). Condition comparisons revealed expected significant differences across incongruency comparisons (see Results; $p < 0.05$).



Supplemental Figure 3.3. Conjunctions of back-reconstructed spatial maps for congruent sentences (CWCS and IWCS; blue) and incongruent sentences (CWIS and IWIS; orange) during the N400 temporal window. Findings reveal that congruent sentences elicited N400-related activation in the default mode network (DMN), while incongruent sentences elicited activation in the language network. All results reported at $p < 0.005$.

Area	**BA**	**volume (cc)**	**Left/Right Max Z Value (x, y, z)**
JC1-- N400			
Superior Temporal Gyrus	22, 39, 42	0.4/0.9	3.3 (-51, 4, -4)/4.3 (51, 9, -6)
Precuneus	7	0.1/0.8	3.1 (-2, -68, 38)/4.5 (8, -74, 39)
Middle Temporal Gyrus	21, 22	0.7/0.0	3.4 (-57, -39, 4)/n.s.
Cingulate Gyrus	24, 32	0.4/0.5	3.1 (-2, 23, 32)/3.1 (2, 6, 35)
Postcentral Gyrus	40	0.3/0.4	3.6 (-61, -22, 18)/3.0 (57, -24, 18)
Inferior Frontal Gyrus	45, 46, 47	0.4/0.1	3.0 (-42, 18, 10)/2.6 (53, 17, -6)
Middle Frontal Gyrus	6	0.0/0.1	n.s./3.4 (55, 4, 38)
Superior Frontal Gyrus	8	0.1/0.0	3.2 (-20, 33, 48)/n.s.
Insula	13	0.1/0.1	2.7 (-38, 16, 10)/3.1 (50, -30, 20)
Posterior Cingulate	*	0.0/0.1	n.s./3.1 (14, -58, 7)
Superior Parietal Lobule	7	0.0/0.1	n.s./2.9 (14, -67, 57)
Precentral Gyrus	4, 6	0.1/0.1	2.7 (-59, -3, 15)/2.7 (57, 0, 37)
Medial Frontal Gyrus	11	0.1/0.0	2.7 (-4, 27, 34)/n.s.
Lingual Gyrus	17	0.1/0.0	2.6 (-6, -91, 0)/n.s.
Sub-Gyral	*	0.5/0.0	3.5 (-44, 24, 15)/n.s.
Third Ventricle	*	0.0/0.2	n.s./4.0 (0, -21, -2)
Culmen	*	0.1/0.1	3.1 (-2, -45, -10)/2.8 (2, -45, -10)
Extra-Nuclear	*	0.0/0.1	n.s./2.8 (0, -14, -4)
JC2-- P600a			
Postcentral Gyrus	2, 3, 5, 40, 43	0.0/1.3	n.s./4.7 (61, -21, 16)
Precuneus	7	0.1/1.3	2.7 (-8, -72, 39)/4.6 (14, -66, 36)
Medial Frontal Gyrus	6, 32	0.4/0.4	3.5 (0, -9, 48)/3.5 (2, 14, 47)
Superior Frontal Gyrus	6, 8	0.1/0.4	2.7 (-2, 16, 49)/3.4 (2, 12, 51)
Superior Temporal Gyrus	22, 42	0.4/0.3	3.2 (-59, 2, 0)/3.1 (59, -25, 14)
Lingual Gyrus	17, 18	0.3/0.1	3.8 (-4, -91, 1)/3.5 (4, -87, 1)
Insula	13	0.3/0.1	3.1 (-42, 0, 0)/2.7 (40, -5, 13)
Inferior Parietal Lobule	40	0.0/0.2	n.s./3.3 (38, -40, 57)
Parahippocampal Gyrus	28, 35	0.2/0.1	3.1 (-20, -28, -9)/2.6 (12, -33, 2)
Middle Frontal Gyrus	6	0.0/0.2	n.s./2.7 (28, 20, 54)
Transverse Temporal Gyrus	42	0.0/0.1	n.s./3.5 (63, -11, 13)
Precentral Gyrus	4	0.0/0.1	n.s./3.2 (44, -13, 56)
Paracentral Lobule	*	0.1/0.1	2.7 (-2, -9, 45)/3.0 (2, -9, 45)
Inferior Frontal Gyrus	47	0.0/0.1	n.s./3.0 (30, 9, -16)
Cingulate Gyrus	32	0.1/0.1	2.6 (0, -5, 46)/2.8 (4, 15, 36)
Cuneus	*	0.0/0.1	n.s./2.7 (2, -86, 23)
Culmen	*	0.6/0.9	3.7 (-12, -37, -8)/4.6 (14, -57, -7)
Extra-Nuclear	*	0.1/0.4	2.6 (-8, -35, 7)/4.1 (8, -31, 3)
Nodule	*	0.1/0.2	4.4 (-2, -50, -29)/6.3 (2, -48, -30)

Third Ventricle	*	0.0/0.2	n.s./4.2 (0, -2, -10)
Lateral Ventricle	*	0.1/0.2	3.1 (-16, -30, 22)/3.0 (6, -13, 21)
Thalamus	*	0.0/0.1	n.s./3.0 (14, -33, 9)
Fourth Ventricle	*	0.0/0.1	n.s./2.7 (0, -48, -26)
Uncus	*	0.1/0.0	2.6 (-28, 7, -19)/n.s.
JC3-- P600b			
Inferior Frontal Gyrus	44, 45, 47	2.2/0.1	4.9 (-53, 26, 10)/2.9 (46, 19, -9)
Cuneus	17, 18, 30	0.4/1.6	3.5 (-2, -66, 7)/4.4 (12, -69, 11)
Lingual Gyrus	17, 18, 19	1.1/0.3	3.7 (-18, -54, 3)/3.3 (12, -93, 0)
Superior Parietal Lobule	7	0.1/0.6	2.7 (-20, -67, 57)/4.8 (32, -67, 49)
Posterior Cingulate	23, 30, 31	0.3/0.5	3.3 (-2, -51, 21)/5.1 (12, -66, 11)
Middle Frontal Gyrus	46	0.1/0.4	3.0 (-48, 11, 34)/3.3 (53, 23, 28)
Superior Temporal Gyrus	38	0.3/0.2	3.5 (-44, 17, -13)/3.0 (38, 3, -19)
Fusiform Gyrus	37	0.1/0.3	2.6 (-48, -53, -16)/3.2 (44, -51, -16)
Parahippocampal Gyrus	30	0.2/0.0	3.2 (-22, -54, 5)/n.s.
Precuneus	*	0.0/0.1	n.s./3.8 (28, -69, 50)
Superior Frontal Gyrus	8	0.0/0.1	n.s./3.3 (14, 49, 40)
Inferior Occipital Gyrus	*	0.0/0.1	n.s./3.2 (28, -90, -7)
Middle Temporal Gyrus	21, 22	0.1/0.1	2.9 (-63, -41, 2)/2.6 (63, -39, 4)
Middle Occipital Gyrus	*	0.1/0.1	2.8 (-26, -86, 21)/2.6 (24, -93, 14)
Medial Frontal Gyrus	10	0.0/0.1	n.s./2.7 (4, 60, -6)
Third Ventricle	*	0.0/0.3	n.s./5.3 (0, -19, -1)
Culmen	*	0.1/0.2	3.1 (-2, -50, -21)/4.0 (6, -44, -20)
Nodule	*	0.2/0.1	3.0 (-4, -58, -29)/2.7 (2, -60, -29)
Fourth Ventricle	*	0.1/0.1	4.9 (-2, -42, -20)/7.0 (2, -42, -20)
Cerebellar Lingual	*	0.1/0.1	3.2 (-2, -46, -18)/4.8 (2, -46, -18)
Uvula	*	0.1/0.0	2.9 (-2, -62, -29)/n.s.
Fastigium	*	0.0/0.1	n.s./2.9 (6, -48, -21)
Declive	*	0.1/0.0	2.8 (-42, -57, -22)/n.s.
Extra-Nuclear	*	0.0/0.1	n.s./2.7 (2, -8, -5)
Sub-Gyral	*	0.1/0.0	2.6 (-24, -76, 28)/n.s.
JC4-- P600c			
Cuneus	7, 17, 18, 19, 23	1.7/0.8	5.4 (-2, -74, 30)/4.6 (4, -80, 33)
Precuneus	19, 31	1.2/0.6	4.1 (0, -70, 27)/4.0 (2, -65, 27)
Middle Frontal Gyrus	10	0.4/0.0	3.0 (-42, 42, 18)/n.s.
Postcentral Gyrus	2, 3, 43	0.3/0.2	3.5 (-61, -16, 30)/3.3 (57, -15, 14)
Lingual Gyrus	18	0.3/0.2	3.1 (-14, -72, -6)/2.8 (28, -72, -5)
Middle Temporal Gyrus	39	0.1/0.3	2.7 (-42, -74, 26)/3.1 (46, -71, 26)
Superior Frontal Gyrus	6, 10	0.2/0.1	3.3 (-32, 55, 16)/3.9 (4, -1, 65)
Transverse Temporal Gyrus	41, 42	0.0/0.2	n.s./3.6 (57, -19, 12)

Superior Temporal Gyrus	22, 38	0.2/0.1	2.7 (-40, 3, -12)/2.9 (44, 11, -11)
Fusiform Gyrus	19	0.1/0.0	3.4 (-22, -61, -9)/n.s.
Cingulate Gyrus	*	0.1/0.1	2.9 (-2, -61, 27)/3.2 (2, -61, 27)
Insula	13	0.0/0.1	n.s./2.9 (42, -12, -4)
Precentral Gyrus	4	0.1/0.0	2.8 (-61, -12, 30)/n.s.
Inferior Parietal Lobule	*	0.1/0.0	2.8 (-59, -27, 36)/n.s.
Angular Gyrus	39	0.1/0.0	2.7 (-42, -74, 30)/n.s.
Posterior Cingulate	30	0.0/0.1	n.s./2.6 (18, -56, 10)
Culmen	*	1.3/0.8	8.8 (-6, -39, -5)/5.0 (2, -39, -6)
Extra-Nuclear	*	0.1/0.3	4.0 (-2, 2, 2)/6.0 (2, 4, 2)
Sub-Gyral	13	0.2/0.3	3.3 (-42, 3, -9)/3.3 (44, -2, -7)
Fourth Ventricle	*	0.1/0.2	4.2 (-2, -44, -20)/7.6 (2, -44, -21)
Cerebellar Lingual	*	0.2/0.1	4.0 (-6, -43, -8)/6.0 (2, -44, -18)
Caudate	*	0.2/0.1	4.2 (-4, 10, 3)/4.1 (6, 4, 2)
Lateral Ventricle	*	0.1/0.1	4.6 (-2, 6, 2)/4.2 (2, 8, 1)

Supplemental Table 3.1. Spatial activations for each joint component, along with the Brodmann Area (BA), cluster volume in cubic centimeters (cc), and maximum z-value size and location for left/right sides. "n.s." signifies that a side was not significant. All results reported at $Z < 2.58$ ($p < 0.005$).

References

Aboud, K., Barquero, L., & Cutting, L. . (2018). Prefrontal mediation of the reading network predicts intervention response in dyslexia. *Cortex*, *101*. https://doi.org/10.1016/j.cortex.2018.01.009

Aboud, K. S., Bailey, S. K., Del Tufo, S. N., Barquero, L. A., & Cutting, L. E. (2019a). Fairy Tales versus Facts: Genre Matters to the Developing Brain. *Cerebral Cortex*. https://doi.org/10.1093/cercor/bhz025

Aboud, K. S., Bailey, S. K., Del Tufo, S. N., Barquero, L. A., & Cutting, L. E. (2019b). Fairy Tales versus Facts: Genre Matters to the Developing Brain. *Cerebral Cortex*. https://doi.org/10.1093/cercor/bhz025

Aboud, K. S., Bailey, S. K., Petrill, S. A., & Cutting, L. E. (2016). Comprehending text versus reading words in young readers with varying reading ability: Distinct patterns of functional connectivity from common processing hubs. *Developmental Science*, 1–25. https://doi.org/10.1111/desc.12422

Amunts, K., & Zilles, K. (2012). Architecture and organizational principles of Broca's region. *Trends in Cognitive Sciences*, *16*(8), 418–426. https://doi.org/10.1016/j.tics.2012.06.005

Artoni, F., Menicucci, D., Delorme, A., Makeig, S., & Micera, S. (2014). Full Length Articles RELICA: A method for estimating the reliability of 3 independent components 4Q1. https://doi.org/10.1016/j.neuroimage.2014.09.010

Bailey, S., Hoeft, F., Aboud, K., & Cutting, L. (2016). Anomalous Gray Matter Patterns in Specific Reading Comprehension Deficits are Independent of Dyslexia. *Annals of Dyslexia*, *66*(3), 256. https://doi.org/10.1007/S11881-015-0114-Y

Balass, M., Nelson, J. R., & Perfetti, C. A. (2010). Word learning: An ERP investigation of word experience effects on recognition and word processing. *Contemporary Educational Psychology*, *35*(2), 126–140. https://doi.org/10.1016/j.cedpsych.2010.04.001

Baldassano, C., Chen, J., Zadbood, A., Pillow, J. W., Hasson, U., & Norman, K. A. (2017a). Discovering Event Structure in Continuous Narrative Perception and Memory. *Neuron*, *95*(3), 709-721.e5. https://doi.org/10.1016/j.neuron.2017.06.041

Baldassano, C., Chen, J., Zadbood, A., Pillow, J. W., Hasson, U., & Norman, K. A. (2017b). Discovering Event Structure in Continuous Narrative Perception and Memory. https://doi.org/10.1016/j.neuron.2017.06.041

Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *NeuroImage*, *37*(1), 90–101. https://doi.org/10.1016/j.neuroimage.2007.04.042

Binder, J. R., Desai, R. H., Graves, W. W., & Conant, L. L. (2009). Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. *Cerebral Cortex (New York, N.Y. : 1991)*, *19*(12), 2767–2796. https://doi.org/10.1093/cercor/bhp055

Bitan, T., Booth, J. R., Choy, J., Burman, D. D., Gitelman, D. R., & Mesulam, M.-M. (2005). Shifts of effective connectivity within a language network during rhyming and spelling. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *25*(22), 5397–5403. https://doi.org/10.1523/JNEUROSCI.0864-05.2005

Broadway, J. M., Franklin, M. S., & Schooler, J. W. (2015). Early event-related brain potentials and hemispheric asymmetries reveal mind-wandering while reading and predict comprehension. *Biological Psychology*, *107*, 31–43.

https://doi.org/10.1016/j.biopsycho.2015.02.009

Brouwer, H., Fitz, H., & Hoeks, J. (2012). Getting real about Semantic Illusions: Rethinking the functional role of the P600 in language comprehension. *Brain Research*, *1446*, 127–143. https://doi.org/10.1016/j.brainres.2012.01.055

Brouwer, H., & Hoeks, J. C. J. (2013). A time and place for language comprehension: mapping the N400 and the P600 to a minimal cortical network. *Frontiers in Human Neuroscience*, *7*, 758. https://doi.org/10.3389/fnhum.2013.00758

Brown, J. I. (1960). *The Nelson-Denny Reading Test.* Oxford, England: Houghton Mifflin. Retrieved from https://psycnet.apa.org/record/1960-06748-000

Burkhardt, P. (2007). The P600 reflects cost of new information in discourse memory. *NeuroReport*, *18*(17), 1851–1854. https://doi.org/10.1097/WNR.0b013e3282f1a999

Cain, K., & Oakhill, J. (2006). Profiles of children with specific reading comprehension difficulties. *The British Journal of Educational Psychology*, *76*(Pt 4), 683–696. https://doi.org/10.1348/000709905X67610

Calhoun, V D, Adali, T., Pearlson, G. D., & Kiehl, K. A. (2006). Neuronal chronometry of target detection: fusion of hemodynamic and event-related potential data. *NeuroImage*, *30*(2), 544–553. https://doi.org/10.1016/j.neuroimage.2005.08.060

Calhoun, Vince D., Adali, T., Kiehl, K. A., Astur, R., Pekar, J. J., & Pearlson, G. D. (2006). A method for multitask fMRI data fusion applied to schizophrenia. *Human Brain Mapping*, *27*(7), 598–610. https://doi.org/10.1002/hbm.20204

Calhoun, Vince D, Liu, J., & Adali, T. (2009). A review of group ICA for fMRI data and ICA for joint inference of imaging, genetic, and ERP data. *NeuroImage*, *45*(1 Suppl), S163-72. https://doi.org/10.1016/j.neuroimage.2008.10.057

Catts, H., Adlof, S. M., & Ellis Weismer, S. (2006). Language deficits in poor comprehenders: a case for the simple view of reading. *Journal of Speech, Language, and Hearing Research : JSLHR*, *49*(2), 278–293. https://doi.org/10.1044/1092-4388(2006/023)

Catts, H., Hogan, T., & Adlof, S. M. (2005). Developmental changes in reading and reading disabilities. In H. Catts & A. Kamhi (Eds.), *The Connections Between Language and Reading Disabilities.* (pp. 25–40). Mahwah, NJ: Lawrence Erlbaum Associates.

Christopher, M. E., Miyake, A., Keenan, J. M., Pennington, B., DeFries, J. C., Wadsworth, S. J., … Olson, R. K. (2012). Predicting word reading and comprehension with executive function and speed measures across development: a latent variable analysis. *Journal of Experimental Psychology. General*, *141*(3), 470–488. https://doi.org/10.1037/a0027375

Cole, M. W., Repov, G., & Anticevic, A. (2014). The Frontoparietal Control System : A Central Role in Mental Health. *The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology and Psychiatry*. https://doi.org/10.1177/1073858414525995

Cole, M. W., Reynolds, J. R., Power, J. D., Repovs, G., Anticevic, A., & Braver, T. S. (2013). Multi-task connectivity reveals flexible hubs for adaptive task control. *Nature Neuroscience*, *16*(9), 1348–1355. https://doi.org/10.1038/nn.3470

Cutting, L. E., Clements-Stephens, A., Pugh, K. R., Burns, S., Cao, A., Pekar, J. J., … Rimrodt, S. L. (2013a). Not all reading disabilities are dyslexia: distinct neurobiology of specific comprehension deficits. *Brain Connectivity*, *3*(2), 199–211. https://doi.org/10.1089/brain.2012.0116

Cutting, L. E., Clements-Stephens, A., Pugh, K. R., Burns, S., Cao, A., Pekar, J. J., … Rimrodt, S. L. (2013b). Not all reading disabilities are dyslexia: distinct neurobiology of specific comprehension deficits. *Brain Connectivity*, *3*(2), 199–211.

https://doi.org/10.1089/brain.2012.0116

Cutting, L. E., Materek, A., Cole, C. A. S., Levine, T. M., & Mahone, E. M. (2009). Effects of fluency, oral language, and executive function on reading comprehension performance. *Annals of Dyslexia*, *59*(1), 34–54. https://doi.org/10.1007/s11881-009-0022-0

Davey, J., Cornelissen, P. L., Thompson, H. E., Sonkusare, S., Hallam, G., Smallwood, J., & Jefferies, E. (2015). Automatic and Controlled Semantic Retrieval: TMS Reveals Distinct Contributions of Posterior Middle Temporal Gyrus and Angular Gyrus. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *35*(46), 15230–15239. https://doi.org/10.1523/JNEUROSCI.4705-14.2015

Davey, J., Thompson, H. E., Hallam, G., Karapanagiotidis, T., Murphy, C., De Caso, I., … Jefferies, E. (2016). Exploring the role of the posterior middle temporal gyrus in semantic cognition: Integration of anterior temporal lobe with executive processes. *NeuroImage*, *137*, 165–177. https://doi.org/10.1016/j.neuroimage.2016.05.051

DeLong, K. A., Quante, L., & Kutas, M. (2014). Predictability, plausibility, and two late ERP positivities during written sentence comprehension. *Neuropsychologia*, *61*, 150–162. https://doi.org/10.1016/j.neuropsychologia.2014.06.016

Dien, J., & O’Hare, A. J. (2008). Evidence for automatic sentence priming in the fusiform semantic area: convergent ERP and fMRI findings. *Brain Research*, *1243*, 134–145. https://doi.org/10.1016/j.brainres.2008.09.045

Donchin, E., & Coles, M. G. H. (1988). Is the P300 component a manifestation of context updating? *Behavioral and Brain Sciences*, *11*(3), 357–374. https://doi.org/10.1017/S0140525X00058027

Dorjee, D., Devenney, L., & Thierry, G. (2010). Written words supersede pictures in priming semantic access: A P300 study. *NeuroReport*, *21*(13), 887–891. https://doi.org/10.1097/WNR.0b013e32833da46a

Duncan, C. C., Barry, R. J., Connolly, J. F., Fischer, C., Michie, P. T., Näätänen, R., … Van Petten, C. (2009). Event-related potentials in clinical research: Guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400. *Clinical Neurophysiology*, *120*(11), 1883–1908. https://doi.org/10.1016/j.clinph.2009.07.045

Edwards, B. G., Calhoun, V. D., & Kiehl, K. A. (2012). Joint ICA of ERP and fMRI during error-monitoring. *NeuroImage*, *59*(2), 1896–1903. https://doi.org/10.1016/j.neuroimage.2011.08.088

Fadiga, L., Craighero, L., Destro, M. F., Finos, L., Cotillon-Williams, N., Smith, A. T., & Castiello, U. (2006). Language in shadow. *Social Neuroscience*, *1*(2), 77–89. https://doi.org/10.1080/17470910600976430

Ferstl, E. C., Neumann, J., Bogler, C., & von Cramon, D. Y. (2008). The extended language network: a meta-analysis of neuroimaging studies on text comprehension. *Human Brain Mapping*, *29*(5), 581–593. https://doi.org/10.1002/hbm.20422

Friederici, A. D. (2002a). Towards a neural basis of auditory sentence processing. *Trends in Cognitive Sciences*, *6*(2), 78–84. https://doi.org/10.1016/S1364-6613(00)01839-8

Friederici, A. D. (2002b, February 1). Towards a neural basis of auditory sentence processing. *Trends in Cognitive Sciences*. https://doi.org/10.1016/S1364-6613(00)01839-8

Friederici, A. D. (2011). The brain basis of language processing: from structure to function. *Physiological Reviews*, *91*(4), 1357–1392. https://doi.org/10.1152/physrev.00006.2011

Friederici, A. D., & Gierhan, S. M. E. (2013). The language network. *Current Opinion in Neurobiology*, *23*(2), 250–254. https://doi.org/10.1016/j.conb.2012.10.002

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J. -P, Frith, C. D., & Frackowiak, R. S. J. (1994). Statistical parametric maps in functional imaging: A general linear approach. *Human Brain Mapping*, *2*(4), 189–210. https://doi.org/10.1002/hbm.460020402

Gouvea, A. C., Phillips, C., Kazanina, N., & Poeppel, D. (2010). The linguistic processes underlying the P600. *Language and Cognitive Processes*, *25*(2), 149–188. https://doi.org/10.1080/01690960902965951

Hagoort, P. (2013). *MUC (Memory, Unification, Control) and beyond*. *Front Psychol* (Vol. 4). Elsevier Inc. https://doi.org/10.3389/fpsyg.2013.00416

Hagoort, Peter. (2005). On Broca, brain, and binding: a new framework. *Trends in Cognitive Sciences*, *9*(9), 416–423. https://doi.org/10.1016/j.tics.2005.07.004

Hagoort, Peter. (2013). MUC (Memory, Unification, Control) and beyond. *Frontiers in Psychology*, *4*, 416. https://doi.org/10.3389/fpsyg.2013.00416

Hagoort, Peter, & Indefrey, P. (2014). The neurobiology of language beyond single words. *Annual Review of Neuroscience*, *37*, 347–362. https://doi.org/10.1146/annurev-neuro-071013-013847

Hill, H., Strube, M., Roesch-Ely, D., & Weisbrod, M. (2002). Automatic vs. controlled processes in semantic priming - Differentiation by event-related potentials. *International Journal of Psychophysiology*, *44*(3), 197–218. https://doi.org/10.1016/S0167-8760(01)00202-1

Himberg, J., Hyvärinen, A., & Esposito, F. (2004). Validating the independent components of neuroimaging time series via clustering and visualization. *NeuroImage*, *22*(3), 1214–1222. https://doi.org/10.1016/J.NEUROIMAGE.2004.03.027

Hoeks, J. C. ., Stowe, L. A., & Doedens, G. (2004). Seeing words in context: the interaction of lexical and sentence level information during reading. *Cognitive Brain Research*, *19*(1), 59–

73. https://doi.org/10.1016/j.cogbrainres.2003.10.022

Hogan, T. P., Adlof, S. M., & Alonzo, C. N. (2014). On the importance of listening comprehension. In *International Journal of Speech-Language Pathology* (Vol. 16, pp. 199–207). Informa Healthcare. https://doi.org/10.3109/17549507.2014.904441

Hoover, W. a., & Gough, P. B. (1990). The simple view of reading. *Reading and Writing*, *2*(2), 127–160. https://doi.org/10.1007/BF00401799

Horowitz-Kraus, T., Buck, C., & Dorrmann, D. (2016). Altered neural circuits accompany lower performance during narrative comprehension in children with reading difficulties: an fMRI study. *Annals of Dyslexia*, *66*(3), 301–318. https://doi.org/10.1007/s11881-016-0124-4

Horowitz-Kraus, T., Eaton, K., Farah, R., Hajinazarian, A., Vannest, J., & Holland, S. K. (2015). Predicting better performance on a college preparedness test from narrative comprehension at the age of 6 years: An fMRI study. *Brain Research*, *1629*, 54–62. https://doi.org/10.1016/j.brainres.2015.10.008

Horowitz-Kraus, T., Vannest, J. J., & Holland, S. K. (2013). Overlapping neural circuitry for narrative comprehension and proficient reading in children and adolescents. *Neuropsychologia*, *51*(13), 2651–2662. https://doi.org/10.1016/j.neuropsychologia.2013.09.002

Jefferies, E. (2013). The neural basis of semantic cognition: converging evidence from neuropsychology, neuroimaging and TMS. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *49*(3), 611–625. https://doi.org/10.1016/j.cortex.2012.10.008

Justice, L., Mashburn, A., & Petscher, Y. (2013). Very early language skills of fifth-grade poor comprehenders. *Journal of Research in Reading*, *36*(2), 172–185. https://doi.org/10.1111/j.1467-9817.2011.01498.x

Kang, S. H. K., Eglington, L. G., & Yap, M. J. (2018). Forward versus backward semantic priming: What movement dynamics during lexical decision reveal. *Quarterly Journal of Experimental Psychology*, *71*(7), 1506–1511. https://doi.org/10.1177/1747021818775051

Kendeou, P., van den Broek, P., Helder, A., & Karlsson, J. (2014). A Cognitive View of Reading Comprehension: Implications for Reading Difficulties. *Learning Disabilities Research & Practice*, *29*(1), 10–16. https://doi.org/10.1111/ldrp.12025

Kielar, A., Panamsky, L., Links, K. A., & Meltzer, J. A. (2015). Localization of electrophysiological responses to semantic and syntactic anomalies in language comprehension with MEG. *NeuroImage*, *105*, 507–524. https://doi.org/10.1016/j.neuroimage.2014.11.016

Kim, A. E., Oines, L., & Miyake, A. (2018). Individual differences in verbal working memory underlie a tradeoff between semantic and structural processing difficulty during language comprehension: An ERP investigation. *Journal of Experimental Psychology: Learning Memory and Cognition*, *44*(3), 406–420. https://doi.org/10.1037/xlm0000457

Kovelman, I., Norton, E. S., Christodoulou, J. A., Gaab, N., Lieberman, D. A., Triantafyllou, C., … Gabrieli, J. D. E. (2012). Brain basis of phonological awareness for spoken language in children and its disruption in dyslexia. *Cerebral Cortex (New York, N.Y. : 1991)*, *22*(4), 754–764. https://doi.org/10.1093/cercor/bhr094

Kuperberg, G. R. (2007). Neural mechanisms of language comprehension: Challenges to syntax. *Brain Research*, *1146*, 23–49. https://doi.org/10.1016/J.BRAINRES.2006.12.063

Kuperberg, G. R., Sitnikova, T., Caplan, D., & Holcomb, P. J. (2003). Electrophysiological distinctions in processing conceptual relationships within simple sentences. *Cognitive Brain Research*, *17*(1), 117–129. https://doi.org/10.1016/S0926-6410(03)00086-7

Kutas, M, & Hillyard, S. (1980). Reading senseless sentences: brain potentials reflect semantic incongruity. *Science*. https://doi.org/10.1126/science.7350657

Kutas, Marta, & Federmeier, K. D. (2011). Thirty years and counting: finding meaning in the N400 component of the event-related brain potential (ERP). *Annual Review of Psychology, 62*, 621–647. https://doi.org/10.1146/annurev.psych.093008.131123

Landi, N., & Perfetti, C. (2007). An electrophysiological investigation of semantic and phonological processing in skilled and less-skilled comprehenders. *Brain and Language*, *102*(1), 30–45. https://doi.org/10.1016/j.bandl.2006.11.001

Landi, N., & Ryherd, K. (2017). Understanding specific reading comprehension deficit: A review. https://doi.org/10.1111/lnc3.12234

Lau, E., Almeida, D., Hines, P. C., & Poeppel, D. (2009). A lexical basis for N400 context effects: evidence from MEG. *Brain and Language*, *111*(3), 161–172. https://doi.org/10.1016/j.bandl.2009.08.007

Lau, E. F., Gramfort, A., Hämäläinen, M. S., & Kuperberg, G. R. (2013). Automatic semantic facilitation in anterior temporal cortex revealed through multimodal neuroimaging. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *33*(43), 17174–17181. https://doi.org/10.1523/JNEUROSCI.1018-13.2013

Lau, E. F., Holcomb, P. J., & Kuperberg, G. R. (2013). Dissociating N400 effects of prediction from association in single-word contexts. *Journal of Cognitive Neuroscience, 25*(3), 484–502. https://doi.org/10.1162/jocn_a_00328

Lau, E. F., Phillips, C., & Poeppel, D. (2008). A cortical network for semantics: (de)constructing the N400. *Nature Reviews Neuroscience*, *9*(12), 920–933. https://doi.org/10.1038/nrn2532

Lau, E. F., Weber, K., Gramfort, A., Hämäläinen, M. S., & Kuperberg, G. R. (2016).

Spatiotemporal Signatures of Lexical-Semantic Prediction. *Cerebral Cortex (New York, N.Y. : 1991)*, *26*(4), 1377–1387. https://doi.org/10.1093/cercor/bhu219

Leckey, M., & Federmeier, K. D. (2019). The P3b and P600(s): Positive contributions to language comprehension. *Psychophysiology*. Blackwell Publishing Inc. https://doi.org/10.1111/psyp.13351

Liu, L., Vira, A., Friedman, E., Minas, J., Bolger, D., Bitan, T., & Booth, J. (2010). Children with reading disability show brain differences in effective connectivity for visual, but not auditory word comprehension. *PloS One*, *5*(10), e13492. https://doi.org/10.1371/journal.pone.0013492

Locascio, G., Mahone, E. M., Eason, S. H., & Cutting, L. E. (2010). Executive dysfunction among children with reading comprehension deficits. *Journal of Learning Disabilities*, *43*(5), 441–454. https://doi.org/10.1177/0022219409355476

Malins, J. G., Gumkowski, N., Buis, B., Molfese, P., Rueckl, J. G., Frost, S. J., … Mencl, W. E. (2016). Dough, tough, cough, rough: A “fast” fMRI localizer of component processes in reading. *Neuropsychologia*, *91*, 394–406. https://doi.org/10.1016/j.neuropsychologia.2016.08.027

Mar, R. A. (2011). The Neural Bases of Social Cognition and Story Comprehension. *Annual Review of Psychology*, *62*, 103–134. https://doi.org/10.1146/annurev-psych-120709-145406

McGrew, K. S., Schrank, F. A., & Woodcock, R. W. (2007). *Woodcock-Johnson III Normative Update*. Rolling Meadows, Illinois, United States: Riverside Publishing.

Mijović, B., Vanderperren, K., Novitskiy, N., Vanrumste, B., Stiers, P., Bergh, B. Van den, … Vos, M. De. (2012). The “why” and “how” of JointICA: results from a visual detection task. *NeuroImage*, *60*(2), 1171–1185. https://doi.org/10.1016/j.neuroimage.2012.01.063

Milivojevic, B., Varadinov, M., Vicente Grabovetsky, A., Collin, S. H. P., & Doeller, C. F. (2016). Coding of Event Nodes and Narrative Context in the Hippocampus. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *36*(49), 12412–12424. https://doi.org/10.1523/JNEUROSCI.2889-15.2016

Molfese, P. J., Fletcher, J. M., & Denton, C. A. (2013). Adequate versus inadequate response to reading intervention: An event-related potentials assessment. *Developmental Neuropsychology*, *38*(8), 534–549. https://doi.org/10.1080/87565641.2013.825260

Mossbridge, J. A., Grabowecky, M., Paller, K. A., & Suzuki, S. (2013). Neural activity tied to reading predicts individual differences in extended-text comprehension. *Frontiers in Human Neuroscience*, *7*, 655. https://doi.org/10.3389/fnhum.2013.00655

Nation, K, Adams, J. W., Bowyer-Crane, C. a, & Snowling, M. J. (1999). Working memory deficits in poor comprehenders reflect underlying language impairments. *Journal of Experimental Child Psychology*, *73*(2), 139–158. https://doi.org/10.1006/jecp.1999.2498

Nation, K, Clarke, P., Marshall, C. M., & Durand, M. (2004). Hidden Language Impairments in Children: Parallels between Poor Reading Comprehension and Specific Language Impairment? *Journal of Speech, Language, and Hearing Research*, *47*(1), 199–211. https://doi.org/10.1044/1092-4388(2004/017)

Nation, Kate, Snowling, M. J., & Clarke, P. (2007). Dissecting the relationship between language skills and learning to read: Semantic and phonological contributions to new vocabulary learning in children with poor reading comprehension†. *International Journal of Speech-Language Pathology*, *9*(2), 131–139. https://doi.org/10.1080/14417040601145166

Oakhill, J. V., Cain, K., & Bryant, P. E. (2003). The dissociation of word reading and text comprehension: Evidence from component skills. *Language and Cognitive Processes*, *18*(4), 443–468. https://doi.org/10.1080/01690960344000008

Oakhill, J. V., & Cain, K. (2012). The Precursors of Reading Ability in Young Readers: Evidence From a Four-Year Longitudinal Study. *Scientific Studies of Reading*, *16*(2), 91–121. https://doi.org/10.1080/10888438.2010.529219

Osterhout, L. (1997). On the Language Specificity of the Brain Response to Syntactic Anomalies: Is the Syntactic Positive Shift a Member of the P300 Family? *Brain and Language*, *59*, 494–522. Retrieved from https://pdfs.semanticscholar.org/4b9b/dfacb648516f8f472b49b9bd16f97534d9da.pdf

Osterhout, Lee, & Holcomb, P. J. (1992). Event-related brain potentials elicited by syntactic anomaly. *Journal of Memory and Language*, *31*(6), 785–806. https://doi.org/10.1016/0749-596X(92)90039-Z

Osterhout, Lee, Kim, A., & Kuperberg, G. (2012). The Neurobiology of Sentence Comprehension. *Cambridge Handbook of Psycholinguistics*, 365–389.

Osterhout, Lee, McLaughlin, J., Kim, A., Greenwald, R., & Inoue, K. (2004). *Sentences in the brain: Event-related potentials as real-time reflections of sentence comprehension and language learning*. *The On-line Study of Sentence Comprehension: Eyetracking, ERPs and Beyond*. https://doi.org/10.4324/9780203509050

Ouyang, X., Chen, K., Yao, L., Hu, B., Wu, X., Ye, Q., & Guo, X. (2015). Simultaneous changes in gray matter volume and white matter fractional anisotropy in Alzheimer's disease revealed by multimodal CCA and joint ICA. *Neuroscience, 301*, 553–562. https://doi.org/10.1016/j.neuroscience.2015.06.031

Patael, S. Z., Farris, E. A., Black, J. M., Hancock, R., Gabrieli, J. D. E., Cutting, L. E., & Hoeft, F. (2018). Brain basis of cognitive resilience: Prefrontal cortex predicts better reading comprehension in relation to decoding. *PLOS ONE, 13*(6), e0198791. https://doi.org/10.1371/journal.pone.0198791

Perfetti, C. A., Wlotko, E. W., & Hart, L. A. (2005). Word learning and individual differences in word learning reflected in event-related potentials. *Journal of Experimental Psychology: Learning Memory and Cognition*, *31*(6), 1281–1292. https://doi.org/10.1037/0278-7393.31.6.1281

Pobric, G., Jefferies, E., & Ralph, M. A. L. (2007). Anterior temporal lobes mediate semantic representation: mimicking semantic dementia by using rTMS in normal participants. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(50), 20137–20141. https://doi.org/10.1073/pnas.0707383104

Polich, J. (2007, October). Updating P300: An integrative theory of P3a and P3b. *Clinical Neurophysiology*. https://doi.org/10.1016/j.clinph.2007.04.019

Polich, J. (2012). Neuropsychology of P300. In *The Oxford Handbook of Event-Related Potential Components*. Oxford University Press. https://doi.org/10.1093/oxfordhb/9780195374148.013.0089

Price, C. J. (2012). A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading. *NeuroImage*, *62*(2), 816–847. https://doi.org/10.1016/j.neuroimage.2012.04.062

Ptak, R. (2012). The frontoparietal attention network of the human brain: action, saliency, and a priority map of the environment. *The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology and Psychiatry*, *18*(5), 502–515. https://doi.org/10.1177/1073858411409051

Richlan, F. (2012). Developmental dyslexia: dysfunction of a left hemisphere reading network.

Frontiers in Human Neuroscience, *6*, 120. https://doi.org/10.3389/fnhum.2012.00120

Richlan, F., Kronbichler, M., & Wimmer, H. (2009). Functional abnormalities in the dyslexic brain: a quantitative meta-analysis of neuroimaging studies. *Human Brain Mapping*, *30*(10), 3299–3308. https://doi.org/10.1002/hbm.20752

Richlan, F., Kronbichler, M., & Wimmer, H. (2011). Meta-analyzing brain dysfunctions in dyslexic children and adults. *NeuroImage*, *56*(3), 1735–1742. https://doi.org/10.1016/j.neuroimage.2011.02.040

Richlan, F., Kronbichler, M., & Wimmer, H. (2013). Structural abnormalities in the dyslexic brain: a meta-analysis of voxel-based morphometry studies. *Human Brain Mapping*, *34*(11), 3055–3065. https://doi.org/10.1002/hbm.22127

Ricketts, J., Sperring, R., & Nation, K. (2014). Educational attainment in poor comprehenders. *Frontiers in Psychology*, *5*, 445. https://doi.org/10.3389/fpsyg.2014.00445

Rimrodt, S. L., Clements-Stephens, A. M., Pugh, K. R., Courtney, S. M., Gaur, P., Pekar, J. J., & Cutting, L. E. (2009). Functional MRI of sentence comprehension in children with dyslexia: beyond word recognition. *Cerebral Cortex (New York, N.Y. : 1991)*, *19*(2), 402–413. https://doi.org/10.1093/cercor/bhn092

Ritchie, S. J., & Bates, T. C. (2013). Enduring Links From Childhood Mathematics and Reading Achievement to Adult Socioeconomic Status. *Psychological Science*, *24*(7), 1301–1308. https://doi.org/10.1177/0956797612466268

Rogers, T. T., Patterson, K., Jefferies, E., & Ralph, M. A. L. (2015). Disorders of representation and control in semantic cognition: Effects of familiarity, typicality, and specificity. *Neuropsychologia*, *76*, 220–239. https://doi.org/10.1016/j.neuropsychologia.2015.04.015

Ryherd, K., Jasinska, K., Van Dyke, J. A., Hung, Y.-H., Baron, E., Mencl, W. E., … Landi, N.

(2018). Cortical regions supporting reading comprehension skill for single words and discourse. *Brain and Language*, *186*, 32–43. https://doi.org/10.1016/J.BANDL.2018.08.001

Saxe, R., Moran, J. M., Scholz, J., & Gabrieli, J. (2006). Overlapping and non-overlapping brain regions for theory of mind and self reflection in individual subjects. *Social Cognitive and Affective Neuroscience*, *1*(3), 229–234. https://doi.org/10.1093/scan/nsl034

SAXE, R., & WEXLER, A. (2005). Making sense of another mind: The role of the right temporo-parietal junction. *Neuropsychologia*, *43*(10), 1391–1399. https://doi.org/10.1016/j.neuropsychologia.2005.02.013

Schlaggar, B. L., & McCandliss, B. D. (2007). Development of neural systems for reading. *Annual Review of Neuroscience*, *30*, 475–503. https://doi.org/10.1146/annurev.neuro.28.061604.135645

Schrank, F. A., Mather, N., & McGrew, K. S. (2014). *Woodcock-Johnson IV Test of Achievement*. Rolling Meadows, IL: Riverside Publishing.

Seghier, M. L. (2013). The angular gyrus: multiple functions and multiple subdivisions. *The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology and Psychiatry*, *19*(1), 43–61. https://doi.org/10.1177/1073858412440596

Service, E., Helenius, P., Maury, S., & Salmelin, R. (2007). Localization of syntactic and semantic brain responses using magnetoencephalography. *Journal of Cognitive Neuroscience*, *19*(7), 1193–1205. https://doi.org/10.1162/jocn.2007.19.7.1193

Sesma, H. W., Mahone, E. M., Levine, T., Eason, S. H., & Cutting, L. E. (2009). The Contribution of Executive Skills to Reading Comprehension. *Child Neuropsychology*, *15*(3), 232–246. https://doi.org/10.1080/09297040802220029.THE

Shaheen, E. A., Shohdy, S. S., Abd Al Raouf, M., Mohamed El Abd, S., & Abd Elhamid, A.

(2011). Relation between language, audio-vocal psycholinguistic abilities and P300 in children having specific language impairment. *International Journal of Pediatric Otorhinolaryngology*, *75*(9), 1117–1122. https://doi.org/10.1016/j.ijporl.2011.06.001

Shankweiler, D., Mencl, W. E., Braze, D., Tabor, W., Pugh, K. R., & Fulbright, R. K. (2008). Reading differences and brain: Cortical integration of speech and print in sentence processing varies with reader skill. In *Developmental Neuropsychology* (Vol. 33, pp. 745–775). https://doi.org/10.1080/87565640802418688

Shen, W., Fiori-Duharcourt, N., & Isel, F. (2016). Functional significance of the semantic P600. *NeuroReport*, *27*(7), 548–558. https://doi.org/10.1097/WNR.0000000000000583

Simony, E., Honey, C. J., Chen, J., Lositsky, O., Yeshurun, Y., Wiesel, A., & Hasson, U. (2016). Dynamic reconfiguration of the default mode network during narrative comprehension. *Nature Communications*, *7*(1), 12141. https://doi.org/10.1038/ncomms12141

Skeide, M. A., Brauer, J., & Friederici, A. D. (2014). Syntax gradually segregates from semantics in the developing brain. *NeuroImage*, *100*, 106–111. https://doi.org/10.1016/j.neuroimage.2014.05.080

Smallwood, J., Brown, K., Baird, B., & Schooler, J. W. (2012). Cooperation between the default mode network and the frontal-parietal network in the production of an internal train of thought. *Brain Research*, *1428*, 60–70. https://doi.org/10.1016/j.brainres.2011.03.072

Smallwood, J., Gorgolewski, K. J., Golchert, J., Ruby, F. J. M., Engen, H., Baird, B., … Margulies, D. S. (2013). The default modes of reading: Modulation of posterior cingulate and medial prefrontal cortex connectivity associated with comprehension and task focus while reading. *Frontiers in Human Neuroscience*, (NOV). https://doi.org/10.3389/fnhum.2013.00734

Spencer, M., Quinn, J. M., & Wagner, R. K. (2014). Specific Reading Comprehension Disability: Major Problem, Myth, or Misnomer? *Learning Disabilities Research & Practice*, *29*(1), 3–9. https://doi.org/10.1111/ldrp.12024

Spreng, R. N., Stevens, W. D., Chamberlain, J. P., Gilmore, A. W., & Schacter, D. L. (2010). Default network activity, coupled with the frontoparietal control network, supports goal-directed cognition. *NeuroImage*, *53*(1), 303–317. https://doi.org/10.1016/j.neuroimage.2010.06.016

Stafura, J. Z., & Perfetti, C. A. (2014a). Word-to-text integration: Message level and lexical level influences in ERPs. *Neuropsychologia*, *64C*, 41–53. https://doi.org/10.1016/j.neuropsychologia.2014.09.012

Stafura, J. Z., & Perfetti, C. A. (2014b). Word-to-text integration: Message level and lexical level influences in ERPs. *Neuropsychologia*, *64*, 41–53. https://doi.org/10.1016/j.neuropsychologia.2014.09.012

Stafura, J. Z., Rickles, B., & Perfetti, C. A. (2015). ERP evidence for memory and predictive mechanisms in word-to-text integration. *Language, Cognition and Neuroscience*, *30*(10), 1273–1290. https://doi.org/10.1080/23273798.2015.1062119

Stanovich, K. E. (1980). Toward an Interactive-Compensatory Model of Individual Differences in the Development of Reading Fluency. *Reading Research Quarterly*, *16*(1), 32. https://doi.org/10.2307/747348

Stothard, S. E., & Hulme, C. (1995). A comparison of phonological skills in children with reading comprehension difficulties and children with decoding difficulties. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *36*(3), 399–408.

Stuebing, K. K., Barth, A. E., Trahan, L. H., Reddy, R. R., Miciak, J., & Fletcher, J. M. (2015).

Are Child Cognitive Characteristics Strong Predictors of Responses to Intervention? A Meta-Analysis. *Review of Educational Research*, *85*(3), 395–429. https://doi.org/10.3102/0034654314555996

Swanson, H. L., Cochran, K. F., & Ewers, C. a. (1989). Working memory in skilled and less skilled readers. *Journal of Abnormal Child Psychology*, *17*(2), 145–156. https://doi.org/10.1007/BF00913790

U.S. Department of Education. (2019). *Data Point: Adult Literacy in the United States*. Washington D.C.

Vagharchakian, L., Dehaene-Lambertz, G., Pallier, C., & Dehaene, S. (2012). A temporal bottleneck in the language comprehension network. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *32*(26), 9089–9102. https://doi.org/10.1523/JNEUROSCI.5685-11.2012

Van Petten, C., Coulson, S., Rubin, S., Plante, E., & Parks, M. (1999). Time course of word identification and semantic integration in spoken language. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *25*(2), 394–417. https://doi.org/10.1037/0278-7393.25.2.394

Van Petten, C., & Luka, B. J. (2006). Neural localization of semantic context effects in electromagnetic and hemodynamic studies. *Brain and Language*, *97*(3), 279–293. https://doi.org/10.1016/j.bandl.2005.11.003

Van Petten, C., Weckerly, J., Mclsaac, H. K., & Kutas, M. (1997). Working memory capacity dissociates lexical and sentential context effects, *8*(3).

Vandermosten, M., Boets, B., Wouters, J., & Ghesquière, P. (2012). A qualitative and quantitative review of diffusion tensor imaging studies in reading and dyslexia.

Neuroscience and Biobehavioral Reviews, 36(6), 1532–1552. https://doi.org/10.1016/j.neubiorev.2012.04.002

Verleger, R., Jaśkowski, P., & Wascher, E. (2005). Evidence for an integrative role of P3b in linking reaction to perception. *Journal of Psychophysiology, 19*(3), 165–181. https://doi.org/10.1027/0269-8803.19.3.165

Visser, M., Jefferies, E., Embleton, K. V, & Lambon Ralph, M. A. (2012). Both the middle temporal gyrus and the ventral anterior temporal area are crucial for multimodal semantic processing: distortion-corrected fMRI evidence for a double gradient of information convergence in the temporal lobes. *Journal of Cognitive Neuroscience, 24*(8), 1766–1778. https://doi.org/10.1162/jocn_a_00244

Vogel, A. C., Petersen, S. E., & Schlaggar, B. L. (2014). The VWFA: it's not just for words anymore. *Frontiers in Human Neuroscience, 8*, 88. https://doi.org/10.3389/fnhum.2014.00088

Warren, D. E., Power, J. D., Bruss, J., Denburg, N. L., Waldron, E. J., Sun, H., … Tranel, D. (2014). Network measures predict neuropsychological outcome after brain injury. *Proceedings of the National Academy of Sciences, 111*(39). https://doi.org/10.1073/pnas.1322173111

Welcome, S. E., Chiarello, C., Thompson, P. M., & Sowell, E. R. (2011). Reading skill is related to individual differences in brain structure in college students. *Human Brain Mapping, 32*(8), 1194–1205. https://doi.org/10.1002/hbm.21101

Welcome, S. E., & Joanisse, M. F. (2012). Individual differences in skilled adult readers reveal dissociable patterns of neural activity associated with component processes of reading. *Brain and Language, 120*(3), 360–371. https://doi.org/10.1016/j.bandl.2011.12.011

Whitfield-Gabrieli, S., & Nieto-Castanon, A. (2012). Conn: a functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connectivity*, *2*(3), 125–141. https://doi.org/10.1089/brain.2012.0073

Whitney, C., Huber, W., Klann, J., Weis, S., Krach, S., & Kircher, T. (2009). Neural correlates of narrative shifts during auditory story comprehension. *NeuroImage*, *47*(1), 360–366. https://doi.org/10.1016/j.neuroimage.2009.04.037

Whitney, C., Kirk, M., O'Sullivan, J., Lambon Ralph, M. A., & Jefferies, E. (2011). The neural organization of semantic control: TMS evidence for a distributed network in left inferior frontal and posterior middle temporal gyrus. *Cerebral Cortex (New York, N.Y. : 1991)*, *21*(5), 1066–1075. https://doi.org/10.1093/cercor/bhq180

Whitney, C., Kirk, M., O'Sullivan, J., Lambon Ralph, M. A., & Jefferies, E. (2012). Executive semantic processing is underpinned by a large-scale neural network: revealing the contribution of left prefrontal, posterior temporal, and parietal cortex to controlled retrieval and selection using TMS. *Journal of Cognitive Neuroscience*, *24*(1), 133–147. https://doi.org/10.1162/jocn_a_00123

Yang, C. L., Perfetti, C. A., & Liu, Y. (2010). Sentence integration processes: An ERP study of Chinese sentence comprehension with relative clauses. *Brain and Language*, *112*(2), 85–100. https://doi.org/10.1016/j.bandl.2009.10.005

Yovanoff, P., Duesbery, L., Alonzo, J., & Tindal, G. (2005). Grade-Level Invariance of a Theoretical Causal Structure Predicting Reading Comprehension With Vocabulary and Oral Reading Fluency. *Educational Measurement: Issues and Practice*, *24*(3), 4–12. https://doi.org/10.1111/j.1745-3992.2005.00014.x

Zhang, S., & Li, C. R. (2012). Functional connectivity mapping of the human precuneus by resting state fMRI. *NeuroImage*, *59*(4), 3548–3562.

https://doi.org/10.1016/j.neuroimage.2011.11.023