Improving Sentence Comprehension Post-Stroke Using Neuroimaging and Neuropsychological Approaches

by

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ABSTRACT

Cognitive deficits often accompany language impairments post-stroke. Past research has focused on working memory in aphasia, but attention is largely underexplored. Therefore, this dissertation will first quantify attention deficits post-stroke before investigating whether preserved cognitive abilities, including attention, can improve auditory sentence comprehension post-stroke. In Experiment 1a, three components of attention (alerting, orienting, executive control) were measured in persons with aphasia and matched-controls using visual and auditory versions of the well-studied Attention Network Test. Experiment 1b then explored the neural resources supporting each component of attention in the visual and auditory modalities in chronic stroke participants. The results from Experiment 1a indicate that alerting, orienting, and executive control are uniquely affected by presentation modality. The lesion-symptom mapping results from Experiment 1b associated the left angular gyrus with visual executive control, the left supramarginal gyrus with auditory alerting, and Broca's area (pars opercularis) with auditory orienting attention post-stroke. Overall, these findings indicate that perceptual modality may impact the lateralization of some aspects of attention, thus auditory attention may be more susceptible to impairment after a left hemisphere stroke.

Prosody, rhythm and pitch changes associated with spoken language may improve spoken language comprehension in persons with aphasia by recruiting intact cognitive abilities (e.g., attention and working memory) and their associated non-lesioned brain regions post-stroke. Therefore, Experiment 2 explored the relationship between cognition, two unique prosody manipulations, lesion location, and auditory sentence comprehension in persons with chronic stroke and matched-controls. The combined results from Experiment 2a and 2b indicate that stroke participants with better auditory orienting attention and a specific left fronto-parietal network intact had greater comprehension of sentences spoken with sentence prosody. For list prosody, participants with deficits in auditory executive control and/or short-term memory and the left angular gyrus and globus pallidus relatively intact, demonstrated better comprehension of sentences spoken with list prosody. Overall, the results from Experiment 2 indicate that following a left hemisphere stroke, individuals need good auditory attention and an intact left fronto-parietal network to benefit from typical sentence prosody, yet when cognitive deficits are present and this fronto-parietal network is damaged, list prosody may be more beneficial.

DEDICATION

To my computer, who has been there every step of the way.

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CHAPTER 1

INTRODUCTION

Aphasia is classically thought to be a language-specific disorder, yet, several studies also identify individuals with aphasia to have co-occurring cognitive impairments including impairments in attention, short-term memory, working memory, executive functions, and processing speed (Caplan, DeDe, Waters, Michaud, & Tripodis, 2011; Caplan, Michaud, & Hufford, 2013; Caplan & Waters, 2013; Fridriksson, Nettles, Davis, Morrow, & Montgomery, 2006; Mayer & Murray, 2012; Moser, Fridriksson, & Healy, 2007; Murray, 2012; Nicholas, Hunsaker, & Guarino, 2015; Villard & Kiran, 2017). Of the potential cognitive impairments, much emphasis has been placed on understanding the role of working memory in language deficits post-stroke. Replicating work in neurotypical adults (see Just & Carpenter, 1992; King & Just, 1991 for a review), these studies largely conclude that individuals with aphasia with deficits in working memory exhibit poorer language abilities than those with relatively good working memory abilities (Caplan et al., 2011, 2013; Caplan & Waters, 2013; Mayer & Murray, 2012).

Working memory is a complex process that includes the maintenance and manipulation of information. Working memory is also known to interact with other cognitive functions including attention. For example, one prominent model of working memory details a central executive component that is necessary for directing attention towards information contained within either the phonological loop or visuospatial sketchpad (i.e., the working memory components of the model) (Baddeley, 2003, 2010). This prominent model of working memory nicely highlights how attention is a more rudimentary ability underlying more complex processes such as working memory and language and further suggests that some of the deficits observed in working memory post-stroke may be related to attention. This necessitates the need to more clearly understand the nature of attention deficits in patients with aphasia and/or chronic stroke.

In terms of attention and aphasia, research is beginning to link attention deficits with language deficits post-stroke (Murray, 2012; Villard & Kiran, 2017). These studies largely conclude that individuals with aphasia who have poorer attention abilities demonstrate poorer language abilities than individuals with aphasia who have relatively preserved attention (Laures, 2005; Murray, 2012; Murray, Holland, & Beeson, 1997; Peach, Nathan, & Beck, 2017; Peach, Rubin, & Newhoff, 1994). Collectively, these studies clearly outline patients with aphasia to have attention deficits, yet attention is not a homogenous process.

Several models of attention exist which break attention into various subcomponents. One such prominent model includes dividing attention into three components: alerting, orienting, and executive control (Petersen & Posner, 2012; Posner & Petersen, 1990). Alerting attention is involved in the initial engagement of attentional resources and vigilance towards an external stimulus, orienting attention includes selecting specific information from a given stimulus, and executive control involves mitigating conflict when relevant and irrelevant information conflict within a stimulus (Petersen & Posner, 2012; Posner & Petersen, 1990). Subdividing attention into these smaller components, prompts the question: Do persons with aphasia and/or chronic stroke demonstrate equal deficits in all three aspects of attention?

The Attention Network Test (ANT) was developed with the goal of assessing alerting, orienting, and executive control using a single cued flanker task (Fan, McCandliss, Sommer, Raz, & Posner, 2002). The ANT has been found to reliably assess all three aspects of attention in both neurotypical adults and patient populations, including stroke (Chica et al., 2012; Fan et al., 2002; Fan & Posner, 2004; Ishigami & Klein, 2011; Roberts, Summerfield, & Hall, 2006; Spagna, Mackie, & Fan, 2015; Stewart & Amitay, 2015). One limitation of the traditional ANT test is that it solely assesses all three components of attention in the visual modality. A matched-version of the visual ANT has since been developed in the auditory modality (Roberts et al., 2006). Results from neurotypical adults completing the auditory ANT are mixed with one study identifying significant auditory alerting, orienting, and executive control effects (Roberts et al., 2006) and another just significant executive control effects (Stewart & Amitay, 2015). This suggests that auditory and visual attention are not necessarily equivalent and should be separately assessed in all perceptual modalities of interest. Assessing attention in all perceptual modalities of interest is particularly important in patients with aphasia and/or chronic stroke as stroke lesion patterns may differentially affect visual and auditory attention. Therefore, the first purpose of this dissertation is to quantify visual and auditory attention using matched-versions of the well-studied ANT in chronic stoke participants with and without aphasia and matched-controls. In Experiment 1a, alerting, orienting, and executive control will be assessed behaviorally in both the visual and auditory modalities. In Experiment 1b, the neural resources supporting visual and auditory attention will be explored using lesion-symptom mapping techniques.

A wealth of research has focused on characterizing language and cognitive deficits in patients with aphasia and/or chronic stroke, as well as how to treat these deficits. Much of the treatment research focuses on treating language production with fewer studies focusing on how to improve auditory comprehension in patients with aphasia (Adelt, Hanne, & Stadie, 2018). This is concerning since auditory comprehension abilities are the number one predictor of quality of life post-stroke (Charidimou et al., 2014; Elman & Bernstein-Ellis, 1995; Thompson & Mckeever, 2014). Therefore, the second purpose of this dissertation is to investigate methods to improve language comprehension post-stroke.

Clinicians use several methodologies to improve auditory comprehension in persons with aphasia. These methodologies include reducing speech rate and using simpler sentence structures while speaking. Prosody, rhythm and pitch changes associated with spoken language, has also been shown to improve spoken language comprehension in neurotypical adults and persons with aphasia. In neurotypical adults, regular sentence prosody improves sentence comprehension (i.e., faster and more accurate responses) compared to irregular prosodic patterns (Carlson, 2009; Kjelgaard & Speer, 1999; Roncaglia-Denissen, Schmidt-Kassow, & Kotz, 2013; Speer, Kjelgaard, & Dobroth, 1996). In persons with aphasia, exaggerated linguistic stress has been shown to improve auditory comprehension of sentences and paragraphs independent of speech rate (Lasky, Weider, & Johnson, 1976; Pashek & Brookshire, 1982). Collectively, this evidence indicates that prosody manipulations likely improve auditory comprehension post-stroke, yet the exact mechanisms driving this phenomenon are understudied.

Previous research indicates that prosody may improve comprehension by reducing demands placed on cognitive resources during sentence comprehension (Cohen, Douaire, & Elsabbagh, 2001; Kjelgaard & Speer, 1999; Roncaglia-Denissen et al., 2013; Speer et al., 1996). The relationship between cognition and prosody has largely been studied using syntactically ambiguous sentence structures. In syntactically ambiguous sentences, prosody manipulations have been found to bias the listener to one interpretation over another (Kjelgaard & Speer, 1999; Price, Ostendorf, & Fong, 1991; Speer et al., 1996), with prosody being particularly beneficial for syntactically complex sentence structures compared to syntactically simple sentence structures (Roncaglia-Denissen et al., 2013). This ability of prosody to bias interpretations of ambiguous sentences may also extend to other types of sentences, specifically complex non-canonical sentences (i.e., sentences with subject-object-verb word order), in which persons with aphasia have relatively specific comprehension deficits (Caramazza & Zurif, 1976). Therefore, in Experiment 2a the relationship between cognition, prosody, and comprehension of non-canonical sentence structures will be investigated in persons with chronic stroke with and without aphasia and matched-controls.

In addition to behaviorally improving auditory comprehension abilities, unique prosodic manipulations have also been shown to recruit distinct neural computations (den Ouden, Dickey, Anderson, & Christianson, 2016; Geiser, Zaehle, Jancke, & Meyer, 2008; Humphries, Love, Swinney, & Hickok, 2005; Meyer, Steinhauer, Alter, Friederici, & von Cramon, 2004). For example, typical sentence prosody has been shown to recruit left frontal and anterior temporal cortices while left posterior temporal and inferior parietal cortices respond to irregular prosodic patterns such as monotone prosody and/or list prosody (i.e., monotone prosody which lacks pitch inflections and meaningful prosodic boundaries) (den Ouden et al., 2016; Humphries et al., 2005; Meyer et al., 2004). This ability of different prosody manipulations to engage distinct neural computations may be particularly advantageous following stroke. More specifically, unique prosodic manipulations may be able to engage relatively intact brain regions post-stroke to improve auditory comprehension. Experiment 2b will therefore identify stroke lesion patterns associated with prosody manipulations that result in improved sentence comprehension for persons with aphasia and/or chronic stroke. Before discussing each experiment, I have included a review of the literature which details existing research related to these experiments.

CHAPTER 2

LITERATURE REVIEW

Sentence Comprehension

Sentence structure, or syntax, is essential for sentence comprehension as it provides information regarding the hierarchical grouping of individual words and phrases (Frazier & Rayner, 1990). For example, to successfully comprehend the following sentence *While Chris washed the dog played outside,* the listener needs to identify that there are two clauses, a main clause and a subordinate clause, and that the main verb of the subordinate clause (i.e., *played*) is intransitive (i.e., verbs that do not take direct objects) and reflexive (i.e., verbs in which the direct object is the same as the subject) to correctly identify the main clause (i.e. *While Chris washed*) and the subordinate clause (i.e., *the dog played outside*).

The above example also highlights the role of syntactic ambiguity in sentence processing. Sentence structures which are ambiguous (e.g., garden-path sentences) have increased processing demands (e.g., longer reading times) compared to unambiguous sentence structures as the location of the syntactic boundary is not initially clear (Frazier & Rayner, 1982). In the above example, the sentence structure is ambiguous as the word *dog* can function as the object of the main clause or the subject of the subordinate clause. The sentence remains ambiguous until the verb *played* is encountered, at which point the sentence's meaning is disambiguated and reanalysis occurs.

It is also well-established that comprehension performance is typically better when sentences have a canonical structure (e.g., subject-verb-object in English) compared to a non-canonical structure (e.g., subject-object-verb in English) (Caramazza

& Zurif, 1976; Ferreira, 2003; Gleason, Goodglass, Green, Ackerman, & Hyde, 1975; Goodglass & Berko, 1960; Kean, 1977, 1995; King & Just, 1991; Rogalsky et al., 2018; Roncaglia-Denissen et al., 2013; Wilson et al., 2010; Wilson et al., 2014; Wilson et al., 2016). In general, simple sentence structures, including canonical, subject-first, and right-branching sentences, are easier to parse than their complex counterparts (i.e., non-canonical, object-first, center-embedded sentences). In control subjects, comprehension of canonical sentence structures is marked by decreased reaction times and increased accuracies compared to non-canonical structures (Ferreira, 2003; King & Just, 1991; Wilson et al., 2010). Similarly, patients with aphasia, including Broca's aphasia and conduction aphasia, demonstrate declines in accuracy for non-canonical sentence structures compared to canonical structures (Bradley, Garrett, & Zurif, 1980; Caramazza & Zurif, 1976). These differences in accuracy as well as reaction time between canonical and non-canonical structures likely reflects an increase in processing load associated with complex sentence structures (Caplan, Alpert, Waters, & Olivieri, 2000; Caplan & Waters, 1999; Gibson, 1998). This relationship between cognitive resources and sentence comprehension will be discussed below in the "Cognitive Resources Supporting Sentence Comprehension" section.

Neurobiology of Sentence Comprehension

Language is primarily supported by a left lateralized fronto-temporo-parietal network (Friederici, 2012; Hickok & Poeppel, 2007). Prominent models of speech processing, including Hickok and Poeppel's (2007) dorsal-ventral model, characterize two pathways supporting language within this network. The first pathway, the dorsal stream, is left lateralized and involved in auditory-motor integration and speech production. The second pathway, the ventral stream is more bilaterally organized and maps sound to meaning, thereby facilitating speech comprehension. Within the dorsal stream, speech information moves from primary auditory cortex to the temporal-parietal junction to the frontal cortex (premotor, anterior insula, and inferior frontal gyrus). Information flow within the ventral stream is bilateral and begins in primary auditory cortex before simultaneously moving to the temporal-parietal junction and to middle and inferior temporal gyri; speech information additionally moves back and forth between the temporal-parietal junction and primary auditory cortex and the temporal-parietal junction and middle and inferior temporal gyri. It also is noteworthy that, within the left hemisphere, speech information additionally moves between the left inferior temporal gyrus and left anterior temporal lobe (Hickok & Poeppel, 2007).

Evidence used to develop the dorsal-ventral model of speech processing largely stems from the functional neuroimaging and lesion literatures. Functional neuroimaging studies of language comprehension, particularly fMRI studies, either identify language to be supported by a left lateralized fronto-temporo-parietal network (Ben-Shachar, Hendler, Kahn, Ben-Bashat, & Grodzinsky, 2003; Ben-Shachar, Palti, & Grodzinsky, 2004; Blank, Balewski, Mahowald, & Fedorenko, 2016; Constable et al., 2004; Goucha & Friederici, 2015; Obleser, Meyer, & Friederici, 2011; Price, 2012; Santi & Grodzinsky, 2007) or solely left temporal and parietal cortices (Brennan et al., 2012; Brennan, Stabler, Van Wagenen, Luh, & Hale, 2016; Crinion, Lambon-Ralph, Warburton, Howard, & Wise, 2003). While functional neuroimaging studies of language provide great insights into the neurobiology of language, they are limited in that they can solely identify brain regions involved in language. Alternatively, lesion studies in both chronic and acute stroke patients can tell us which brain regions are critical to language comprehension.[1] Crucially, results from lesion-symptom mapping studies consistently identify the left temporal and parietal cortices to be critical to language comprehension (Dronkers, Wilkins, Van Valin, Redfern, & Jaeger, 2004; Magnusdottir et al., 2013; Pillay, Binder, Humphries, Gross, & Book, 2017; Rogalsky et al., 2018; Thothathiri, Kimberg, & Schwartz, 2012) with the left anterior temporal and posterior temporal cortices gaining the most attention.

The left posterior superior temporal cortex and sentence comprehension. The left posterior superior temporal cortex has classically been associated with language comprehension deficits. This is because patients with damage to this brain region are thought to have Wernicke's aphasia, which is characterized by poor comprehension of even the simplest sentence structures (Goodglass, 1993). Recent large-scale lesion-symptom mapping studies have largely confirmed the association between Wernicke's area in the left posterior superior temporal and inferior parietal cortices and sentence comprehension deficits. For example, in 79 patients with chronic aphasia, Thothathiri et al. (2012) identified posterior temporal and inferior parietal regions to be associated with processing both canonical and non-canonical sentences. Rogalsky et al. (2018) found the same pattern in 66 patients with chronic stroke, but not necessarily aphasia. Furthermore, in patients with acute stroke, Magnusdottir et al. (2013) found similar findings: canonical sentence comprehension was supported by left posterior and inferior parietal regions

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[1] Lesion studies in chronic stroke patients can be confounded by functional reorganization and neural compensation, however, results from lesion studies in chronic stroke patients largely align with results in patients with acute stroke (e.g., Magnusdottir et al., 2013; Rogalsky et al., 2018; Pillay et al., 2017).

while non-canonical sentence comprehension was supported by the left anterior and inferior temporal cortices (plus the left inferior frontal gyrus).

This classic association of the left posterior superior temporal cortex and comprehension deficits is also supported by functional neuroimaging studies as bilateral temporal cortices reliably activate when contrasting auditory speech/language versus rest (Price, 2012). However, the exact role of the left posterior superior temporal cortex in language comprehension is not entirely clear from functional neuroimaging studies as this increase in activation could be attributed to phonological, semantic, and/or syntactic computations. For example, increased left posterior superior temporal gyrus activation is reliably observed for sentences compared to word lists, sentences containing an error compared to grammatically correct sentences, and complex sentences compared to simple sentence structures (Bornkessel-Schlesewsky & Schlesewsky, 2013; Friederici, 2011). Regarding semantics, the left posterior superior temporal gyrus demonstrates increased activation in response to semantically ambiguous sentences and sentences containing semantic errors (e.g., errors related to verb-argument agreement) compared to unambiguous sentences and sentences without semantic errors (Friederici, Rüschemeyer, Hahne, & Fiebach, 2003). In terms of phonological processing, pseudowords reliably activate the left posterior superior temporal gyrus, suggesting it may also play a role in phonological processing, separate from semantic and syntactic computations (Buchsbaum, Hickok, & Humphries, 2001; Graves, Grabowski, Mehta, & Gupta, 2008).

Lesion studies also provide mixed evidence regarding the role of the left posterior temporal cortex in language comprehension. For example, in a recent lesion-symptom mapping study, Hickok and colleagues (2018) identified the left posterior superior temporal cortex (plus left frontal and parietal regions) to be involved in processing the auditory syllable /pa/; supporting fMRI findings indicating the involvement of this region in phonological processing. In terms of semantics, Baldo, Schwartz, Wilkins, and Dronkers (2006) associated the left posterior temporal cortex with semantic-based word retrieval (i.e., performance on a category fluency task). Regarding sentence structure, Pillay et al. (2017) suggest a role for the left posterior superior temporal cortex in processing sentence structure as this region of the brain still contributed to sentence comprehension deficits even after controlling for some cognitive and language processes (e.g., semantics, phonological processes associated with a picture naming task). Collectively, functional neuroimaging and lesion-symptom mapping studies suggest that the left posterior superior temporal cortex has a multifaceted contribution to language comprehension.

The left anterior temporal lobe and sentence comprehension. The left anterior temporal lobe has also been implicated in language comprehension, yet similar to the left posterior superior temporal cortex, its exact involvement in somewhat unclear. Numerous neuroimaging studies, including lesion studies, largely associate the left anterior temporal lobe with comprehending sentence structures, particularly complex sentence structures (Dronkers et al., 2004; Magnusdottir et al., 2013) and many functional neuroimaging studies confirm these findings by showing that the left anterior temporal lobe consistently activates more in response to sentences compared to word lists (Friederici, Meyer, & von Cramon, 2000; Humphries, Binder, Medler, & Liebenthal, 2006; Humphries et al., 2005; Mazoyer, Tzourio, Frak, & Syrota, 1993) and pseudosentences compared to pseudoword lists and scrambled pseudoword sentences (Friederici et al., 2000; Humphries et al., 2006, 2005; Rogalsky, Rong, Saberi, & Hickok, 2011). Error detection paradigms also tie the left anterior temporal lobe to processing sentence structure. In a study looking at event-related potentials, Friederici and colleagues (2003) demonstrated syntactic anomalies to elicit an early left anterior negativity, which has been previously associated with the left anterior temporal and left inferior frontal gyrus (Friederici & Kotz, 2003). Similarly, fMRI studies demonstrate increased activation in response to sentences containing syntactic violations (Friederici et al., 2003; Meyer, Friederici, & von Cramon, 2000). Collectively, these findings suggest that at least a portion of the left anterior temporal lobe responds selectively to sentence structure.

It has also been hypothesized that the role of the left anterior temporal lobe in language comprehension may be due to combinatorial semantics, i.e., the process of combining semantic and syntactic information to deduce the meaning of a sentence. For example, in addition to identifying a sub-region of the left anterior temporal lobe which preferentially responded to sentence structure, Vandenberghe, Nobre, and Price (2002) also found a second, separate sub-region within the left anterior temporal lobe which responded more for semantically coherent sentences compared to their scrambled versions but not for semantically incoherent sentences compared to their scrambled versions. Humphries and colleagues (2006) found similar results, although their sub-regions differed from Vandenberghe et al. (2002): semantically congruent sentences resulted in greater activation compared to sentences with random semantic content and/or pseudoword sentences in one sub-region of the left anterior temporal lobe; importantly, this sub-region differed from the sub-region they showed to support syntactic processing. Vandenberghe et al. (2002) and Humphries et al. (2006) both suggest that this preferential response of distinct sub-regions of the left anterior temporal lobe to sentence structures with meaningful semantic content suggests that the left anterior temporal lobe also supports sentence/language comprehension by combining semantic and syntactic information (Vandenberghe et al., 2002).

Broca’s area and sentence comprehension. Another region within the dorsal-ventral model of speech processing that has gained considerable attention for its role in sentence comprehension is Broca’s area (defined as the posterior two-thirds of the left inferior frontal gyrus; pars opercularis and triangularis). The classic agrammatic pattern associated with Broca’s aphasia was first attributed to sentence production, however, more recent evidence identifies persons with Broca’s aphasia to also demonstrate agrammatic comprehension, i.e., greater comprehension of sentences with canonical compared to non-canonical word order (Bradley et al., 1980; Caramazza & Zurif, 1976; Rogalsky et al., 2018). This distinctive characteristic of Broca’s aphasia, and to a lesser extent conduction aphasia, is particularly pronounced when sentences are semantically reversible and have a complex sentence structure as meaning can only be deduced from the syntactic information (Bradley et al., 1980; Caramazza & Zurif, 1976). These classic results demonstrating agrammatic comprehension to be associated with lesions to Broca’s area has led to the view that Broca’s area contributes to language comprehension due to language-specific computations. However, we now know that focal lesions to Broca’s area do not result in classic Broca’s aphasia (Dronkers, Shapiro, Redfern, & Knight, 1992) and that damage to Broca’s area is not necessary for Broca’s aphasia (Fridriksson, Bonilha, & Rorden, 2007; Mohr et al., 1978). Furthermore, individuals with Broca’s aphasia have relatively preserved abilities in making grammaticality judgments, suggesting some level of preserved syntactic knowledge (Linebarger, Schwartz, & Saffran, 1983; Wulfeck, 1988) and an alternative role for Broca's area in sentence processing.

As previously outlined, functional neuroimaging studies of language provide mixed results regarding the exact role of given brain regions in sentence comprehension and no region has produced more seemingly discrepant results than Broca's area. For example, some fMRI studies identify a left lateralized fronto-temporo-parietal network to support sentence comprehension (Ben-Shachar et al., 2003, 2004; Blank et al., 2016; Constable et al., 2004; Goucha & Friederici, 2015; Obleser et al., 2011; Santi & Grodzinsky, 2007) while others solely identify left temporal and parietal cortices (Brennan et al., 2012; Brennan et al., 2016; Crinion et al., 2003). This discrepancy regarding the involvement of the left frontal cortex in sentence comprehension may at least partially stem from task demands. For example, studies which identify the left frontal cortex to support language comprehension largely employ active tasks (i.e., tasks such as comprehension probes, which require participants to make a response) (Ben-Shachar et al., 2003, 2004; Blank et al., 2016; Buchsbaum et al., 2001; Constable et al., 2004; Goucha & Friederici, 2015; Obleser et al., 2011; Santi & Grodzinsky, 2007; Uchiyama et al., 2008) while studies using passive listening paradigms (i.e., participants listen to the speech stimulus as naturally as possible) identify just left temporal and parietal regions to be involved in language comprehension (Brennan et al., 2012; Brennan et al., 2016; Crinion et al., 2003). Furthermore, the use of active tasks is known to confound neuroimaging results in the frontal cortex (Hasson, Nusbaum, & Small, 2006). Therefore, this discrepancy within the functional neuroimaging literature may be explained by the fact that active tasks recruit additional cognitive resources that are not necessarily critical to comprehending language, but are critical to completing the associated task (e.g., comprehension probe, n-back, grammaticality judgment).

As previously mentioned, functional neuroimaging studies of language provide great insights into the neurobiology of language but are limited in that they can solely identify brain regions involved in sentence comprehension. Alternatively, lesion studies in both chronic and acute stroke patients can tell us which brain regions are critical. Notably, results from lesion-symptom mapping studies largely align with the research from functional neuroimaging studies which do not use any tasks in that they consistently identify the left temporal and parietal cortices to be critical to language comprehension (Dronkers et al., 2004; Magnusdottir et al., 2013; Pillay et al., 2017; Rogalsky et al., 2018; Thothathiri et al., 2012).

Importantly, lesion-symptom mapping studies do identify the left frontal cortex as being involved in language comprehension, however, they identify its involvement to be due to cognitive resources. For example, Rogalsky et al. (2018) recently associated response bias with the left frontal cortex, specifically Broca's area. Response bias has previously been associated with cognitive deficits (Venezia, Saberi, Chubb, & Hickock, 2012) likely because inhibiting the preferred response draws on cognitive resources including executive functions (Friedman & Miyake, 2017; Miyake et al., 2000). An example of response bias in Rogalsky et al.'s (2018) plausibility judgment task is a patient primarily saying all sentences are plausible, even when the sentence is implausible. This inability to inhibit a preferred response in favor of the correct, non-preferred response suggests these patients likely have underlying deficits in executive functions. These results additionally align with the subset of functional neuroimaging studies which do not use active tasks; collectively linking Broca's area with domain-general cognitive resources recruited during sentence comprehension to support task demands.

To better understand the role of domain-general cognitive processes in sentence comprehension, Thothathiri et al. (2012) contrasted one-proposition (i.e., active and passive) and two-proposition (i.e., subject-relative and object-relative) sentences. Importantly, their sentence constructions did not require participants to process the second proposition in the two-proposition sentences in order to successfully comprehend the sentences during a sentence-picture matching task. Therefore, they propose that regions involved in processing two-proposition but not one-proposition sentences should be cognitive in nature as the longer duration of the two-proposition sentences will require them to be maintained in memory for a longer period of time. Their results indicate that damage to Broca's area was associated with two-proposition but not one-proposition sentence comprehension suggesting that Broca's area is not being recruited due to the more complex construction of the sentence, but instead because of additional domain-general task demands such as maintaining the sentence in memory until the pictures appear or comparing the results of the picture analysis with a stored representation of the sentence; Waters, Rochon, and Caplan (1998) have previously linked processing two-proposition sentences with working memory resources. These results further link the recruitment of Broca's area in language comprehension to domain-general cognitive processes and once again nicely align with the functional neuroimaging literature which do not use active tasks.

Controversy over the role of Broca's area and adjacent regions in sentence comprehension largely stems from functional neuroimaging studies which contrast sentences with canonical and non-canonical structures. In these studies, canonical sentences largely activate left temporal and parietal cortices while non-canonical sentence constructions additionally activate Broca's area in the left inferior frontal gyrus (Ben-Shachar et al., 2003, 2004; Blank et al., 2016; Constable et al., 2004; Goucha & Friederici, 2015; Obleser et al., 2011; Santi & Grodzinsky, 2010). This relatively specific activation of Broca's area for non-canonical sentences is often interpreted to mean that Broca's area is involved in sentence comprehension via language-specific computations (e.g., linguistic-specific computations which are needed for thematic role assignment). However, this interpretation is not without fault. Not only does evidence from lesion studies not support the idea that Broca's area's role in sentence comprehension is language-specific, but behavioral studies also suggest that Broca's area supports sentence comprehension as a function of domain-general cognitive processes. In general, behavioral studies which compare canonical and non-canonical sentence processing find shorter response times and greater accuracy for canonical sentences in both neurotypical adults and patients with aphasia (Fiebach, Schlesewsky, Lohmann, von Cramon, & Friederici, 2005; Kinno, Kawamura, Shioda, & Sakai, 2008; Rogalsky, Matchin, & Hickock, 2008; Wilson et al., 2010; Wilson et al., 2014). Notably, these processing differences may be accounted for by individual differences in cognitive capacity. For example, studies comparing individuals with low and high working memory capacity show individuals with higher working memory capacities to have greater comprehension of complex sentence structures (e.g., object-relative) compared to individuals with low working memory capacities, however, no comprehension differences exist for relatively simple sentence structures (e.g., subject-relative) (King & Just, 1991). These results suggest that extra cognitive resources are required to successfully comprehend complex sentence structures and these extra cognitive resources may further explain the activation differences between simple and complex sentences observed in Broca's area during functional neuroimaging.

To better understand the relationship between cognition and sentence comprehension within Broca's area, January, Trueswell, and Thompson-Schill (2009) compared syntactic (sentence comprehension task with syntactically ambiguous sentences) and non-syntactic (Stroop task) conflict during fMRI. Their results indicate a domain-general conflict resolution mechanism to subserve both syntactic and non-syntactic conflict resolution as the same pattern of conflict resolution was observed for both the Stroop and sentence comprehension tasks within the Stroop and sentence comprehension region of interests (both of which were within Broca's area). For example, for the Stroop task, participants demonstrated the greatest activation for incongruent trials and the least activation for neutral trials in both the Stroop and sentence comprehension regions of interest. For the sentence comprehension task, sentences with high syntactic ambiguity had the greatest levels of activation while sentences with low syntactic ambiguity elicited the least amount of activation within both the sentence comprehension and Stroop regions of interest (January et al., 2009). These findings, in conjunction with results from lesion studies indicate that the role of the left frontal cortex, specifically Broca's area in sentence comprehension is secondary to cognitive processes such as working memory, attention, and executive functions, and therefore the increased activation in response to non-canonical sentences is likely due to the recruitment of additional cognitive resources needed to parse the sentence (e.g., mentally manipulating the sentence to assign thematic roles). This interpretation also explains the discrepancy between functional neuroimaging results and lesion-symptom mapping results which demonstrate left temporal and parietal cortices to be critical to sentence comprehension, while the left inferior frontal gyrus supports sentence comprehension via cognitive resources which support task demands.

Cognitive Resources Supporting Sentence Comprehension

Cognitive abilities play an important role in sentence comprehension and are believed to be particularly important for comprehension of complex sentence structures. In a study comparing individuals with low and high working memory capacity, King and Just (1991) demonstrated that individuals with lower working memory capacities had longer reading times and lower accuracies for complex object-relative sentences; no comprehension differences between the groups were observed for the simpler subject-relative sentences. Furthermore, individuals with high working memory capacities demonstrated reduced sentence comprehension when asked to simultaneously complete a working memory task (King & Just, 1991). These results indicate that a reduction in the cognitive resources available for comprehending language results in an overall decrease in comprehension.

In addition to comparing individuals with high and low cognitive capacities, another population of interest is older adults as approximately three-quarters of all strokes occur in adults over the age of 65 (Centers for Disease Control and Prevention, 2017); therefore, it is important to understand cognitive changes associated with the normal aging process. Cognitive capacity, including working memory, attention, and other executive functions are known to decrease due to the normal aging process. In older adults, more basic aspects of attention such as orienting attention (i.e., the ability to select specific information from a given stimulus) appear to be stable across the lifespan (Zhou, Fan, Lee, Wang, & Wang, 2011). However, more complex aspects of attention, including selective attention, i.e., the ability to attend to a target stimulus while disregarding irrelevant/distracting stimuli, appear to decline with advancing age (Geerligs, Saliasi, Maurits, Renken, & Lorist, 2014; Glisky, 2007). For example, on selective attention tasks such as the Stroop color word task, older adults are slower to respond (Glisky, 2007) and have greater difficulty suppressing irrelevant information on incongruent trials when compared to younger adults (Geerligs et al., 2014; Zhou et al., 2011). Older adults also demonstrate deficits in divided attention: the ability to process more than one set of stimuli or perform more than one task at the same time. Under dual task conditions, older adults perform more slowly and have decreased accuracy compared to younger adults and compared to older adults performing each task in isolation; these differences are exacerbated as task demands increase (Glisky, 2007).

Older adults also demonstrate declines in working memory as part of the normal aging process (Park et al., 2002). Of the two components of working memory, maintenance and manipulation of information, older adults are believed to have specific deficits in the manipulation of information and not maintenance of information. For example, age did not predict performance on simple span tasks such as forward and backward digit span, which are primarily maintenance tasks, however, age was a significant predictor of performance on n-back tasks (Dobbs & Rule, 1989), letter rotation, line span, computation span, and reading span tasks, which all require maintenance plus manipulation of information (Park et al., 2002). Given the relatively preserved nature of short-term memory in older adults (as measured by simple span tasks), it is largely believed that older adults demonstrate deficits in the manipulation of information and not maintenance of information.

Older adults also demonstrate deficits in elements of executive functions including inhibition. Deficits in inhibition are postulated to underlie the deficits observed in working memory (Hasher, Rose, & May, 1999) and attention (Geerlings et al., 2014). For example, Hasher and colleagues (1999) suggest that older adults demonstrate deficits in working memory because they have difficulty suppressing irrelevant stimuli, which may build up in working memory trial after trial. The same occurs for attention: on incongruent trials in the Stroop color word task, older adults are unable to inhibit reading the word while focusing on saying the color of the ink the word is printed in (Geerlings et al., 2014). Since older adults demonstrate deficits in updating, they are unable to remove the irrelevant information resulting in a reduced capacity for target stimuli.

Processing speed, i.e., how efficiently a person can process information, is also susceptible to the normal aging process (Salthouse, 1996). For example, in digit symbol coding task, participants match a series of symbols to a corresponding number. This is a timed task and the number of digits and symbols that a person can match is a measure of their processing speed (i.e., more matches indicates greater processing speed). Overall, older adults perform more slowly and less accurately on tests of processing speed compared to younger adults suggesting that processing speed is vulnerable to age-related declines associated with the normal aging process. Importantly, Salthouse (1996) postulates that deficits in processing speed underlie all the cognitive deficits associated with aging.

These declines in cognitive abilities observed in older adults likely stem from structural and functional changes that occur in the brain as people age. For example, the fronto-parietal network has been associated with attention (Dosenbach et al., 2007; Power et al., 2011; Yeo et al., 2011). More specifically, the fronto-parietal network is activated when tasks require cognitive control and goal-directed cognition, both of which rely heavily on attention (Dosenbach et al., 2007; Geerligs et al., 2014). With advancing age, the fronto-parietal network demonstrates decreased within network connectivity and increased between network connectivity, indicating declines in efficiency as a result of increasing age (Geerlings et al., 2014). Therefore, the vulnerability of the fronto-parietal network likely underlies selective and divided attention deficits in older adults as declines in the neural resources result in declines in behavioral performance.

Working memory is believed to be supported by regions in the frontal and parietal lobes, including prefrontal cortex (Cappell, Gmeindl, & Reuter-Lorenz, 2010). Grey and white matter volume within the frontal cortices are known to decrease as a function of increasing age (Head et al., 2004; Raz, Rodrigue, Head, Kennedy, & Acker, 2004). Furthermore, functional patterns of activation differ between older adults with high and low working memory capacities and also younger adults. For example, high performing older adults demonstrate a more bilateral pattern of activation in prefrontal cortex compared to low performing older adults and young adults (Cappell et al., 2010; Reuter-Lorenz & Park, 2010). This over activation observed in high performing older adults suggests that high performing older adults maintain task performance by demonstrating cognitive flexibility and recruiting additional neural resources. Comparatively, low performing older adults demonstrate a pattern of activation on par with younger adults (i.e., left prefrontal cortex activation), however, their working memory behavioral performance is significantly worse. These distinct patterns of activation provide evidence for neural decline in prefrontal cortices underlying deficits in working memory as when older adults do not recruit additional resources their behavioral performance is significantly worse than younger adults, likely due to structural changes in prefrontal cortex such as decreased grey and white matter volume (Martins, Joanette, & Monchi, 2015).

In summary, neuroimaging and neuropsychological measures suggest a relationship between brain and behavior as vulnerability in one generally corresponds with vulnerabilities in the other. Notably, this relationship can be disrupted when older adults demonstrate the ability to recruit additional neural resources, which prevent declines in behavioral performance, thus making the associated cognitive function resilient to age-related declines.

Cognition and Language in Aphasia

Aphasia is classically thought of as a language specific disorder; however, more and more evidence suggests persons with aphasia demonstrate additional deficits in cognition and that these deficits in cognition may at least partially account for some of the deficits observed in terms of communication abilities. Over the last ten years, the link between cognition and language has become clearer with several studies demonstrating associations between behavioral measures of cognition (Caplan et al., 2013; Fridriksson et al., 2006; Murray, 2012; Murray et al., 1997; Villard & Kiran, 2017), brain activation

(Brownsett et al., 2014), functional connectivity (Geranmayeh, Brownsett, & Wise, 2014; Geranmayeh & Wise, 2015; Saur et al., 2006), and structural integrity (Gläscher et al., 2009; Leff et al., 2008) with communication abilities in aphasia.

Several studies have demonstrated a relationship between behavioral measures of cognition and overall communication abilities. Fridriksson and colleagues (2006) investigated the relationship between executive functioning skills and functional communication abilities in 25 persons with aphasia. Functional communication abilities were assessed using the ASHA FACS, a measure of an individual's ability to use any modality to produce and comprehend communication. The *Color Trails Test* was used to assess executive functioning abilities including sequencing, inhibition, planning, cognitive flexibility, working memory, sustained attention, and perceptual tracking. Executive functioning was also assessed using the *Wisconsin Card Sorting Task*, which measures abstract reasoning ability, cognitive set shifting abilities, and working memory. Results indicate that performance on the *Color Trails Test* significantly correlated with functional communication abilities in that participants who made more errors and required more prompts to complete the *Color Trails Test* demonstrated poorer functional communication abilities. The relationship between executive functions as measured by the *Wisconsin Card Sorting Task* and functional communication abilities largely confirmed the previous results, suggesting greater executive functioning abilities correspond with greater functional communication abilities.

Like Fridriksson et al. (2006), Murray and colleagues (1997, 2012) have identified a similar relationship between attention and communication abilities. Murray et al. (1997) investigated the relationship between attention and auditory processing of single words in 16 persons with aphasia and eight controls. All participants completed semantic and lexical judgment tasks in isolation and under dual task conditions (designed to tap focused and divided attention). Results indicate that persons with aphasia perform similarly to controls when tasks are completed in isolation, however, when tasks require focused and divided attention (i.e., dual task conditions), persons with aphasia perform more poorly than controls. These results indicate that deficits in attention correspond with deficits in auditory processing abilities. To extend these findings, Murray (2012) looked at the relationship between attention and more complex language abilities. Attention was assessed using the *Test of Everyday Attention* and language and communication abilities were measured using the *Aphasia Diagnostic Profiles* and *ASHA FACS*, respectively. Results indicate that performance on the *Test of Everyday Attention* significantly predicted language and communication abilities as measured by the *Aphasia Diagnostic Profiles* and *ASHA FACS*; persons with aphasia with more impaired attention abilities demonstrated more severe deficits in language and functional communication, suggesting language and communication deficits may partially stem from deficits in attention.

Memory has additionally been associated with speech comprehension abilities in aphasia. In 61 persons with aphasia, Caplan et al. (2013) assessed the relationship between short-term memory and working memory abilities with the ability to comprehend simple and complex sentence structures. Short-term memory was assessed using tasks that require immediate serial recall such as the forward digit span. Working memory was assessed using tasks that require maintenance plus manipulation of information such as the backward digit span. Regardless of the task employed, both short-term memory and working memory abilities significantly predicted sentence comprehension performance: persons with aphasia with greater short-term memory and working memory abilities demonstrated greater auditory sentence comprehension, indicating a relationship between working memory performance and auditory sentence comprehension in persons with aphasia. Collectively, these behavioral studies demonstrate cognitive deficits, including deficits in executive functioning skills, attention, short-term memory, and working memory, partially underlie the language and communication deficits associated with aphasia and further suggest that aphasia is not a language specific disorder.

Lesion-symptom mapping techniques nicely compliment results from behavioral studies of cognitive deficits and language/communication abilities in aphasia. For example, Leff et al. (2010) quantified language and cognitive abilities in 210 stroke patients. Language abilities were assessed using the *Comprehensive Aphasia Test* and cognitive abilities, i.e., short-term memory, were measured using the forward digit span. The results identified a common neural substrate, the left posterior superior temporal gyrus to subserve both language comprehension and auditory short-term memory. Furthermore, the structural integrity of the left posterior superior temporal gyrus predicted both auditory short-term memory capacity and auditory sentence comprehension: patients with greater grey matter density in left posterior superior temporal gyrus performed better on the forward digit span and on a measure of auditory sentence comprehension. These findings identify a shared neural substrate for auditory short-term memory and sentence comprehension and further confirm the notion that cognitive deficits at least partially subserve language deficits in aphasia.

Using similar methodologies, Gläscher and colleagues (2009) identified a similar structure-function relationship between cognition and language abilities post-stroke. Gläscher et al. (2009) tested 241 stroke patients on the *Wechsler Adult Intelligence Scale-III*. Lesion-deficit maps overlapped for the working memory and vocabulary indices in left anterior frontal cortices (including Broca's area), left posterior temporal cortex, and left parietal cortex. Importantly, patients with lesions to these areas performed worse on each index, while patients with lesions sparing these regions demonstrated higher performance on each index. These results identify common neural substrates supporting working memory and vocabulary and further implicate deficits in cognitive resources to at least partially contribute to the language deficits observed in aphasia.

Functional connectivity analyses of functional MRI data further support the notion that deficits in cognitive processes partially underlie deficits in language abilities in aphasia. The cingulo-opercular network is one network believed to support cognitive skills such as maintaining task goals. Nodes within the cingulo-opercular network include the dorsal anterior cingulate cortex and the adjacent medial superior frontal gyrus, bilateral anterior insula, and bilateral inferior frontal gyrus (Geranmayeh et al., 2014). In a study of 16 chronic stroke patients, Brownsett and colleagues (2014) investigated the relationship between the cingulo-opercular network and communication abilities. Prior to scanning participants completed a picture description task. During scanning, participants listened and repeated sentences. Region of interest analyses using two nodes within the cingulo-opercular network, the dorsal anterior cingulate cortex and superior frontal gyrus, revealed that activation of the dorsal anterior cingulate cortex and superior frontal gyrus significantly predicted picture description scores: patients with greater activation had more complex picture descriptions. Collectively, these results suggest that preserved functional connectivity of cognitive networks results in greater communication abilities post-stroke and further suggests that deficits in language secondary to aphasia may at least partially stem from cognitive deficits.

A study of language recovery provides further support for the relationship between the cingulo-opercular network and communicative abilities. Saur et al. (2006) scanned patients at three time points: a few days post-stroke, two weeks post-stroke, and one year post-stroke. The primary task of interest was patient's abilities to detect semantic violations within auditory sentences. Results indicated that in the acute stage, language scores significantly correlated with activation in bilateral inferior frontal gyri and anterior insula. However, by the second scan, language scores correlated with activation of nodes within the cingulo-opercular network. These results indicate an initial reliance on language networks to support language functions immediately post-stroke, however, as recovery occurs, there is a shift towards regions involved in more domain-general cognitive processes supporting language abilities. Furthermore, the results from Saur et al. (2006) in the subacute phase largely support the findings of Brownsett et al. (2014) and Geranmayeh and Wise (2015) in chronic stroke patients.

The fronto-parietal network is a second cognitive network which has also been shown to support language functions. The fronto-parietal network is thought to support language via adaptive control (i.e., the ability to adjust control moment to moment) and includes bilateral dorsolateral prefrontal cortex, inferior parietal lobule, precuneus, and middle cingulate cortex (Dosenbach et al., 2007; Power et al., 2011; Yeo et al., 2011). In a study of 13 patients with aphasia, Zhu et al. (2014) investigated the relationship between the left fronto-parietal network and language comprehension one-month and two-months post-stroke. Their results indicate stronger within network functional connectivity of the left fronto-parietal network to be associated with greater language comprehension abilities in persons with aphasia (Zhu et al., 2014). Furthermore, their results associate increases in within network connectivity of the left fronto-parietal network with recovery of language comprehension abilities (Zhu et al., 2014). Collectively, these resting-state and task-based fMRI studies link the presence of intact cognitive networks with greater language functioning in aphasia, suggesting language deficits in aphasia may not be language specific and instead may stem from cognitive deficits as well.

Prosody and Sentence Comprehension

In addition to sentence structure and cognitive abilities, prosody (i.e., rhythm and pitch changes associated with spoken language) also affects how we comprehend sentences. Behavioral studies of prosody demonstrate that regular prosodic patterns facilitate sentence comprehension compared to irregular patterns in neurotypical adults (Carlson, 2009; Carlson, Frazier, & Clifton, 2009; Kjelgaard & Speer, 1999; Roncaglia-Denissen et al., 2013; Speer et al., 1996). This may be because prosodic cues, including pitch inflections and prosodic boundaries perceptually divide sentences into smaller phrases and focus listener attention to critical time points within a sentence. Additionally, the strategic placement of prosodic boundaries can influence the less preferred meaning of syntactically ambiguous sentence structures (Beach, 1991; Kjelgaard & Speer, 1999; Speer et al., 1996). For example, participants demonstrate faster response times for the less preferred meaning of the sentence *Whenever the guard checks the door it's/is locked* (i.e., *Whenever the guard checks, the door is locked)* when a prosodic boundary is placed after *checks* as they do not need to reanalyze the sentence when the disambiguating word *is* is encountered. Without the prosodic boundary after *checks* participants will favor the preferred meaning of the sentence *Whenever the guard checks the door, it's locked* as this meaning does not require reanalysis at the point of disambiguation.

Prosody may facilitate sentence comprehension by reducing cognitive demands associated with sentence processing (Cohen et al., 2001; Kjelgaard & Speer, 1999; Speer et al., 1996; Roncaglia-Denissen et al., 2013). For example, prosody may serve as a placeholder in working memory while other linguistic analyses (i.e., syntactic and semantic) occur (Schafer, 1997). Once linguistic analyses are complete, the information is reintegrated into working memory and the presence of a prior mental representation of prosodic cues facilitates comprehension (Cohen et al., 2001; Frazier et al., 2006; Kjelgaard & Speer, 1999; Speer et al, 1996). This interaction between prosody and cognition may be particularly important for complex sentences, such as the syntactically ambiguous sentence discussed in the preceding paragraph, as the strategic placement of pitch inflections and prosodic boundaries may help listeners to parse the sentence correctly on the first pass, preventing the need for reanalysis which draws heavily on cognitive resources (Caplan & Waters, 1999).

In a recent study, Roncaglia-Denissen and colleagues (2013) compared simple (i.e., subject-first) and complex (i.e., object-first) sentences spoken with regular and irregular speech rhythms. The regular rhythm condition consisted of one stressed syllable followed by three unstressed syllables; note, the rhythm was metrically regular, but is not considered normal sentence prosody. Sentences with irregular rhythm were created by replacing proper and common nouns in the regular rhythm sentences with proper and common nouns which differed in terms of lexical stress and number of syllables (e.g., replacing the proper noun Antonio with Nicole). Their behavioral results demonstrate that the addition of irregular speech rhythms decreases comprehension of both syntactically ambiguous subject-first and object-first sentences (Roncaglia-Denissen et al., 2013). While the rhythmic manipulation did not interact with sentence structure behaviorally (as measured by reaction time; the interaction statistics were not reported for accuracy), simultaneous electrophysiological recordings identified an interaction driven by a decreased P600 mean amplitude for rhythmically regular object-first sentences compared to their irregular counterparts, but no differences in amplitude between rhythmically regular and irregular subject-first sentences (Roncaglia-Denissen et al., 2013). These findings suggest that irregular rhythms are costly to language comprehension as they require increased processing time, however, they do not inhibit comprehension as a successful parse is eventually achieved.

Prosody not only impacts behavioral measures of sentence comprehension, but also the neural computations supporting sentence comprehension. For example, the closure positive shift is an event related potential sensitive to prosodic information and demonstrates a right hemisphere bias for prosodic information as well as larger event related potentials in response to irregular rhythms compared to regular rhythms (Honbolygó, Török, Bánréti, Hunyadi, & Csépe, 2016). While prosody is classically associated with the right hemisphere (Friederici & Alter, 2004; Gandour et al., 2004; Ross, 1981; Sammler, Kotz, Eckstein, Ott, & Friederici, 2010; Wildgruber et al., 2004; Wildgruber, Ethofer, Grandjean, & Kreifelts, 2009), different functions of prosody appear to be differentially lateralized (Kristensen, Wang, Petersson, & Hagoort, 2013). For example, fMRI indicates affective or emotional prosody to be more right lateralized while linguistic prosody (e.g., prosody which determines the form of an utterance) is more left lateralized (Belyk & Brown, 2014; Wildgruber et al., 2004). These findings align with the asymmetric sampling in time hypothesis, which proposes left hemisphere dominance for short temporal information (e.g., phonemes, syllables, pitch inflections, prosodic boundaries) and right hemisphere dominance for longer temporal segments (e.g., sentence level prosody) (Poeppel, 2003). Furthermore, this specialization of each hemisphere for particular temporal durations may be advantageous for patients with brain damage, including aphasia, as manipulating the temporal structure of a sentence may alter the brain regions recruited during sentence processing.

Functional neuroimaging studies provide some insight into the response of specific brain regions to different prosodic patterns. In general, acoustically rich sentences activate bilateral temporal and parietal regions, with greater activity in the right hemisphere when compared to sentences with less spectral detail (Lee, Min, Wingfield, Grossman, & Peelle, 2016). Within this bilateral temporal-parietal network, specific brain regions have been identified to preferentially respond to specific prosodic patterns. For example, Humphries et al. (2005) identified list prosody (i.e., monotone prosody lacking pitch inflections and prosodic boundaries) to activate the left posterior superior temporal gyrus while typical sentence prosody activated the left anterior temporal lobe. Meyer et al. (2004) found flattened speech to activate bilateral posterior superior temporal gyri and inferior parietal lobe, left middle frontal gyrus, left superior parietal lobe, and right inferior frontal gyrus. A direct comparison of typical sentence prosody and monotone prosody in neurotypical adults revealed increased activation of the left superior frontal cortex, left anterior temporal lobe, left insula, left Heschl's gyrus, and bilateral anterior cingulate cortex for sentence prosody compared to monotone prosody (den Ouden et al., 2016). These studies largely highlight the following pattern in neurotypical adults: left frontal and anterior temporal cortices respond preferentially to typical prosodic cues while left posterior temporal and inferior parietal cortices respond to irregular prosodic patterns such as monotone prosody and list prosody. Collectively, these results suggest that the brain networks involved in sentence processing may be modulated to some extent by prosody.

Prosody and Aphasia

Pitch inflections may facilitate sentence comprehension by providing cues about new or contrasting information (Dahan, 2015; Dahan, Tanenhaus, & Chambers, 2002; Ito & Speer, 2008; Weber, Braun, & Crocker, 2006). Failure to perceive these pitch inflections may lead to comprehension deficits. For example, individuals with left hemisphere lesions demonstrate decreased sensitivity to prosodic cues such as rising pitch contours differentiating a question from a statement (Heilman, Bowers, Speedie, & Coslett, 1984; Pell & Baum, 1997; Perkins, Baran, & Gandour, 1996). This decreased sensitivity to prosodic cues suggests communication impairments associated with left hemisphere lesions (which are traditionally associated with deficits in sentence comprehension, particularly for non-canonical sentences) may actually stem from a combination of deficits in processing prosody and non-canonical sentence structures, as prosodic cues may fail to initially guide the listener to a correct interpretation. Given this finding, prosodic cues, including pitch inflections and prosodic boundaries, may be particularly important during sentence comprehension for individuals with reduced cognitive capacities as their ability to maintain the representation of a sentence in working memory is diminished (Caplan & Waters, 1999; Haarmann, Just, & Carpenter, 1997; Just & Carpenter, 1992; King & Just, 1991; Miyake, Carpenter, & Just, 1994). Therefore, using typical prosodic cues to reduce the processing loads associated with sentence processing may be particularly important for this clinical population.

Previous research suggests that patients with aphasia benefit from prosodic cueing: patients with aphasia demonstrate increased comprehension accuracy when sentences (Lasky et al., 1976) and paragraphs (Pashek & Brookshire, 1982) are presented with a reduced speech rate and exaggerated linguistic stress. Importantly, exaggerated linguistic stress increased sentence comprehension independent of speech rate (Lasky et al., 1976; Pashek & Brookshire, 1982). The exaggerated linguistic stress (i.e., exaggerated pitch inflections) may be facilitating auditory comprehension as prosodic cues may be used by intact attentional resources to direct the patient's attention to important sentential information; however, the relationship between prosody and cognition is unclear from this study as cognition was not measured.

Prosody may also facilitate sentence comprehension in aphasia through temporal expectancy. Previous research indicates that temporal expectancy can be created through rhythmic cueing prior to the stimulus, which subsequently improves speech comprehension (Cason & Schön, 2012). Temporal expectancy may also be embedded within the speech stimulus itself (e.g., regular intervals created by placing equal emphasis and stress on each word within a sentence). Temporal expectancy may facilitate comprehension in patients with aphasia by helping them to chunk words/phrases into smaller, more manageable units, that can be maintained by intact working memory resources (Gilbert, Boucher, & Jemel, 2014), particularly when attentional control is diminished and thus typical prosodic information cannot be utilized as attentional cues.

As previously discussed, prosody may improve language comprehension in neurotypical adults by reducing cognitive demands associated with sentence processing (Cohen et al., 2001; Kjelgaard & Speer, 1999; Roncaglia-Denissen et al., 2013; Speer et al., 1996). However, for persons with aphasia, who may have cognitive deficits, prosodic cues may instead help to selectively engage relatively intact cognitive resources. Furthermore, different prosody manipulations have been shown to recruit distinct brain regions (den Ouden et al., 2016; Humphries et al., 2005; Meyer et al., 2004). Collectively, this evidence suggests that prosody may be able to improve auditory comprehension post-stroke by selectively engaging relatively preserved cognitive resources and/or distinct brain regions.

Present Study

Cognitive deficits frequently co-occur with language deficits in aphasia. Much of this research has focused on more complex processes such as working memory and executive functions, leaving attention largely unexplored. Previous research does identify some relationship between attention and overall communication abilities: persons with aphasia with poorer attention abilities demonstrate poorer overall communication (Laures, 2005; Murray, 2012; Murray et al., 1997; Villard & Kiran, 2017). These studies further detail that different types of attention are differentially affected by stroke, likely due to somewhat distinct neural resources supporting each type of attention. Furthermore, somewhat distinct neural resources are also known to support attention in different perceptual modalities (Fritz, Elhilali, David, & Shamma, 2007; Petersen & Posner, 2012; Roberts & Hall, 2008; Thiel & Fink, 2007). Yet, questions remain regarding the effects of presentation modality on attention post-stroke, particularly since auditory attention has been mostly unstudied in stroke patients. Therefore, Experiment 1a will explore the effects of presentation modality (visual and auditory) on attention post-stroke. Experiment 1b will then investigate the neural resources supporting attention in each domain.

Patients with aphasia who have better cognitive abilities typically demonstrate better overall communication abilities. Therefore, Experiment 2 will explore whether relatively preserved cognitive abilities, including attention, can be used to improve sentence comprehension post-stroke. In neurotypical adults, prosody has been shown to possibly improve language comprehension by reducing demands placed on the cognitive resources associated with sentence processing (Cohen et al., 2001; Kjelgaard & Speer, 1999; Roncaglia-Denissen et al., 2013; Speer et al., 1996). However, in aphasia, prosody may instead improve language comprehension by recruiting relatively preserved cognitive resources. For example, sentence prosody may recruit attentional control resources during sentence comprehension as the pitch inflections and prosodic boundaries may direct listener attention towards important sentential information (Schafer, 1997). Alternatively, list prosody may recruit relatively preserved working memory resources by creating temporal expectancy effects that facilitate the chunking of sentence-level information within working memory resources (Gilbert et al., 2014). Therefore, Experiment 2a will behaviorally investigate the relationship between cognition, prosody, and auditory sentence comprehension in persons with chronic stroke (with and without aphasia) and matched-controls. Experiment 2b will extend the findings from Experiment 2a by identifying stroke lesion patterns associated with prosody manipulations that result in improved sentence comprehension for persons with chronic stroke (with and without aphasia).

CHAPTER 3

EXPERIMENT 1A: VISUAL AND AUDITORY ATTENTION IN PERSONS WITH APHASIA

Introduction

Aphasia is classically thought to be a language-specific disorder. Yet, it is well established that persons with aphasia demonstrate impaired performance on a variety of cognitive skills including attention (Murray, 2012; Murray et al., 1997), memory (Caplan et al., 2013), and executive functions (Fridriksson et al., 2006). Of these cognitive skills, attention is particularly important for studies of aphasia as it is a necessary foundation for other executive functions. For example, attention allows an individual to maintain alertness while completing a task or selectively respond to an incoming stimulus (e.g., language), while ignoring irrelevant and/or distracting information (e.g., background noise); both of which are basic abilities necessary for the execution of more complex tasks such as language.

Attention was once thought to be a uniform construct, however, three distinct subsets have since been identified: alerting, orienting, and executive control (Petersen & Posner, 2012; Posner & Petersen, 1990). Alerting involves maintaining vigilance towards external stimuli while orienting is the selection of specific information from a given stimulus (Fan et al., 2002; Fan & Posner, 2004; Posner & Petersen, 1990). Executive control is hypothesized to be a more complex form of attention and is a measure of how efficiently a correct response is achieved when relevant stimulus information conflicts with irrelevant stimulus information (Fan et al., 2002; Posner & Petersen, 1990).

Each type of attention has traditionally been assessed in neurotypical adults using cueing tasks in both the visual and auditory modalities. Collectively, these studies indicate that levels of alertness can be modulated by both visual and auditory cues (Fernandez-Duque & Posner, 1997). Similarly, one's ability to orient to specific information has been observed in both the visual (Rosen et al., 1999) and auditory (McDonald & Ward, 1999) modalities. In control subjects, the executive control component of attention has traditionally been studied in the visual modality using tasks such as the flanker, Stroop, and Simon paradigms (MacLeod, 1991), but similar behavioral results also have been produced in the auditory modality (McClain, 1983).

Neuroimaging and lesion evidence indicate that each type of attention is associated with a unique neural network: alerting with the thalamus, brainstem, and right fronto-parietal cortices (Petersen & Posner, 2012; Rinne et al., 2013; Sturm & Willmes, 2001); orienting with the right temporal-parietal junction, interparietal sulcus, superior parietal lobe, and frontal eye fields (Petersen & Posner, 2012; Rinne et al., 2013); and executive control with bilateral prefrontal cortex (Rinne et al., 2013) as well as the fronto-parietal and cingulo-opercular networks (Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008; Petersen & Posner, 2012). However, the exact neural resources supporting each type of attention can vary depending on sensory modality (Fritz et al., 2007; Petersen & Posner, 2012). For example, visual alerting cues activate bilateral inferior occipital gyri and posterior parietal cortices while auditory alerting cues activate bilateral superior temporal gyri and frontal cortices (Thiel & Fink, 2007). These modality-specific effects on the neural resources supporting attention indicate the need for reliable assessments of each subtype of attention within both the auditory and visual modalities as stroke lesions may differentially impact visual and auditory attention, with the latter being particularly important for spoken language comprehension.

Clinically, attention is commonly assessed using visual tests such as the color-word Stroop or Attention Network Test (ANT) (Stewart & Amitay, 2015). Solely assessing attention in the visual domain is problematic because both alerting and orienting attention have been shown to be domain-specific processes (Roberts et al., 2006; Spagna et al., 2015). The *Test of Everyday Attention (TEA)* is an improvement on visual-only assessments as it assesses attention in both the visual and auditory domains (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994). However, the *TEA* is limited in that it assumes attention to be domain-general and therefore does not fully measure attention in either modality (i.e., visual and auditory subtests are combined to provide measures of each type of attention). The lack of a reliable assessment of auditory attention in clinical populations is problematic, particularly for aphasia patients, for whom it is important to understand how cognitive deficits such as attention may be contributing to their auditory-dependent language impairments (i.e., impairments in speech production and auditory speech comprehension).

The ANT was developed to measure alerting, orienting, and executive control attention using a cued flanker task in the visual modality (Fan et al., 2002). Clinically, the ANT has been used to assess the integrity of each subtype of attention in a variety of populations including stroke (Fan & Posner, 2004; Rinne et al., 2013). An auditory-visual combination ANT, which tests alerting in the auditory modality and orienting and executive control in the visual modality has been used with stroke patients with right hemisphere disorder; alerting, orienting, and executive control effects were reliably identified (Chica et al., 2012). A similar version of the auditory-visual ANT, the double-modality ANT, which tests alerting in the auditory and visual domains, but only tests orienting and executive control in the visual modality has been used on younger and older adults and reliably finds auditory alerting, visual alerting, visual orienting, and visual executive control effects (Callejas, Lupiàñez, Funes, & Tudela, 2005; Ishigami et al., 2016; Ishigami & Klein, 2011). An auditory-only version of the ANT, based on Fan et al.'s (2004) visual ANT, has been developed which uses a cued auditory Stroop task (Roberts et al., 2006; Stewart & Amitay, 2015), but to our knowledge it has not been implemented in aphasia patients or after stroke more generally.

Further evidence for the need to assess attention in both auditory and visual modalities is that studies of neurotypical adults comparing matched versions of the visual and auditory ANT produce conflicting results. While studies typically find significant alerting, orienting, and executive control effects in the visual domain (Roberts et al., 2006; Spagna et al., 2015; Stewart & Amitay, 2015), results differ within the auditory modality. For example, Roberts and colleagues (2006) found significant alerting, orienting, and executive control effects in the auditory modality. However, Spagna et al. (2015) solely identified significant alerting and executive control effects and Stewart and Amitay (2015) found just significant executive control effects in the auditory modality.

In these studies of neurotypical adults, correlations between the two modalities further suggest a separation of visual and auditory attention. Both Roberts et al. (2006) and Spagna et al. (2015) found executive control to be correlated across the two modalities suggesting it is unaffected by test modality and likely a domain-general cognitive process. Roberts et al. (2006) found similar results for alerting across the two modalities, however, Spagna and colleagues (2015) did not find alerting attention abilities to correlate across modalities. Both Roberts et al., (2006) and Spagna et al. (2015) identified orienting attention to be uncorrelated across the two modalities suggesting it may be a domain-specific process. Using a factor analysis approach, Stewart and Amitay (2015) found that only auditory and visual executive control ("conflict resolution" in their terms) load on the same component. These findings further necessitate separate examination of visual and auditory attention in persons with chronic aphasia, particularly when trying to relate attentional abilities to auditory language performance. Thus, the purpose of the present study was to determine whether alerting, orienting, and executive control attention abilities are influenced by presentation modality in persons with chronic aphasia and matched control subjects. This study is the first, to my knowledge, to examine auditory attention in aphasia patients using the well-studied ANT paradigm. It was hypothesized that: (1) the aphasia group would perform significantly worse on all trial types (longer reaction times and more errors) than age-matched controls on both the visual and auditory ANTs; (2) both alerting and orienting attention will not correlate across the visual and auditory modalities, but executive control attention will correlate; and (3) significant effects of alerting, orienting, and executive control will be measured by both the visual and auditory ANTs in both groups, which would indicate that the auditory ANT is a feasible and potentially informative clinical measure.

Method

Participants

Participants were 22 chronic aphasia patients (12 females) who experienced a single left hemisphere cerebral stroke[2] at least 6 months prior to testing (Table 1). Aphasia participants ranged in age from 28 to 80 years (*M* = 54.64, *sd* = 12.97). Aphasia participants were pre-morbidly right-handed, native speakers of American English, 18+ years of age, with no history of neurological disease, head trauma, or psychiatric disturbances prior to their stroke. An additional 20 controls (14 females) ranging in age from 31 to 79 years (*M* = 51.40, *sd* = 12.82) who were also right-handed, native speakers of American English, 18+ years of age, with no history of neurological disease, head trauma, or psychiatric disturbances were also recruited. There were no significant differences between the aphasia and control groups in age, gender, education, or hearing status (Table 2). All participants were monetarily compensated for their participation. Arizona State University's Institutional Review Board approved all procedures.

Table 1. Aphasia group demographics.

	Gender	Age	Months Post Stroke	Years of Education	Aphasia Diagnosis
AZ1003	Female	48	110	19	Broca's
AZ1006	Male	60	138	14	Broca's
AZ1011	Female	73	53	16	Anomic
AZ1012	Male	77	85	16	Wernicke's
AZ1013	Female	47	258	17	Broca's
AZ1016	Male	37	142	14	Broca's
AZ1018	Female	43	29	14	Broca's
AZ1022	Female	46	79	14	Broca's
AZ1028	Female	80	19	24	Wernicke's
AZ1030	Male	56	32	16	Broca's
AZ1031	Female	40	63	20	Broca's

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[2] One participant (AZ1033) had two strokes ten years apart.

AZ1032	Male	28	20	13	Anomic
AZ1033	Male	57	180; 60	14	Global
AZ1034	Female	59	110	15	Anomic
AZ1035	Female	41	72	17	Broca’s
AZ1036	Male	65	158	15	Broca’s
AZ1037	Male	57	13	16	Broca’s
AZ1038	Male	54	155	14	Broca’s
AZ1039	Female	66	48	14	Anomic
AZ1040	Female	54	45	14	Broca’s
AZ1041	Female	59	24	12	Anomic
AZ1042	Male	55	37	14	Broca’s

Table 2. Demographic comparisons between aphasia and control groups.

	Aphasia (n=22)	Controls (n=20)	Statistic
Age	54.64 (12.97)	51.40 (12.82)	$t(40)=.81, p=.42$
Gender (male/female)	10/12	6/14	$\chi^2(1)=1.06, p=.30$
Education (years)	15.54 (2.67)	15.20 (2.17)	$t(40)=.46, p=.65$
Hearing Status[a]	16.53 (12.15)	13.44 (9.07)	$t(40)=.93, p=.36$

[a]Pure tone average for better ear; 500-4000 Hz

Experimental Design

Participants completed the visual (Fan et al., 2002; Roberts et al., 2006) and auditory ANTs (Roberts et al., 2006) as part of a larger neuropsychological test battery. In both ANTs, each trial begins with the presentation of a cue (double cue, center cue, spatial cue, no cue) and asks participants to make a judgment about a target within a specific task (visual: flanker task; auditory: Stroop task). This setup allows each trial to be analyzed by cue type (double cue, center cue, spatial cue, no cue) and target condition (congruent, incongruent, and neutral). Comparing different combinations of cues provides measures of alerting (no cue – double cue trials) and orienting (center cue – spatial cue trials) attention. Comparing different target conditions provides a measure of executive control attention (incongruent – neutral trials). For alerting and orienting attention, larger scores indicate faster responses for the alerting or orienting cue compared to the comparison cue (i.e., no cue for alerting and center cue for orienting). For executive control, scores closer to zero reflect better executive control attention as this indicates participants have similar mean correct reaction times for the incongruent and neutral trials (Fan & Posner, 2004). Specifics of the visual and auditory tasks are described below.

Visual Attention Network Task (ANT). The visual ANT set-up was modeled after Roberts et al., (2006) and was very similar to the visual ANT reported by Fan et al. (2002) (Figure 1). Each trial began with a fixation cross jittered between 2400-3600 milliseconds. Following the offset of the fixation cross, a visual cue was presented in the middle of the screen for 100 milliseconds. Visual cue conditions were as follows: (1) center cues (single asterisk presented in the middle of the screen), (2) double cues (simultaneous presentation of one asterisk above the fixation cross and one asterisk below the fixation cross), (3) spatial cue (single asterisk presented either above or below the fixation cross; spatial cues always predicted the location of the flanker task), and (4) no cue (fixation cross remains in the middle of the screen, but no cueing is provided). Following the offset of the visual cue, the fixation cross was presented on the screen for 400 milliseconds after which time participants completed the flanker task. In the flanker task, participants saw a series of five arrows and indicated via button press whether the center arrow was pointing left or right. A congruent trial occurred when the center arrow was pointing the same direction as the flanking arrows. An incongruent trial occurred when the center arrow was pointing the opposite direction of the flanking arrows. A neutral trial occurred when the center arrow was not flanked by any arrows. Participants completed a total of 180 trials where all cue types and flanker conditions were presented equally. Trial presentation was randomized for each participant. Verbal and written instructions, examples of all stimuli, and 10 practice trials preceded the start of the experiment.

Auditory Attention Network Task (ANT). The auditory ANT set-up was modeled after the auditory ANT used by Roberts et al. (2006) (Figure 1). In the auditory ANT, the flanker task is replaced by an auditory Stroop task; participants are instructed to ignore the meaning of the stimulus and determine whether the stimulus was spoken in a high or low pitched voice. Each trial began with a 500 Hz fixation tone jittered between 400-1600 milliseconds. Following the offset of the fixation tone, an auditory cue was presented for 50 milliseconds. Auditory cues were bursts of speech-shaped noise, cosine gated for 10 milliseconds at the onset and offset. Auditory cue conditions were as follows: (1) center cues (correlated noise bursts perceived in the center of the head), (2) double cues (uncorrelated noise burst perceived as separate signals in each ear), (3) spatial cue (single noise burst) presented in the left or right ear (spatial cue always predicted the location of the auditory Stroop task), and (4) no cue. Conflict to measure executive control was generated using an auditory Stroop task. In this task, participants heard the words “high,” “low,” and “day” spoken in either a high pitched or a low pitched voice. A single female speaker recorded each word in a high and low pitch. The average fundamental frequency of the high pitch words was 353.67 Hz; the average for the low pitch words was 217 Hz. The participants’ task was to ignore the semantic content (i.e., the spoken word “high,” “low,” or “day”) and indicate via a button press whether the speaker's voice was high or low in pitch. Participants completed a total of 180 trials where all cue types and Stroop conditions were presented equally. Trial presentation was randomized for each participant. Verbal and written instructions, examples of all stimuli, and 10 practice trials preceded the start of the experiment.

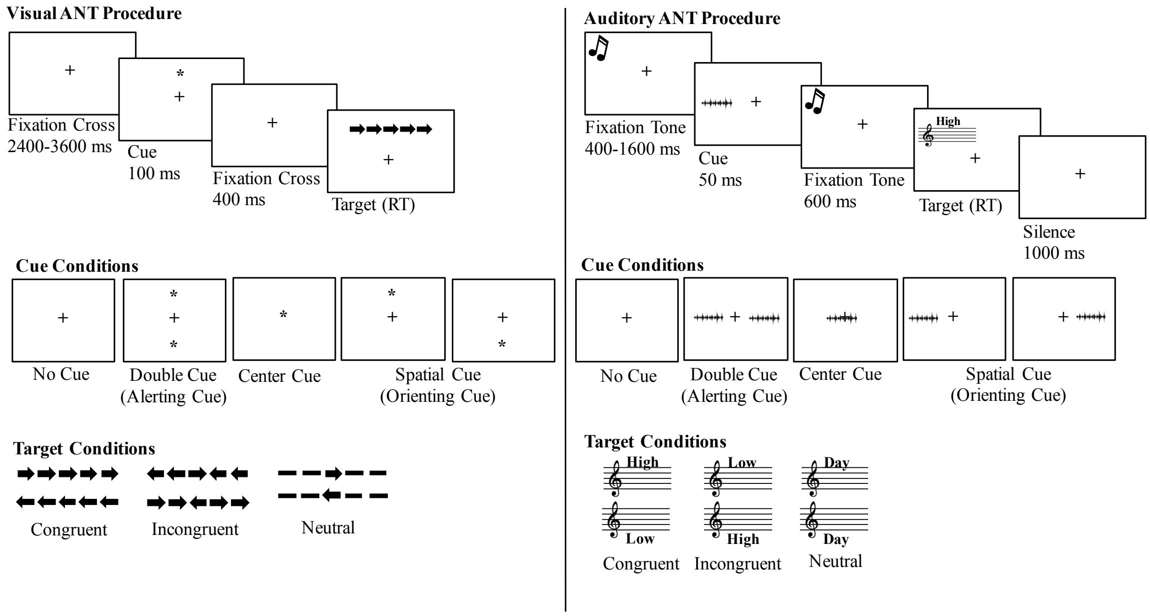

Figure 1. Illustration of the procedure, cue conditions, and target conditions for the visual and auditory ANTs. Adapted from Roberts et al. (2006).

Data Analysis

Reaction times associated with incorrect responses and those greater than 2.5 standard deviations from each participant's mean were excluded from the analyses; this data trimming procedure was determined *a priori* based on it being a standard, well-studied approach in psycholinguistic research (Baayen & Milin, 2010; Lachaud & Renaud, 2011; Ratcliff, 1993). This approach aims to capture the middle 85% of the distribution of the reaction time measurements and is based on the assumption that the process of interest is being captured, not other extraneous factors (e.g., brief distractions, button press mistakes, etc.). Consistent with this aim, 14.56% of the data was removed for the auditory ANT and 3.47% for the visual ANT for the aphasia group. For the control group, 4.39% of the data was removed for the auditory ANT and 2.58% for the visual ANT. Reaction times from the remaining correct responses were used to calculate measures of alerting, orienting, and executive control.

To facilitate comparisons with previous studies (e.g. Roberts et al., 2006; Spagna et al., 2015; Stewart & Amitay, 2015), we first used paired samples *t*-tests to determine, within each group, if significant effects of alerting (no cue versus double cue), orienting (center cue versus spatial cue), and executive control (incongruent versus neural) were evident in each modality. We then transformed these contrasts into relative difference scores (i.e., ratio scores) to compare the two groups. Relative difference scores are more advantageous for patient versus control group comparisons than absolute difference scores (i.e., a subtraction of reaction times between the two conditions of interest) because the relative difference approach scales the score such that individual differences related to the speed of general response selection processes and motor planning and execution are controlled. Independent samples *t*-tests were used to compare alerting ((no cue – double cue)/double cue), orienting ((center cue – spatial cue)/spatial cue), and executive control ((incongruent – neutral)/neutral) attention between the aphasia and control groups. Paired samples *t*-tests and Pearson correlations were used to analyze the relationship across modality between alerting, orienting, and executive control attention, respectively, within each group.

Results

Visual and Auditory ANT in Patients with Aphasia and Matched-controls

Mean reaction times and standard deviations of the mean for all cues and targets in the visual and auditory modality are reported in Table 3 for both groups. Replicating previous work using the visual ANT, the control group demonstrated significant effects of alerting (i.e., better performance on double cue trials compared to no cue trials), orienting (i.e., better performance on spatial cue trials compared to center cue trials), and executive control (i.e., slower responses for incongruent trials compared to neutral trials). For the aphasia group, significant orienting and executive control effects were observed, however, unlike in controls, the alerting effect was not significant in the visual modality. In the auditory modality, significant executive control effects were observed for both groups, but the alerting and orienting effects were not significant for either group (Table 4).

Table 3. Mean reaction times and standard deviations of the mean for all cues and targets in the visual and auditory modality for both groups.

	Condition	Visual Modality Mean (sd)	Auditory Modality Mean (sd)
Control Group (n = 20)	No Cue	634.24 (174.44)	804.50 (149.51)
	Double Cue	597.59 (173.45)	796.59 (157.46)
	Center Cue	601.32 (172.62)	803.09 (169.06)
	Spatial Cue	571.53 (171.36)	809.52 (165.54)
	Congruent Target	570.55 (165.34)	743.47 (153.21)
	Incongruent Target	670.27 (177.83)	902.55 (185.84)
	Neutral Target	565.09 (162.60)	776.55 (149.95)
Aphasia Group (n = 22)	No Cue	1253.10 (692.75)	1233.78 (407.77)
	Double Cue	1185.45 (618.01)	1207.52 (376.38)
	Center Cue	1212.23 (628.63)	1222.30 (387.35)
	Spatial Cue	1171.84 (649.23)	1197.64 (355.81)

Congruent Target	1160.04 (614.29)	1160.20 (384.88)
Incongruent Target	1344.77 (758.43)	1328.85 (414.33)
Neutral Target	1115.53 (578.99)	1183.12 (370.85)

The Effect of Presentation Modality

For the control group, alerting benefits (i.e., better performance on double cue trials compared to no cue trials) significantly differed between the two modalities with the control group benefiting more from the alerting cue (i.e., double cue) in the visual than the auditory modality [*t*(19)=2.67, *p*=.02]. Orienting benefits (i.e., better performance on spatial cue trials compared to center cue trials) also significantly differed between the two modalities for the control group with participants benefiting more from the orienting cue (i.e., spatial cue) in the visual than the auditory modality [*t*(19)=3.93, *p*<.001]. Note, that auditory orienting attention had a negative mean (Figure 2) suggesting control participants were actually distracted by the spatial cue in the auditory modality but the spatial cue in the visual modality facilitated responses as expected. Executive control costs (i.e., slower responses for incongruent trials compared to neutral trials) did not significantly differ between the two modalities for the control group [*t*(19)=1.52, *p*=.15]. For the aphasia group, alerting [*t*(21)=.91, *p*=.38], orienting [*t*(21)=1.01, *p*=.32], and executive control [*t*(21)=1.50, *p*=.15] did not significantly differ between the two modalities.

For the control group, there were no significant correlations across the two modalities for alerting [*r*(18) = -.08, *p*=.74], orienting [*r*(18) = .17, *p*=.49], and executive control [*r*(18) = -.35, *p*=.13]. For the aphasia group, alerting positively correlated across the two modalities [*r*(20) = .46, *p*=.03], however, the correlations for orienting [*r*(20) = -.18, *p*=.42] and executive control [*r*(20) = .10, *p*=.65] were not significant (Figure 2).

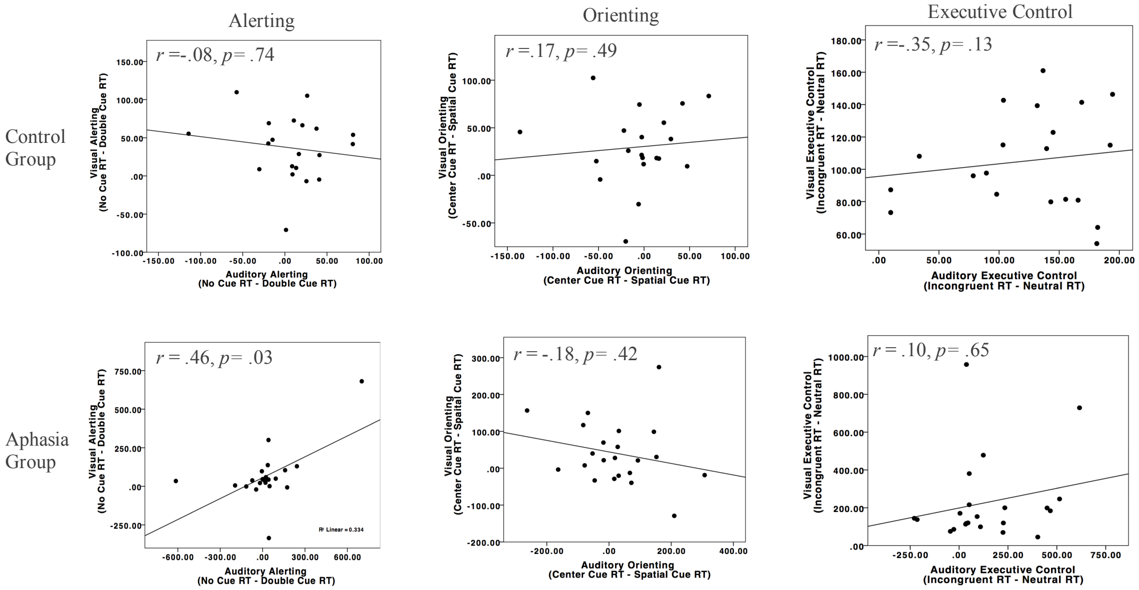

Figure 2. Alerting, orienting, and executive control between modality correlations for the control and aphasia groups.

Aphasia versus Control

Overall, the control group was significantly faster than the aphasia group in both the auditory [*t*(40) = 3.78, *p*<.001] and visual [*t*(40) = 4.13, *p*<.001] modalities. But, alerting benefits [auditory: *t*(40) = .39, *p*=.70; visual: *t*(40) = .58, *p*=.57], orienting benefits [auditory: *t*(40) = 1.09, *p*=.28; visual: *t*(40) = .52, *p*=.61], and executive control costs [auditory: *t*(40) = .73, *p*=.47; visual: *t*(40) = .02, *p*=.99] did not significantly differ between the two groups in either modality (Figure 3). The aphasia group made more errors than the control group on the auditory ANT overall [*t*(40) = 2.78, *p*=.008], but overall error rate did not significantly differ between the two groups in the visual modality [*t*(40) = .53, *p*=.60].

Table 4. Alerting benefits, orienting benefits, and executive control costs for each group in each modality. For alerting, cue 1 is no cue and cue 2 is double cue. For orienting, cue 1 is center cue and cue 2 is spatial cue. For executive control, cue 1 is incongruent target and cue 2 is neutral target.

			Cue 1	Cue 2	Paired *t*-test
Control Group (n=20)	Visual ANT	Alerting (no cue- double)	634.24 (39.00)	597.59 (38.78)	*t*(19)=3.92, *p*<.001*
		Orienting (center – spatial)	601.32 (38.60)	571.53 (38.32)	*t*(19)=3.37, *p*=.003*
		Executive Control (incongruent – neutral)	670.27 (39.76)	565.09 (36.36)	*t*(19)=15.61, *p*<.001*
	Auditory ANT	Alerting (no cue- double)	804.50 (33.43)	796.59 (35.21)	*t*(19)=.80, *p*=.43
		Orienting (center – spatial)	803.09 (37.80)	809.52 (37.01)	*t*(19)=.64, *p*=.53
		Executive Control (incongruent – neutral)	902.55 (41.55)	776.55 (33.53)	*t*(19)=10.85, *p*<.001*
Aphasia Group (n=22)	Visual ANT	Alerting (no cue- double)	1253.10 (147.70)	1185.45 (131.76)	*t*(21)=1.82, *p*=.08
		Orienting (center – spatial)	1212.23 (134.02)	1171.58 (138.36)	*t*(21)=2.21, *p*=.04*
		Executive Control (incongruent – neutral)	1344.77 (161.70)	1115.53 (123.44)	*t*(21)=4.77, *p*<.001*
	Auditory ANT	Alerting (no cue- double)	1233.78 (86.94)	1207.52 (80.24)	*t*(21)=.55, *p*=.59
		Orienting (center – spatial)	1222.30 (82.58)	1200.27 (76.50)	*t*(21)=.83, *p*=.42
		Executive Control (incongruent – neutral)	1328.85 (88.34)	1183.12 (79.06)	*t*(21)=3.04, *p*=.006*

*significant at *p*<.05

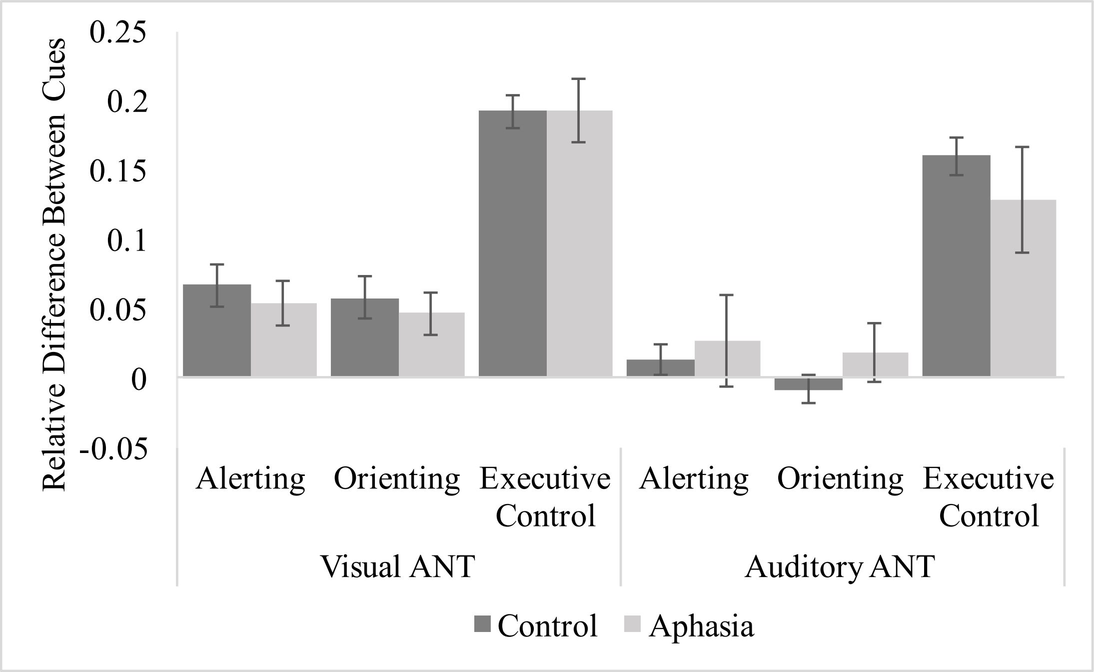

Figure 3. Aphasia and control group measures of alerting ((no cue – double cue)/double cue), orienting ((center cue – spatial cue)/spatial cue), and executive control ((incongruent – neutral)/neutral) from the visual and auditory ANT. Error bars represent +/- one standard error.

Discussion

The purpose of this study was to investigate whether alerting, orienting, and executive control are domain-specific or domain-general subsets of attention in patients with chronic aphasia and matched-controls. To this end, aphasia patients and matched-control participants completed visual and auditory versions of the well-studied Attention Network Test (ANT).

For the control group, significant effects of alerting and orienting were only observed in the visual modality, while executive control costs were observed in both the visual and auditory modalities. The significant effects of alerting, orienting, and executive control in the visual modality replicate previous work (Fan et al., 2002; Roberts et al., 2006; Spagna et al., 2015; Stewart & Amitay, 2015). The lack of a significant alerting and orienting effect in the present auditory task coincides with Stewart and Amitay's (2015) results but not with Roberts et al.'s (2006) and Spagna et al.'s (2015) results who found significant alerting effects but non-significant orienting effects. The fact that this study replicates the findings from one previous study but not others is likely due to differences in statistical procedures, namely using mean versus median reaction times to calculate the three attention measures; this is discussed in more detail below.

The aphasia group demonstrated a similar pattern of results as the control group: orienting benefits were observed in the visual modality, but not the auditory modality, and executive control costs were present in both modalities. However, unlike the control group, significant alerting benefits were not observed in either modality in the aphasia group. The failure to identify significant alerting and orienting effects (in either group) in the auditory ANT likely stems from the increased difficulty of this task compared to the visual version leading to greater variability in individual subject performance and suggests that modifications (discussed below) may need to be considered when administering the auditory ANT to clinical populations.

The Effect of Presentation Modality

Significant modality differences for the control group were identified for alerting and orienting with controls benefiting more from the alerting (i.e., double cue) and orienting (i.e., spatial cue) cues in the visual than auditory modality. The difference between executive control abilities (i.e., scores closer to zero for incongruent trials minus neutral trials) across modalities in the control group was not significant. The between modality difference for orienting in the control group appears to be driven by a lack of spatial cue benefits in the auditory domain. Hearing levels could possibly explain the decreased spatial cue benefit; however, pure tone averages did not correlate with the auditory spatial cues for either ear. Therefore, a more likely explanation is that neurotypical adults benefit equally from the cues used to calculate orienting attention: both the spatial cue and the center cue may serve as auditory orienting cues for the upcoming stimulus, thus no further significant gain is provided by the spatial orienting cue (i.e., spatial cue).

In the control group, the between-modality correlations for alerting, orienting, and executive control were non-significant suggesting each construct (at least as it is operationally defined by the ANT) is domain-specific. This conclusion corresponds with previous work for alerting and orienting attention (Roberts et al., 2006; Spagna et al., 2015; Stewart & Amitay, 2015), but, the executive control conclusions differ somewhat. While previous work concludes that executive control is a domain-general construct (Roberts et al., 2006; Spagna et al., 2015; Stewart & Amitay, 2015), the non-significant correlation across modalities for executive control suggests that the auditory and visual executive control tasks may be engaging domain-specific attention resources. This discrepancy between previous findings in younger adults and our aphasia and control results could be due to age-related changes. For example, on the visual ANT, older adults demonstrate greater difficulty mitigating the conflict generated by incongruent trials compared to younger adults (Zhou et al., 2011). Executive control performance also interacts with cue type in older adults: relative to congruent trials, orienting cues improve performance on incongruent trials but alerting cues do not (Mahoney, Verghese, Goldin, Lipton, & Holtzer, 2010). Older adults have also been shown to employ executive control resources differently than younger adults based on task demands (Isingrini et al., 2015) and this difference in resource allocation could be due to structural changes in the frontal cortex, which supports executive control (Raz, 2000; Resnick, Pham, Kraut, Zonderman, & Davatzikos, 2003). However, future work is needed to better understand age-related changes in executive control; specifically regarding the influence of task and perceptual modality effects.

The modality effects within the aphasia group differed from the control group in a few notable ways. For the aphasia group, there were no significant differences in alerting, orienting, or executive control effects between the visual and auditory modalities (unlike the control group that exhibited significant differences in alerting and orienting effects across modalities). The significant modality differences in alerting and orienting in controls but not in the aphasia group indicate that both alerting and orienting attention in each modality may engage distinct, yet likely adjacent, neural resources in neurotypical adults. Proximity, or at least shared arterial pathways, between anatomically distinct auditory and visual attention resources may mean that a specific type of attention (e.g., alerting or orienting) in both modalities is affected by the same stroke despite being behaviorally dissociable in controls. It also is notable that a significant positive correlation was observed for alerting between the two modalities in the aphasia group, whereas no significant correlations were found between modalities for the control group. This may suggest that post-stroke functional reorganization may include shared resources that support both auditory and visual alerting. Future work is needed to better understand the neural resources supporting each type of attention following brain injury, but these findings indicate that in older populations, alerting, orienting, *and* executive control performance are each affected by modality, and that this relationship between auditory and visual attention abilities, particularly alerting, may be different in patients with aphasia. Altogether these findings indicate that it is necessary to asses all three aspects of attention in all perceptual modalities of interest, and that the auditory ANT may be a promising clinical tool to provide a more complete picture of attention abilities in patient populations.

The Auditory Modality

While the present study's auditory ANT effects coincide with Stewart and Amitay's (2015) results, the failure to reliably identify significant alerting effects (in either group) in the auditory domain is notable as it contradicts other previous studies in controls (Callejas et al., 2005; Chica et al., 2012; Ishigami et al., 2016; Ishigami & Klein, 2011; Roberts et al., 2006; Spagna et al., 2015), which all found either an alerting or orienting effect, or both. The lack of a significant auditory alerting effect in the present experiment may be due to the auditory ANT being more difficult overall than the visual ANT, and/or statistical procedures used to calculate the measures of attention. We will begin by comparing statistical procedures among studies using the same auditory ANT task and then discuss studies using the double-modality ANT: Roberts et al. (2006) calculated each of their attention effects using trimmed median reaction times (and found a significant alerting effect) while Stewart and Amitay (2015) used trimmed mean reaction times (and found a non-significant alerting effect). In the present study, we utilized trimmed mean reaction times, like Stewart and Amitay (2015), and find no alerting effect in the auditory modality. Median reaction times are often used when data is skewed, however, because of this, median reaction times can be more easily biased by skewed data and can lead to an inflation in the probability of finding significant effects (Miller, 1988; Whelan, 2008). The data in the present experiment have a normal distribution, making mean reaction time the more appropriate approach. Since the present study's statistical procedure corresponds with Stewart and Amitay's (2015) and the same auditory effects are observed, it is possible that the discrepancy in alerting findings between this study and Roberts et al. (2006) may be due to differences in how the attention measures were calculated (i.e., median versus mean reaction times).

Age-related changes are another possible explanation for why significant auditory alerting effects were not observed in the present experiment. To my knowledge, the version of the auditory ANT utilized in this experiment has not been used in older adults or patients with aphasia. However, a double-modality ANT has been used to investigate the three measures of attention in older adults (Chica et al., 2012; Ishigami et al., 2016; Ishigami & Klein, 2011) and stroke patients with right hemisphere disorder (Chica et al., 2012). The double-modality ANT does not allow for a direct comparison with the present study's auditory ANT as it measures alerting in the auditory and visual modalities, but solely measures orienting and executive control in the visual domain; yet, it does provide some insight into auditory alerting effects. Using the double-modality ANT, significant alerting effects have been identified by comparing auditory cue trials to no cue trials in both older adults (Chica et al., 2012; Ishigami et al., 2016; Ishigami & Klein, 2011) and stroke patients with right hemisphere disorder (Chica et al., 2012). These findings suggest that the integrity of auditory alerting attention may not necessarily decline with age, but healthy aging is associated with deterioration of the frontal lobes (Raz, 2000; Resnick et al., 2003) which have also been shown to support auditory alerting attention (Thiel & Fink, 2007). Therefore, age-related declines in the frontal cortex may still explain the lack of a significant auditory alerting effect in the present experiment (in either group), especially since older adults demonstrate reduced visual alerting abilities compared to younger adults (Zhou et al., 2011). However, future work is needed to parse the relationship between auditory attention and healthy aging using behavioral and neuroimaging methodologies.

Discrepancies between our findings and the findings from the double-modality ANT may be due to differences in statistical/experimental procedures. While all the double-modality ANT studies utilize trimmed mean reaction times to calculate the measures of attention, they differ from our trimmed means in that the double-modality ANT procedure forces participants to respond within 1700 milliseconds (Ishigami et al., 2016; Ishigami & Klein, 2011) and 4000 milliseconds (Chica et al., 2012). Forcing a response within a given time frame reduces reaction time variability leading to decreased standard deviations and a greater likelihood of detecting statistically significant effects. The standard deviations for the auditory ANT in the present experiment are much greater than the standard deviations for the double-modality ANT, likely because a response was not forced and participants were instead instructed to make fast and accurate responses. Furthermore, visual inspection of the means on this study's auditory ANT conditions indicates that there were faster reaction times on the alerting cue (i.e., double cue) trials compared to the no cue trials for both the aphasia and matched-control group. So, although the effect is not significant, a similar trend is observed; further suggesting differences in experimental paradigms and statistical procedures may be contributing to the discrepant results.

Another plausible explanation for the discrepancy in auditory alerting findings on this study's task compared to the double-modality ANT in older adults and right hemisphere stroke patients could possibly be hearing abilities. Hearing levels are known to decrease with age (Lin, Niparko, & Ferrucci, 2011; Lin, Thorpe, Gordon-Salant, & Ferrucci, 2011). Presumably, if participants have a hearing loss, they may not be able to reliably perceive the alerting cue, leading all trials to be perceived as "no cue" trials. This may subsequently prevent an auditory alerting effect from being identified. I screened the hearing of all participants from 500 to 4000 Hz and pure tone averages did not correlate with reaction times for trials with any of the auditory cues for either group, but hearing did correlate with auditory alerting in the aphasia group only. The non-significant correlations between auditory cues and hearing levels indicate that all participants were able to perceive the cues. However, the fact that hearing levels did positively correlate with auditory alerting in the aphasia group indicates that hearing abilities, perhaps related to stroke-induced brain lesions, still may be contributing to auditory alerting impairments. Thus, future work is needed to explore the relationship between hearing loss, brain injury, and higher order cognitive abilities, including attention, especially since hearing loss is linked to cognitive decline more generally (Lin et al., 2013).

The time frame between cue offset and target onset in the auditory ANT is another possible explanation for the failure to find a significant alerting effect in the present experiment. Alerting effects have been shown to peak around 300-400 milliseconds and last no more than 900 milliseconds (Callejas et al., 2005; Fuentes &

Campoy, 2008; Wang et al., 2014). In the present experiment, there was 600 milliseconds between cue offset and target onset; corresponding to previous work using this version of the auditory ANT in controls (Roberts et al., 2006; Stewart & Amitay, 2015). While 600 milliseconds is within the 900 millisecond timeframe for alerting benefits, it is greater than the 300-400 millisecond peak. Therefore, it is possible that the alerting cue has diminished prior to the onset of the target, essentially making all conditions “no cue” conditions. Older adults and individuals with brain damage may experience increased alerting cue decay rates compared to younger neurotypical adults. Again, future work is needed to better understand how auditory alerting attention changes with hearing loss, age, and brain injury.

Aphasia versus Control

As expected, aphasia participants had slower response rates than the control group in both presentation modalities; however, error rates only differed for the auditory ANT with aphasia participants making more errors overall. The effects of alerting, orienting, and executive control did not significantly differ between the control group and the aphasia group in either modality. This likely reflects the bilateral organization of attention resources (Cieslik, Mueller, Eickhoff, Langner, & Eickhoff, 2015; Derrfuss, Brass, Neumann, & von Cramon, 2005; Laird et al., 2005).

Visual inspection of the auditory executive control measure reveals the aphasia group to have a lower mean (i.e., better executive control) and greater variability compared to the control group. The lack of a significant between group difference is likely driven by increased variability within the aphasia group, but the seemingly better performance of the aphasia group on the auditory executive control measure warrants some discussion, especially since both groups have nearly identical executive control abilities in the visual modality.

The seemingly better executive control abilities in the aphasia group in the auditory modality may arise because of inherent differences in the demands of the visual and auditory neutral trials. In the auditory ANT, to make the correct response on the neutral trials, participants need to selectively attend to the relevant auditory information (i.e., the pitch of the voice) while inhibiting the irrelevant auditory information (i.e., the semantic content of the stimulus *day)*. Even though *day* does not contain pitch information like *high* and *low*, its presence does add additional irrelevant information, which makes the auditory neutral trials inherently more complex than the visual neutral trials, which solely contain a single left or right pointing center arrow, but no flankers. The need to ignore irrelevant information in the auditory ANT neutral trials likely makes these trials function more closely to incongruent trials than true neutral trials. This is problematic when using the auditory ANT to measure executive control abilities as aphasia participants and others with reduced cognitive abilities may appear to have better auditory executive control abilities than they really do (i.e., they are more likely to have a difference score closer to zero for incongruent – neutral trials). This may be because similar demands are being placed on their executive control attention by both the incongruent *and* neutral trials in the auditory modality and prompts the question: Is there a better baseline condition that can be used to measure auditory executive control in patients with aphasia? While the present experiment is not designed to specifically address this question, I do suggest that calculating “executive control” using a baseline which is less attentionally demanding (e.g., incongruent – congruent) may be more appropriate when trying to compare the performance of a clinical group with a control group and/or executive control abilities across different perceptual modalities. In the current dataset, when auditory executive control is calculated using congruent trials as the baseline instead of neutral trials, I find that the non-significant difference between auditory and visual executive control in the aphasia group becomes even smaller, with nearly identical means (and standard deviations) in each modality. However, additional studies are needed to further explore the potential processing differences between auditory and visual neutral trials and how to best quantify executive control in each modality.

Conclusion

The present study compares visual and auditory attention measures in patients with aphasia and matched-controls using auditory and visual ANT paradigms to assess the alerting, orienting, and executive control components of attention. The results indicate that alerting, orienting, and executive control effects in each modality did not significantly differ between the control and aphasia groups. Furthermore, none of the three components significantly correlated between the auditory and visual modalities in the control group and only alerting had a significant between-modality correlation in the aphasia group, indicating that visual and auditory attention measures are poor predictors of one another, and that their relationship may differ in controls versus aphasia patients. The lack of a correlation between executive control in the auditory and visual paradigms is particularly interesting given that previous literature suggests executive control is a domain-general resource; the lack of correlation in the present study may be related to inherent differences in measuring auditory and visual attention that need to be considered. Overall these findings demonstrate the need to separately assess all three components of attention in all perceptual modalities of interest in both neurotypical older adult and patient populations to gain a complete picture of an individual's attention abilities. The auditory ANT may be an effective measurement of attention in aphasia when administration and scoring modifications are considered.

CHAPTER 4

EXPERIMENT 1B: NEURAL RESOURCES SUPPORTING VISUAL AND AUDITORY ATTENTION POST-STROKE

Introduction

Various theoretical frameworks exist regarding the division of attention into distinct subtypes. One prominent theoretical framework proposed by Posner and Peterson (1990) breaks attention into three separate components: alerting, orienting, and executive control. Alerting attention includes the initial engagement of attentional resources as well as vigilance towards an external stimulus. Orienting attention involves selecting specific information from a given stimulus. Executive control is a measure of how well conflict can be mitigated when a stimulus contains both relevant information and conflicting irrelevant information (Fan, McCandliss, Sommer, Raz, & Posner, 2002; Fan & Posner, 2004; Petersen & Posner, 2012; Posner & Petersen, 1990).

The Attention Network Test (ANT) was developed to measure all three subtypes of attention using a single cued flanker task (Fan et al., 2002). The ANT has been traditionally presented in the visual modality and found to reliably identify alerting, orienting, and executive control effects in neurotypical adults and patient populations, including stroke (Fan et al., 2002; Fan & Posner, 2004; Roberts, Summerfield, & Hall, 2006; Spagna, Mackie, & Fan, 2015; Stewart & Amitay, 2015). An auditory version of the ANT has since been developed based on Fan et al.'s visual ANT. In the auditory modality, the cued flanker task is replaced by a cued auditory Stroop task (Roberts et al., 2006). While significant alerting, orienting, and executive control effects are consistently observed in the visual ANT, the identification of these effects using the auditory ANT in neurotypical adults is more variable with one study identifying significant alerting, orienting, and executive control effects (Roberts et al., 2006) and another only significant executive control effects (Stewart & Amitay, 2015).[3]

Studies looking at the relationship between the visual and auditory versions of the ANT conclude that alerting and orienting attention are domain-specific processes while executive control is a domain-general process (Roberts et al., 2006; Stewart & Amitay, 2015). The results from Experiment 1a confirm that alerting and orienting are modality-specific processes, but we additionally conclude that executive control becomes modality-specific as a function of age and that the independence of alerting attention across modalities is altered post-stroke. These discrepancies in findings between our results in stroke patients and previous findings in neurotypical young adults indicates a need to understand whether the neural resources supporting alerting, orienting, and executive control are affected by presentation modality (visual and auditory) post-stroke.

Both neuroimaging and lesion-based analyses have been used to study alerting, orienting, and executive control as defined by Fan et al.'s (2004) visual ANT. These studies generally conclude that visual attention is supported by a bilateral network, yet a right hemisphere bias is observed (Fan, McCandliss, Fossela, Flombaum, & Posner, 2005; Petersen & Posner, 2012; Posner & Petersen, 1990; Power et al., 2011; Rinne et al., 2013; Yeo et al., 2011). This bilateral visual attention network can be subdivided based on the specific aspects of attention being investigated. More specifically, alerting

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[3] The results from Experiment 1a correspond with the results from Stewart and Amitay (2015): only significant auditory executive control effects were observed in patients with aphasia and matched-controls.

attention has been shown to be supported by the thalamus, brainstem, and bilateral fronto-parietal cortices including bilateral dorsolateral prefrontal cortex, left inferior and superior parietal gyri, and the right posterior superior temporal gyrus (Fan, Mccandliss, Fossella, Flombaum, & Posner, 2005; Petersen & Posner, 2012; Rinne et al., 2013; Sturm & Willmes, 2001); orienting with the right temporal-parietal junction, interparietal sulcus, superior parietal lobe, and frontal eye fields (Fan et al., 2005; Petersen & Posner, 2012; Rinne et al., 2013); and executive control with bilateral prefrontal cortex (Rinne et al., 2013) and anterior cingulate gyrus (Fan et al., 2005). Additionally, executive control has been associated with the functional connectivity of both the fronto-parietal and cingulo-opercular networks as measured by resting-state functional MRI (Dosenbach et al., 2008; Petersen & Posner, 2012). Diffusion tensor imaging studies reveal similar relationships: visual alerting is associated with the integrity of white matter tracts connecting the right thalamus and right supplementary motor area, visual orienting with the structural integrity of white matter connecting the bilateral inferior parietal lobes, and visual executive control with the integrity of white matter underlying the right supramarginal gyrus (Yin et al., 2012). In regards to cortical thickness, visual alerting has been associated with the thickness of the left superior parietal lobe (Westlye, Grydeland, Walhovd, & Fjell, 2011), visual orienting with the thickness of the right angular gyrus (Yin et al., 2012), and visual executive control with the thickness of bilateral anterior cingulate cortex, left superior temporal gyrus, and right middle temporal gyrus (Westlye et al., 2011). Collectively, this evidence indicates that alerting, orienting, and executive control are at least partially supported by distinct neural resources located within both hemispheres; however, questions remain regarding the effects of presentation modality on attention.

In neurotypical control subjects, functional neuroimaging studies indicate that sensory modality influences the specific neural resources supporting each type of attention (Fritz et al., 2007; Petersen & Posner, 2012). For example, visual alerting is supported by bilateral inferior occipital gyri and posterior parietal cortices while auditory alerting is supported by bilateral superior temporal gyri and frontal cortices (Thiel & Fink, 2007). While many studies indicate that executive control is a domain-general resource (Cieslik et al., 2015; Dosenbach et al., 2008; Marek & Dosenbach, 2018; Petersen & Posner, 2012), some modality differences are reported. For example, bilateral prefrontal cortex is involved in conflict resolution in both the visual and auditory modalities, however, visual and auditory conflict resolution activate distinct sub-regions of the right parietal lobe (Roberts & Hall, 2008). These modality-specific findings regarding the neural resources supporting visual and auditory attention in neurotypical adults, plus behavioral findings in stroke patients indicating altered cross-modal relationships between alerting, orienting, and executive control (compared to neurotypical adults), necessitate the need to more fully understand the neural resources supporting both visual *and* auditory attention post-stroke.

Understanding the neural resources supporting alerting, orienting, and executive control in the auditory modality is critical for developing a complete picture of the neural bases of attention and how the neural resources supporting attention may change post-stroke. Thus, the purpose of this study was to determine whether the neural resources supporting alerting, orienting, and executive control attention are influenced by presentation modality in persons with chronic stroke. To my knowledge, this is the first study to examine the neural networks supporting visual and auditory attention post-stroke using matched-versions of the well-studied ANT paradigm. While both visual and auditory attention are known to be supported by bilateral neural networks (Power et al., 2011; Yeo et al., 2011), the present experiment focuses on left hemisphere brain regions that contribute to visual and auditory attention because my overall interest is in understanding the interplay between attention and language and how they are affected by left hemisphere stroke lesion patterns. It was hypothesized that visual alerting would be supported by the left supramarginal gyrus, left angular gyrus, left superior parietal gyrus, and left thalamus. Auditory alerting was hypothesized to be supported by more anterior brain regions including Broca's area (pars opercularis) and the left middle frontal gyrus. Both visual and auditory orienting attention are hypothesized to be supported by the left supramarginal gyrus, left angular gyrus, and left superior parietal gyrus. Auditory orienting attention is expected to be additionally associated with the left anterior cingulate cortex, Broca's area (pars opercularis), and the left middle frontal gyrus. Previous literature suggests that executive control is a domain-general cognitive resource, so in both modalities it is hypothesized to be supported by left prefrontal cortices including the left dorsolateral prefrontal cortex, left middle frontal gyrus, and Broca's area (pars opercularis).

Method

Participants

Twenty-one chronic stroke participants (12 females) who experienced a single left hemisphere cerebral stroke[4] at least six months prior to testing were included in the present study. Participants ranged in age from 28 to 80 years (*M* = 55, *sd* = 13.86), were pre-morbidly right-handed, native speakers of American English, 18+ years of age, with no history of neurological disease, head trauma, or psychiatric disturbances prior to their stroke (Table 5; Figure 4). Participants were monetarily compensated for their participation. Arizona State University's Institutional Review Board approved all procedures.

Table 5. Stroke group demographics.

	Gender	Age	Months Post Stroke	Years of Education	Aphasia Diagnosis
AZ1001	Female	57	77	18	None
AZ1003	Female	48	110	19	Broca's
AZ1006	Male	60	138	14	Broca's
AZ1011	Female	73	53	16	Anomic
AZ1012	Male	77	85	16	Wernicke's
AZ1016	Male	37	142	14	Broca's
AZ1018	Female	43	29	14	Broca's
AZ1022	Female	46	79	14	Broca's
AZ1026	Male	70	50	16	None
AZ1028	Female	80	19	24	Wernicke's
AZ1029	Female	34	174	14	None
AZ1030	Male	56	32	16	Broca's
AZ1031	Female	40	63	20	Broca's
AZ1032	Male	28	20	13	Anomic
AZ1033	Male	57	180; 60	14	Global
AZ1034	Female	59	110	15	Anomic
AZ1037	Male	57	13	16	Broca's
AZ1038	Male	54	155	14	Broca's
AZ1039	Female	66	48	14	Anomic
AZ1040	Female	54	45	14	Broca's

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[4] One participant (AZ1033) had two strokes ten years apart.

AZ1041	Female	59	24	12	Anomic

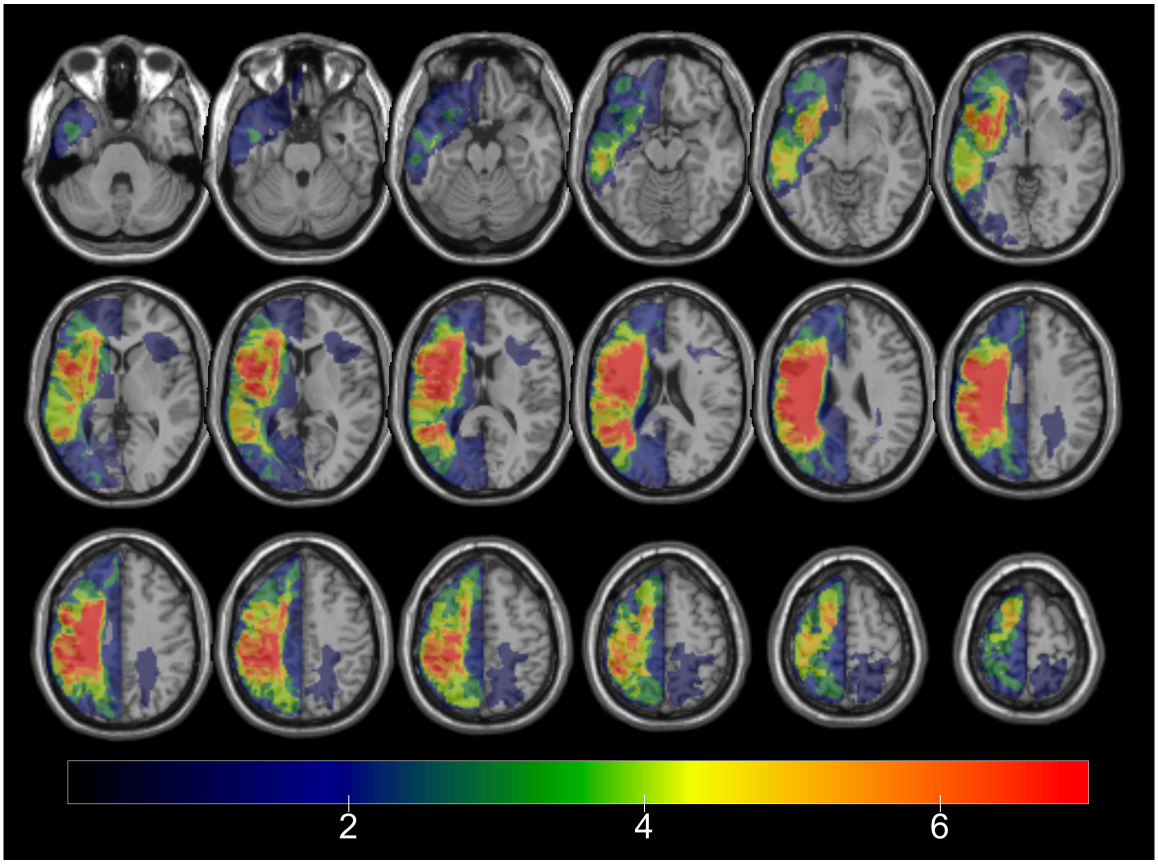

Figure 4. Lesion overlap map for all 21 stroke participants.

Experimental Design

Visual and auditory ANT tasks. The visual and auditory ANT tasks from Experiment 1a provided the measures of visual and auditory alerting (reaction time difference for no cue – double cue trials), orienting (reaction time difference for center cue – spatial cue trials), and executive control (reaction time difference for incongruent – neutral trials).

MRI data collection. Stroke participants underwent MRI scanning using a 3T Phillips Ingenia MRI scanner equipped with a 32 channel radiofrequency head coil located at the Keller Center for Imaging Innovation at the Barrow Neurological Institute in Phoenix, Arizona. Chronic stroke lesions were demarcated on a high-resolution anatomical T1 image (FOV = 270 X 252, TR = 6.7, flip angle = 9, voxel size = 1 x 1 x 1 mm) in MRIcron (Rorden & Brett, 2000).

Lesion identification and normalization. Lesion maps were smoothed with a 3mm full-width half maximum Gaussian kernel to remove jagged edges associated with manual drawing. Enantiomorphic normalization (Nachev, Coulthard, Jäger, Kennard, & Husain, 2008) was conducted using SPM12 in accordance with procedures at the University of South Carolina (Rorden, Bonilha, Fridriksson, Bender, & Karnath, 2012) (i.e., NiiStat's "nii_harvest"). First, a mirrored image of the T1 image (reflected across the midline) was co-registered to the native T1 image. Then, a chimeric image based on the native T1 image with the lesioned tissue replaced by tissue from the mirrored image (using the smoothed lesion map to modulate this blending, feathering the lesion edge) was created. SPM12's unified segmentation-normalization (Ashburner & Friston, 2005) was used to transform this chimeric image to standard space; the resulting spatial transformation was subsequently applied to the T1 image. The normalized lesion map was then binarized, using a 50% probability threshold.

Lesion symptom mapping. Lesion maps were segmented into regions of interest based on the JHU brain atlas, which uses structural-anatomical boundaries to define 189 individual regions of interest (Faria et al., 2012). Nine regions of interest were selected from the JHU brain atlas based on previous literature and *a priori* hypotheses. The nine regions of interest included the left dorsolateral prefrontal cortex (defined by the JHU atlas as the anterior half of the left middle and superior frontal gyri), the posterior half of the left middle frontal gyrus, Broca's area (pars opercularis), left supramarginal gyrus, left angular gyrus, left superior parietal gyrus, left precuneus, left anterior cingulate gyrus, and left thalamus[5] (Figure 5). The percent of each region of interest that was intact was extracted from each patient's lesion map using an "in house" Matlab (MathWorks, Natick, MA) script.

Data Analysis

Multiple regression analyses were used to predict the effects of alerting (reaction time difference for no cue – double cue trials), orienting (reaction time difference for center cue – spatial cue trials), and executive control (reaction time difference for incongruent – neutral trials) attention in both the visual and auditory modalities. The predictors for each regression analysis were the percent of intact tissue within each of the nine regions of interest.

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[5] Several other left hemisphere brain regions other than the nine identified by this study are known to support visual and auditory attention including, but not limited to the left superior frontal lobe (prefrontal cortex) and left posterior cingulate cortex. However, due to a small sample size resulting in a limited number of degrees of freedom, we are restricting our analyses to these nine prominent regions.

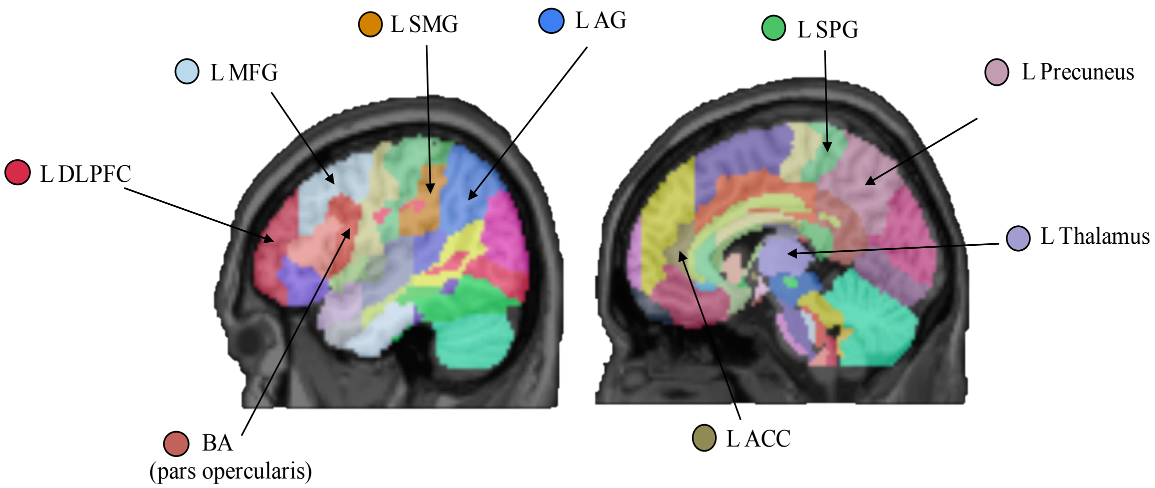

Figure 5. Anatomical regions of interest derived from the JHU atlas (Faria et al., 2012). Peak coordinates for each region of interest are as follows: L ACC (-6, 41, 7); BA pars opercularis (-45, 13, 15); L DLPFC (-35, 47, 12); L MFG (-36, 18, 38); L SMG (-52, -29, 32); L AG (-42, -52, 38); L SPG (-24, -48, 51); L Precuneus (-8, -55, 43); L Thalamus (-12, -18, 7).

Key: L: left; ACC: anterior cingulate cortex; AG: angular gyrus; BA: Broca's area; DLPFC: dorsolateral prefrontal cortex (comprised of the left middle and superior frontal gyri); MFG: middle frontal gyrus; SMG: supramarginal gyrus; SPG: superior parietal gyrus.

Results

Mean reaction times and standard deviations of the mean for alerting, orienting, and executive control in the visual and auditory modalities are reported in Table 6.

Table 6. Mean reaction times and standard deviations of the mean for alerting, orienting, and executive control in the visual and auditory modalities.

Attention Component	Visual Modality Mean (sd)	Auditory Modality Mean (sd)
Alerting	70.00 (178.75)	58.00 (173.37)
Orienting	32.73 (84.05)	36.97 (112.23)
Executive Control	235.90 (228.93)	168.47 (221.84)

Visual Attention

The overall model predicting visual alerting attention was significant [R^2 =.79, F(9,11)=4.45, *p*=.01], however, no individual predictors reached significance. The overall model predicting visual orienting attention was not significant [R^2 =.27, F(9,11)=.45, *p*=.88]. For visual executive control, the overall model was significant [R^2 =.71, F(9,11)=2.92, *p*=.05] with the left angular gyrus being the sole significant predictor (β= -1.16, *p*=.02); the left thalamus was also trending towards significance (β= -.37, *p*=.06) (Table 7).

Table 7. Multiple regression models predicting visual attention.

Visual Alerting (No Cue – Double Cue RT)			
Predictors	β	*t*	*p*
Left anterior cingulate cortex	-.42	-1.94	.08
Left middle frontal gyrus	.29	.65	.53
Left dorsolateral prefrontal cortex	.30	1.06	.31
Broca's area (pars opercularis)	-.16	-.59	.57
Left superior parietal gyrus	.40	.74	.47
Left supramarginal gyrus	.09	.40	.70
Left angular gyrus	-.09	-.27	.80
Left precuneus	-.21	-.57	.58
Left thalamus	-.76	-5.17	<.001[a]
Visual Orienting (Center Cue – Spatial Cue RT)			
Left anterior cingulate cortex	.23	.58	.58
Left middle frontal gyrus	-.15	-.18	.86

Left dorsolateral prefrontal cortex	-.04	-.08	.94
Broca’s area (pars opercularis)	.39	.78	.45
Left superior parietal gyrus	.33	.33	.75
Left supramarginal gyrus	-.28	-.64	.54
Left angular gyrus	.27	.42	.68
Left precuneus	-.75	-1.09	.30
Left thalamus	.22	.82	.43
Visual Executive Control (Incongruent – Neutral RT)			
Left anterior cingulate cortex	.52	2.06	.06
Left middle frontal gyrus	-.36	-.71	.50
Left dorsolateral prefrontal cortex	-.15	-.44	.67
Broca’s area (pars opercularis)	.34	1.07	.31
Left superior parietal gyrus	1.38	2.21	.05[a]
Left supramarginal gyrus	-.33	-1.20	.26
Left angular gyrus	-1.16	-2.84	.02[*]
Left precuneus	-.26	-.60	.56
Left thalamus	-.37	-2.11	.06

*significant at *p*<.05

[a] Region of interest elicits a statistically significant finding in the unexpected direction (i.e., larger percent of intact tissue predicting worse performance). This is a common finding in lesion-symptom mapping and aphasia research due to lesion locations not being independent of one another, but should not be interpreted as intact tissue equaling impairment.

Auditory Attention

The overall model predicting auditory alerting attention was significant [R^2=.89, F(9,11)=9.58, *p*<.001] with the left supramarginal gyrus being the sole significant predictor (β= .50, *p*=.01). The overall model predicting auditory orienting attention was also significant [R^2=.84, F(9,11)=6.30, *p*=.003] with Broca’s area (pars opercularis; β=.72, *p*=.01) being the significant predictor. For auditory executive control, the overall model was not significant [R^2=.31, F(9,11)=.54, *p*=.82] (Table 8).

Table 8. Multiple regression models predicting auditory attention.

Auditory Alerting (No Cue – Double Cue RT)			
Predictors	β	*t*	*p*
Left anterior cingulate cortex	.008	.05	.96
Left middle frontal gyrus	.31	.96	.36
Left dorsolateral prefrontal cortex	.04	.21	.84
Broca's area (pars opercularis)	-.12	-.63	.54
Left superior parietal gyrus	-.003	-.008	.99
Left supramarginal gyrus	.50	2.91	.01*
Left angular gyrus	-.90	-3.55	.005[a]
Left precuneus	.50	1.85	.09
Left thalamus	-.93	-8.70	<.001[a]
Auditory Orienting (Center Cue – Spatial Cue RT)			
Left anterior cingulate cortex	.30	1.61	.14
Left middle frontal gyrus	-.94	-2.48	.03[a]
Left dorsolateral prefrontal cortex	.45	1.86	.09
Broca's area (pars opercularis)	.72	3.11	.01*
Left superior parietal gyrus	.16	.35	.73
Left supramarginal gyrus	-.45	-2.19	.05[a]
Left angular gyrus	-.25	-.82	.43
Left precuneus	.58	1.78	.10
Left thalamus	-.50	-3.91	.002[a]
Auditory Executive Control (Incongruent – Neutral RT)			
Left anterior cingulate cortex	.32	.84	.42
Left middle frontal gyrus	-.79	-1.01	.34
Left dorsolateral prefrontal cortex	.21	.41	.69
Broca's area (pars opercularis)	.48	1.00	.34
Left superior parietal gyrus	1.53	1.60	.14
Left supramarginal gyrus	-.18	-.43	.67
Left angular gyrus	-.19	-.31	.76
Left precuneus	-1.02	-1.52	.16
Left thalamus	.12	.46	.66

*significant at $p<.05$

[a] Region of interest elicits a statistically significant finding in the unexpected direction (i.e., larger percent of intact tissue predicting worse performance). This is a common finding in lesion-symptom mapping and aphasia research due to lesion locations not being independent of one another, but should not be interpreted as intact tissue equaling impairment.

Discussion

The purpose of this experiment was to identify the relationship between relatively intact brain regions post-stroke, presentation modality, and three well-studied aspects of attention (alerting, orienting, and executive control). In the visual domain, there were no significant predictors of alerting or orienting attention. Visual executive control was predicted by having a greater proportion of the left angular gyrus intact. For auditory attention, a more intact left supramarginal gyrus predicted alerting attention and a more intact Broca's area (pars opercularis) predicted orienting attention; there were no significant predictors of auditory executive control.

Visual Attention

Visual attention is generally supported by a bilateral neural network (Corbetta & Shulman, 2002; Petersen & Posner, 2012; Posner & Petersen, 1990; Ungerleider & Haxby, 1994; Vossel, Geng, & Fink, 2014). However, lateralization of the specific neural resources differs depending on the subtype of attention being investigated. For example, in neurotypical controls, visual alerting attention is frequently associated with the right prefrontal and parietal cortices, orienting attention with the right parietal cortex, and executive control with the left prefrontal cortex and anterior cingulate cortex (Fan, Mccandliss, Fossella, Flombaum, & Posner, 2005; Petersen & Posner, 2012; Posner & Petersen, 1990; Rinne et al., 2013). This bilateral organization of visual attention likely makes visual attention more resilient to stroke lesions and may have contributed to fewer brain regions in the left hemisphere being associated with visual attention.

In the present study, stroke patients with a larger proportion of the left angular gyrus intact demonstrated greater visual executive control abilities. The left angular gyrus is not routinely associated with executive control attention in control subjects. But, impairments filtering out irrelevant visual information have been associated with both the left and right angular gyri (Friedman-Hill, Robertson, Desimone, & Ungerleider, 2003; Schiff, Bardi, Basso, & Mapelli, 2011; Studer, Cen, & Walsh, 2014). For example, Friedman-Hill and colleagues (2003) identified a patient with bilateral lesions to the angular gyri to have deficits making visual discriminations in the presence of distractors. Similarly, decision-making deficits have been observed when transcranial magnetic stimulation was applied over both the left and right angular gyri (Schiff et al., 2011; Studer et al., 2014). This evidence suggests that the left angular gyrus is involved in visual executive control to some extent.

The left angular gyrus may support visual executive control via the bilaterally organized fronto-parietal network. While the angular gyrus is traditionally associated with the default mode network (Greicius, Krasnow, Reiss, & Menon, 2003; Power et al., 2011), it has also been linked to the fronto-parietal network (Yeo et al., 2011). The fronto-parietal network plays a role in selecting and maintaining goal relevant information in the presence of distractors (Cieslik et al., 2015). Collectively, this evidence suggests that the left angular gyrus is an important component of a larger neural network that maintains visual executive control abilities post-stroke.

Auditory Attention

Alerting attention is the process of being ready to act on a stimulus and can be deconstructed into tonic and phasic alertness. Tonic alertness is intrinsic alertness, which naturally fluctuates throughout the day (i.e., circadian rhythms) while phasic alertness is the rapid change in attention due to the onset of an external event (Petersen & Posner, 2012). Phasic alertness is commonly studied using paradigms in which a warning cue precedes the target stimulus (as in the current experiment). Visual and auditory tonic and phasic alertness are both associated with the thalamus, brainstem, and bilateral fronto-parietal cortices (Fan, Mccandliss, Fossella, Flombaum, & Posner, 2005; Petersen & Posner, 2012; Rinne et al., 2013; Sturm & Willmes, 2001). Yet, phasic alertness measured using both visual and auditory warning cues has additionally been associated with a left lateralized fronto-parietal network (Coull, Frackowiak, & Frith, 1998; Sturm & Willmes, 2001). Sensory modality has additionally been shown to affect the neural resources supporting alerting attention. Thiel and Fink (2007) associated visual alerting with the bilateral inferior occipital gyri and posterior parietal cortices and auditory alerting with the bilateral superior temporal gyri and frontal cortices. The results from the present experiment partially correspond with Coull et al.'s (1998) and Thiel and Fink's (2007) findings: stroke participants with a larger proportion of the left supramarginal gyrus intact demonstrated better auditory alerting attention abilities.

The other noteworthy finding regarding auditory attention was the relationship between Broca's area (pars opercularis) and auditory orienting attention: participants with a larger proportion of the pars opercularis intact demonstrated greater auditory orienting attention abilities. Visual and auditory orienting attention, characterized as the selection of specific information from a given stimulus (Fan et al., 2002; Posner & Petersen, 1990), is most commonly associated with the bilateral temporal-parietal junction, bilateral interparietal sulcus, bilateral superior parietal lobe, and bilateral frontal eye fields, with a more right hemisphere bias observed in both modalities (Bareham et al., 2018; Fan et al., 2005; Petersen & Posner, 2012; Pugh et al., 1996; Rinne et al., 2013). Auditory orienting has additionally been associated with activation in the bilateral inferior frontal gyrus (pars opercularis) and middle frontal gyrus (Alho, Salmi, Koistinen, Salonen, & Rinne, 2015; Pugh et al., 1996). The findings from the present study associating Broca's area (pars opercularis) with auditory orienting attention align with the work from Alho et al. (2015) and Pugh et al. (1996), and indicate that left prefrontal cortices may be more involved in auditory orienting attention than visual orienting attention.

Orienting attention, in either domain, is supported by a combination of top-down and bottom-up processes: bottom-up processes are engaged in reflexive orienting when cues are not predictable while top-down processes are likely engaged when previously established relationships exist between cues and targets (Chica, Bartolomeo, & Valero-Cabré, 2011). In the present version of the auditory ANT, the spatial cues always predicted the location of the target; no "invalid" cues were presented. The use of only valid cues may reduce demands on bottom-up processes as participants quickly learn that the spatial cue location always predicts the location of the target. Invalid cues may utilize bottom-up and/or post-hoc reorienting processes more than valid cues as they are not predictable and stimulus-driven, therefore the prior knowledge provided by the cue will not necessarily aid in predicting the location of the target. Previous work indicates that when both valid and invalid cues are utilized, Broca's area is not associated with orienting cues (i.e., valid cues), but instead is associated with reorienting cues (i.e., invalid cues) (Mayer, Harrington, Stephen, Adair, & Lee, 2007; Mayer et al., 2009). Stroke patients frequently demonstrate deficits in orienting attention (Villard & Kiran, 2017) and these deficits may inhibit their ability to correctly orient towards the location of the cue in the ANT task. This failure to correctly orient to the cue may cause the presentation of the target stimulus to engage post-hoc reorienting processes, which are partially supported by Broca's area. The results from the present experiment suggest that having a larger proportion of Broca's area intact may be beneficial for reorienting towards the target after failing to first orient towards the location of the cue. However, future work is needed to more clearly parse apart the contributions of top-down and bottom-up processing in auditory orienting attention post-stroke.

In general, auditory attention may be more lateralized to the left hemisphere than visual attention due to the types of stimuli used in the visual flanker (i.e., non-linguistic stimuli; arrows) and auditory Stroop tasks (i.e., linguistic stimuli; high, low, day). The linguistic nature of the auditory Stroop may have caused greater engagement of left hemisphere brain regions which can support both attention and speech processing. Sub-regions of both the left supramarginal gyrus and Broca's area (pars opercularis) are both implicated in attention (alerting and orienting, respectively) (Alho et al., 2015; Coull et al., 1998; Petersen & Posner, 2012; Pugh et al., 1996; Sturm & Willmes, 2001; Thiel & Fink, 2007), and speech and language processing (Hickok & Poeppel, 2007; Oberhuber et al., 2016). Thus, the intactness of these regions may be more advantageous for completing the auditory Stroop task compared to the flanker task as the auditory Stroop likely draws upon speech processing resources to some extent, even though participants are instructed to focus on the pitch of the voice, not the semantic content of the word. However, single word comprehension did not correlate with any measure of auditory attention (alerting, orienting, executive control), suggesting that distinct left hemisphere regions [likely within the left supramarginal gyrus and Broca's area (pars opercularis)] are supporting general auditory attention and the more linguistic aspects of the task.

Nonetheless future work should specifically measure auditory attention using both linguistic (like in the present experiment) and non-linguistic auditory (e.g., determining if the pitch of two sequentially presented tones is congruent or incongruent) stimuli. This comparison will ultimately provide a clearer understanding of the relationship between auditory attention and auditory language processing.

The utilization of primarily left hemisphere regions during the auditory ANT may also explain the increased errors stroke participants made on the auditory ANT compared to the visual ANT in Experiment 1a. Stroke participants may have made increased errors on the auditory ANT as this task primarily relies on a left hemisphere attention network that is disrupted and therefore less efficient post-stroke. Alternatively, their visual attention abilities may remain stable post-stroke because the visual attention network is more bilaterally organized (Corbetta & Shulman, 2002; Petersen & Posner, 2012; Posner & Petersen, 1990; Ungerleider & Haxby, 1994; Vossel et al., 2014), and therefore can more adequately be supported by right hemisphere networks when left hemisphere brain regions are damaged post-stroke. However, further quantification of the neural resources supporting both visual and auditory attention is needed in a larger cohort that includes patients with right hemisphere lesions to test this possibility.

Conclusion

The present experiment investigated the relationship between three components of auditory and visual attention and the neural resources supporting each post-stroke. Using well-studied versions of the ANT task in the visual and auditory modalities, a more intact left angular gyrus was associated with better visual executive control abilities while a more intact left supramarginal gyrus predicted better auditory alerting attention, and a more intact Broca’s area (pars opercularis) predicted better auditory orienting attention abilities. Overall, these findings indicate that auditory alerting and orienting attention may be more left lateralized in the auditory than the visual domain, thus these aspects of auditory attention may be more susceptible to impairment after a left hemisphere stroke.

CHAPTER 5

EXPERIMENT 2A: PROSODY, COGNITION, AND SENTENCE COMPREHENSION POST-STROKE

Introduction

Sentence structure and prosody (i.e., rhythm and pitch changes associated with spoken language) interact to facilitate sentence comprehension in neurotypical adults. For example, the comprehension of some complex, non-canonical sentence structures has been shown to be facilitated when complex sentences are presented with a typical prosody compared to an atypical prosody (LaCroix et al., in revision; Roncaglia-Denissen et al., 2013). It is hypothesized that this interaction is driven by prosody reducing demands placed on cognitive resources such as attention and working memory involved in sentence comprehension (Kjelgaard & Speer, 1999; Roncaglia-Denissen et al., 2013; Speer et al., 1996). However, for persons with aphasia, who may have cognitive deficits, prosodic cues may instead help to selectively engage relatively intact cognitive resources, and thus, facilitate sentence comprehension. The purpose of this experiment was to identify the relationship between prosody and cognition during sentence comprehension in persons with aphasia and matched-controls.

The overall prosody of a sentence may facilitate sentence comprehension by allowing for more efficient use of specific cognitive resources. For example, typical sentence prosody, which contains meaningful pitch inflections and prosodic boundaries, may facilitate sentence comprehension by directing listener attention towards important elements of the sentence (Schafer, 1997). In general, prosodic boundaries (i.e., pauses) aid in the division of sentences into smaller, more manageable units, while pitch inflections focus listener attention. For example, changes in pitch have been shown to cue listeners about new or contrasting information (Dahan, 2015; Dahan et al., 2002; Ito & Speer, 2008; Weber et al., 2006). Pitch inflections have also been shown to resolve ambiguities related to pronoun and clause attachment (Lakoff, 1971; Schafer, 1996).

Like sentence prosody, list prosody (i.e., prosody in which equal emphasis and stress is placed on each word) may also facilitate sentence comprehension. However, instead of directing listeners' attention, list prosody may create temporal expectancy effects that aid the chunking of information within working memory resources (Gilbert et al., 2014). Previous research indicates that temporal expectancy can be created through rhythmic cueing prior to the stimulus, which subsequently improves speech comprehension (Cason & Schön, 2012). Temporal expectancy can also be embedded within the speech stimulus itself; the equal emphasis and stress associated with list prosody creates regularly timed intervals and this leads to the creation of temporal expectation. Individuals naturally group the speech signal into three to four units/chunks of meaningful information (e.g., syllables, words) (Broadbent, 1975; Cowan, 2001). Therefore, the temporal expectancy effects created by list prosody may facilitate sentence comprehension by helping an individual to correctly group information in the sentence in real time. Collectively, this evidence suggests that using prosody to more efficiently engage cognitive resources may be advantageous to sentence comprehension, perhaps because an initial correct parse prevents the need for re-analysis.

Using prosody to prevent the need for re-analysis is particularly important for complex sentence structures. When the sentence structure is simple and contains subject-verb-object word order (e.g., *The boy is kissing the girl who is tall)*, prosodic cues may not be important as the linear structure makes it easy to deduce who is doing what to whom as well as determining who *is tall*. However, for more complex sentence structures with subject-object-verb word order (e.g., *The boy who the girl is kissing is tall)*, prosodic cues are important as the sentence structure is non-linear making the thematic roles and who *is tall* initially unclear. Without sufficient prosodic cues, re-analysis will be required, which may be costly to sentence comprehension as it places extra demands on cognitive resources. For example, to re-analyze the sentence, *The boy who the girl is kissing is tall*, and deduce the relationship between the agent and patient, the listener must actively maintain the sentence in focal attention while simultaneously manipulating the sentence (i.e., attaching *is tall* to *the boy* and assigning *kissing* to *the girl*) in working memory. Re-analysis of the aforementioned complex sentence can be prevented if a prosodic boundary (i.e., pause) is placed after *boy* and *kissing* as this will help the listener assign thematic roles and successfully attach *is tall* to *the boy* during the first presentation of the sentence.

Using prosody to more efficiently engage cognitive resources during sentence comprehension may be particularly important for individuals with reduced cognitive capacities, including individuals with aphasia.[6] Previous research suggests that patients with aphasia benefit from prosodic cueing (Lasky et al., 1976; Pashek & Brookshire, 1982). Patients with aphasia demonstrated increased sentence comprehension accuracy when sentences (Lasky et al., 1976) and paragraphs (Pashek & Brookshire, 1982) were presented with a reduced speech rate and exaggerated linguistic stress. Importantly,

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[6] While aphasia is classically thought to be a language-specific disorder, ample evidence indicates that cognitive deficits frequently co-occur (Caplan, Michaud, & Hufford, 2013; Fridriksson, Nettles, Davis, Morrow, & Montgomery, 2006; Murray, 2012).

exaggerated linguistic stress increased sentence comprehension performance independent of speech rate (Lasky et al., 1976; Pashek & Brookshire, 1982). While cognition was not explicitly measured in this study, the results suggests that strategic placement of pitch inflections and prosodic boundaries in the exaggerated linguistic stress conditions may have increased sentence comprehension as the prosodic cues drew the patients' attention to important sentential information.

Similar findings have been observed regarding working memory and sentence comprehension in neurotypical adults. In a study comparing individuals with low and high working memory capacity, King and Just (1991) demonstrated that individuals with lower working memory capacities had longer reading times and lower comprehension accuracies for complex object-relative sentences; no comprehension differences between the groups were observed for the simpler subject-relative sentences. Furthermore, individuals with high working memory capacities demonstrated reduced sentence comprehension when asked to simultaneously complete a working memory task. These results indicate that a reduction in the cognitive resources available for processing language results in an overall decrease in comprehension for complex non-canonical sentence structures.

Another notable finding from King and Just (1991) was when sentences contain meaningful pragmatic information (i.e., the use of verbs that give clues as to which of the two actors in the sentence completed the task), individuals with low working memory capacity experienced gains in comprehension. An example of a sentence containing meaningful pragmatic information is as follows: "The robber that the fireman *rescued stole* the jewelry." Here the words *rescued* and *fireman* are associated because firemen are more likely to rescue than robbers. The same is true of the verb *stole* and its association with *robber*. However, when the sentence does not contain meaningful pragmatic information, e.g., “The robber that the fireman *detested watched* the program,” it is less obvious who is watching the program as both actors in the sentence are equally likely to do so. King and Just’s (1991) results demonstrate that all participants have greater comprehension when sentences contained meaningful pragmatic information compared to when they did not; however, the gains were greatest for individuals with low working memory capacity. These results suggest that individuals with lower cognitive abilities are less likely to be able to effectively utilize syntactic cues, possibly because they place greater demands on cognitive resources; and instead, depend more on word-level semantic information, which may be less cognitively taxing during sentence comprehension. Prosodic cues may function similarly to word-level semantic information for individuals with impaired cognitive resources (i.e., prosodic cues may provide additional information, beyond syntax, that helps parse the sentence). However, this relationship between prosody and cognition in relation to sentence comprehension has yet to be explored.

The following experiment will examine how prosody-related sentence comprehension differences may be related to working memory and/or attentional control abilities in persons with aphasia and matched-controls. This relationship between prosody and cognition was specifically explored within the context of non-canonical sentence comprehension because patients with aphasia[7] have relatively specific deficits in comprehension of complex, non-canonical sentence structures (Bradley et al., 1980; Caramazza & Zurif, 1976). It was hypothesized that: (1) attentional control abilities will best predict comprehension of non-canonical sentences spoken with sentence prosody while (2) working memory abilities will best predict comprehension of non-canonical sentences spoken with list prosody.

Method

Participants

Participants were 25 chronic stroke patients (14 females) who experienced a single left hemisphere cerebral stroke[8] at least 6 months prior to testing (Table 9). Stroke participants ranged in age from 28 to 80 years (*M* = 54.20, *sd* = 13.23). Stroke participants were pre-morbidly right-handed, native speakers of American English, 18+ years of age, with no history of neurological disease, head trauma, or psychiatric disturbances prior to their stroke. An additional 20 controls (14 females) ranging in age from 31 to 79 years (*M* = 51.40, *sd* = 12.82) who were also right-handed, native speakers of American English, 18+ years of age, with no history of neurological disease, head trauma, or psychiatric disturbances were also recruited. The stroke and control groups did not significantly differ from each other in terms of age, gender, education, and hearing

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[7] Agrammatic comprehension (i.e., complexity-related sentence comprehension deficits) has primarily been studied in persons with Broca's aphasia, but this same phenomenon is also reported in conduction aphasia (Caramazza & Zurif, 1976).

[8] One participant had two strokes ten years apart and a second participant had a single stroke resulting in a bilateral lesion.

status (Table 10). All participants were monetarily compensated for their participation. Arizona State University's Institutional Review Board approved all procedures.

Table 9. Stroke group demographics.

	Gender	Age	Months Post Stroke	Years of Education	Aphasia Diagnosis
AZ1001	Female	57	77	18	None
AZ1003	Female	48	110	19	Broca's
AZ1006	Male	60	138	14	Broca's
AZ1011	Female	73	53	16	Anomic
AZ1012	Male	77	85	16	Wernicke's
AZ1013	Female	47	258	17	Broca's
AZ1016	Male	37	142	14	Broca's
AZ1018	Female	43	29	14	Broca's
AZ1022	Female	46	79	14	Broca's
AZ1026	Male	70	50	16	None
AZ1028	Female	80	19	24	Wernicke's
AZ1029	Female	34	174	14	None
AZ1030	Male	56	32	16	Broca's
AZ1031	Female	40	63	20	Broca's
AZ1032	Male	28	20	13	Anomic
AZ1033	Male	57	180; 60	14	Global
AZ1034	Female	59	110	15	Anomic
AZ1035	Female	41	72	17	Broca's
AZ1036	Male	65	158	15	Broca's
AZ1037	Male	57	13	16	Broca's
AZ1038	Male	54	155	14	Broca's
AZ1039	Female	66	48	14	Anomic
AZ1040	Female	54	45	14	Broca's
AZ1041	Female	59	24	12	Anomic
AZ1042	Male	55	37	14	Broca's

Table 10. Demographic comparisons between stroke and control groups.

	Stroke (n=25)	Controls (n=20)	Statistic
Age	54.52 (13.23)	51.40 (12.82)	*t*(43)=.80, *p*=.43
Gender (male/female)	11/14	6/14	$\chi^2(1)$=.93, *p*=.34
Education (years)	15.6 (2.57)	15.20 (2.17)	*t*(43)=.56, *p*=.58
Hearing Status[a]	15.45 (12.42)	13.43 (9.07)	*t*(43)=.61, *p*=.55

[a] Pure tone average for better ear; 500-4000 Hz

Stimuli

Sentences. Stimuli were a subset of sentences (10 syllables each) representing two sentence structures (canonical and non-canonical) previously reported by Wilson et al. (2010, 2014, 2016). All sentences contained two nouns (boy, girl), one of seven verbs (hit, push, kick, kiss, wash, pull, hug), and one of three color adjectives (blue, green, red); thematic role assignment, verb, and adjective use were balanced across all sentence structures. See Table 9 for descriptions and examples.

Prosody manipulations. All sentences were spoken with both sentence prosody (i.e., natural prosody) and list prosody (i.e., monotone prosody which lacks pitch inflections and meaningful prosodic boundaries). Stimuli were digitally recorded by a classically trained female vocalist in Audacity sound editing software using a 32-bit resolution and 44,100 Hz sampling rate. Loudness was matched across all stimuli.

To generate the sentences with sentence prosody, the speaker spoke each sentence with natural intonation. The speaker was instructed to accentuate key words needed to parse the sentence with pitch inflections and prosodic boundaries. Sentences with list prosody were generated by recording each word in isolation, out of sentence context, and then concatenating the individual words in the order of the experimental sentence. The inter-word interval for the list prosody sentences was 20 milliseconds. Durations for sentences spoken with sentence prosody and sentences spoken with list prosody are reported in Table 11.

Table 11. Sentence stimuli.

Sentence Structure*	Example	Syntactic Parsing	Sentence Prosody Duration	List Prosody Duration
Canonical	The boy who is red is kissing the girl.	Subject-verb-object word order. Active modifying clause can only be attached to the subject.	3.81-4.45 seconds (*M*=4.07, *sd*= .13)	4.52-4.79 seconds (*M*=4.68*, sd*= .07).
Non-Canonical	The girl who the boy is kissing is red.	Subject-object-verb word order. Active modifying clause can be attached to either the subject or object; correct parsing leads to attachment of modifying clause to the subject.	3.88-4.73 seconds (*M*=4.29, *sd*= .15)	4.53-4.80 seconds (*M*=4.72*, sd*= .07).

*The canonical sentences correspond to one of the two types of sentences within Wilson et al.'s (2010) "long easy" sentences. The non-canonical sentences correspond to Wilson et al.'s (2010) "long medium."

Experimental Design

As part of a larger test battery, participants completed a sentence-picture matching task, the auditory Attention Network Test (ANT) from Experiment 1, the *Wechsler Adult Intelligence Scale-IV* Working Memory Index, the Immediate Memory and Attention indices from the *Repeatable Battery for the Assessment of Neuropsychological Status (RBANS),* and the short form of the *Boston Diagnostic Aphasia Examination-III (BDAE-*

III) single-word auditory comprehension subtest. Pure tone audiometric thresholds (500-4000 Hz) were also measured on all participants.

Sentence-picture matching task. The sentence-picture matching task has previously been used by Wilson et al. (2010; 2014). Like the task in Wilson et al. (2010; 2014), each trial began with the simultaneous presentation of an auditory sentence and a target and foil picture (positioned left and right respectively and counterbalanced across trials). Foils were either thematic (i.e., role reversal of agent and patient) or color based (i.e., color assigned to wrong agent/patient) and were counterbalanced across trials. Participants were instructed to decide which picture matched the target sentence as quickly and accurately as possible, with accuracy being emphasized over speed. Response accuracy and reaction time were recorded for each trial via a keyboard button press. After the participant responded, a black fixation cross appeared for one second before initiation of the next trial (Figure 6A). Stimulus presentation was randomized for each participant. Verbal and written instructions, examples of all stimuli, and three practice trials preceded the start of the experiment.

The entire paradigm consisted of 80 experimental trials and 10 rest trials. Of these 80 trials, 40 trials were of interest to this experiment, resulting in four experimental conditions (two sentence structures x two prosody manipulations) with each condition containing 10 sentence presentations. From these four experimental conditions, we isolated the additional processing load associated with non-canonical sentence processing using absolute difference scores to create two dependent variables: (1) non-canonical sentence reaction time – canonical sentence reaction time within sentence prosody and (2) non-canonical sentence reaction time – canonical sentence reaction time within list prosody. For both dependent variables, reaction time difference scores closer to zero reflect better sentence comprehension abilities.

Auditory Attention Network Task (ANT). The same auditory ANT used in Experiment 1 was used to measure alerting (no cue reaction time – double cue reaction time), orienting (center cue reaction time – spatial cue reaction time), and executive control (incongruent target reaction time – congruent target reaction time) attention (Figure 6B). Executive control was calculated using congruent trials as the baseline condition based on the conclusions from Experiment 1 indicating that auditory neutral trials function similarly to auditory incongruent trials, especially for stroke patients. Calculating executive control by subtracting congruent trials from incongruent trials has been implemented in several previous studies (Chica et al., 2012; Ishigami et al., 2016; Ishigami & Klein, 2011; Jennings, Dagenbach, Engle, & Funke, 2007; Spagna et al., 2015; Stewart & Amitay, 2015; Wang et al., 2014; Zhou et al., 2011). As in Experiment 1, larger alerting and orienting reaction time difference scores indicate better alerting and orienting attention abilities (i.e., participants respond faster to the alerting or orienting cue compared to the comparison cue), while reaction time difference scores closer to zero reflect better executive control attention (i.e., similar levels of executive control are necessary for incongruent and congruent trials).

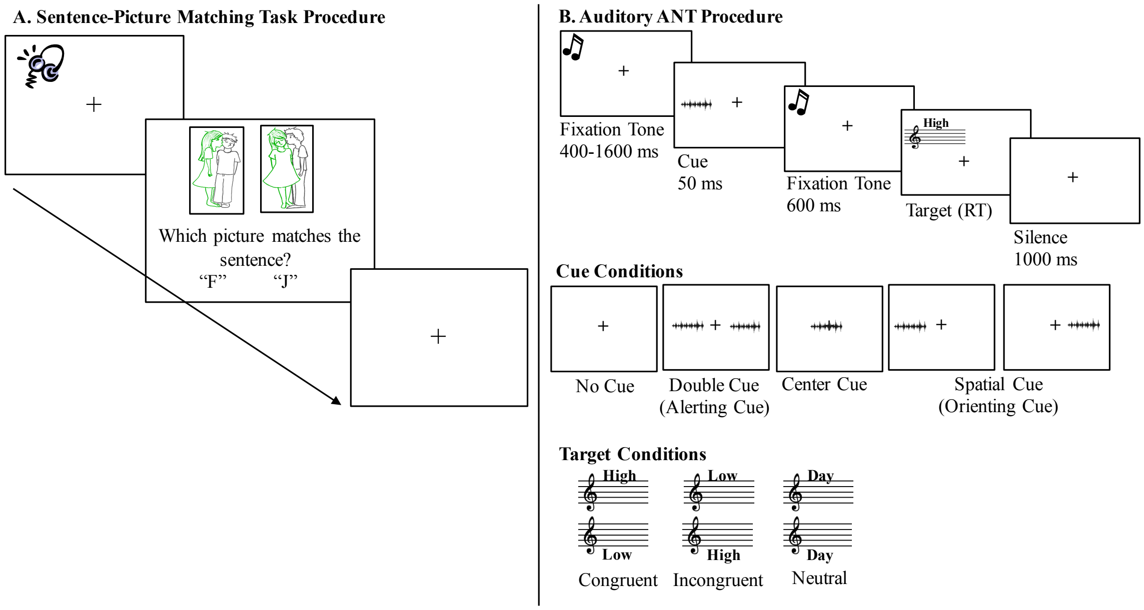

Figure 6. Illustration of the (A) sentence-picture matching task and (B) auditory ANT procedures.

Wechsler Adult Intelligence Scale-IV (WAIS-IV). Working memory was measured using the *WAIS-IV* Working Memory Index. The *WAIS-IV* Working Memory Index is an age-adjusted standardized measure (*M*=100, *sd*=±15) where larger scores represent better working memory abilities. The *WAIS*-IV Working Memory Index is comprised of the Digit Span and Arithmetic subtests. In the Digit Span subtest, participants are read a series of numbers of increasing length and asked to recall the numbers in either the order presented, reverse order, or ascending order. The Arithmetic subtest has participants mentally solve auditorily presented mathematical problems of increasing complexity.

Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Memory and attention were additionally assessed using two indices from the *RBANS*. The

Immediate Memory index, comprised of the list learning and story memory subtests is primarily a measure of short-term memory[9] while the Attention index, comprised of the digit span and coding subtests, is a measure of basic attentional processes (e.g., sustained attention). The *RBANS* was chosen because it is an age-adjusted standardized assessment (with each index being centered around a mean of 100 and standard deviation of ±15; larger scores indicate better cognitive abilities). Additionally, the *RBANS* is routinely available in clinical settings, has a short completion time (30 minutes), and is preferable to other similar tests such as the *Cognitive-Linguistic Quick Test* as it contains a measure of both attention and memory making it a useful screener of initial deficits. The *RBANS* also contains parallel forms, making it easier to track progress over the course of therapy. Therefore, in addition to standard laboratory assessments, attention and memory were assessed using the *RBANS* to meaningfully extend the results into speech-language pathology clinical practice, specifically in the rehabilitation setting.

Boston Diagnostic Aphasia Examination-III (BDAE-III) **Short Form.** The *BDAE-III* short form was used to assess auditory single-word comprehension. In this subtest, participants point to various familiar objects/pictures (e.g., body parts, animals, vehicles, etc.) following a verbal prompt from the examiner (e.g., Point to your shoulder). Participants could achieve a maximum raw score of 16; larger scores represent better single word comprehension. The *BDAE-III* short form does not provide cut-off scores indicating impairment, however, the raw scores do correspond with percentiles to

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[9] Short-term memory has been previously linked to sentence comprehension deficits in aphasia (Caplan et al., 2013; Pettigrew & Hillis, 2014; Potagas, Kasselimis, & Evdokimidis, 2011).

facilitate comparison with the norming sample. For example, a score of 15 out of 16 is equivalent to the 60th percentile (i.e., participants achieving a score of 15, score better or the same as 60% of the population; this indicates that some degree of impairment is associated with one erroneous response on the *BDAE-III* short form). Importantly, auditory single-word comprehension on the *BDAE-III* short form positively correlates (r=.77) with the *BDAE-III* standard form, indicating the short form is a reliable measure of auditory single-word comprehension.

Data Analysis

Sentence-picture matching task analysis. Previous work consistently associates increased processing demands with non-canonical sentences (i.e., longer reactions times and decreased accuracy) compared to canonical sentences in both controls (Ferreira, 2003; King & Just, 1991; Roncaglia-Denissen et al., 2013; Wilson et al., 2010) and patients with aphasia (Caplan et al., 2013; Caramazza & Zurif, 1976; Rogalsky et al., 2018). Similarly, typical sentence prosody is associated with faster reaction times and higher accuracy compared to irregular prosodic patterns (Kjelgaard & Speer, 1999; Roncaglia-Denissen et al., 2013; Speer et al., 1996). To facilitate comparison with previous work, we first analyzed the reaction time data using a repeated-measures ANOVA with two levels of sentence structure (non-canonical, canonical) and two levels of prosody (sentence prosody, list prosody).

Cognitive measures to predict sentence comprehension. The purpose of this study was to investigate the relationship between cognition, prosody, and sentence comprehension. The data was analyzed in two-steps. In step one, bivariate correlations were evaluated between potential covariates [auditory single word comprehension, pure tone audiometry (500-4000 Hz better ear), age, education, time post-stroke] and the dependent variables: (1) non-canonical sentence reaction time – canonical sentence reaction time within sentence prosody (hereafter non-canonical sentences spoken with sentence prosody) and (2) non-canonical sentence reaction time – canonical sentence reaction time within list prosody (hereafter non-canonical sentences spoken with list prosody). Covariates which significantly correlated with at least one of the dependent variables were included in the multiple regression analyses. In step two, multiple regressions were used to predict the dependent variables (non-canonical sentences spoken within sentence prosody and non-canonical sentences spoken within list prosody) from the independent variables (alerting attention, orienting attention, executive control attention, *WAIS-IV* Working Memory Index*, RBANS* Immediate memory and Attention indices).

Reaction times associated with incorrect responses and those greater than 2.5 standard deviations from each participant's mean were excluded from the analyses; this data trimming procedure was determined *a priori* based on it being a standard, well-studied approach in psycholinguistic research (Baayen & Milin, 2010; Lachaud & Renaud, 2011; Ratcliff, 1993). This approach aims to capture the middle 85% of the distribution of the reaction time measurements and is based on the assumption that the process of interest is being captured, not other extraneous factors (e.g., brief distractions, button press mistakes, etc.). Consistent with the above procedure, 14.56% of the data was removed for the auditory ANT and 24.08% from the sentence-picture matching task for the aphasia group; however, it should be noted that the majority of the trials removed were due to errored responses and only .41% of trials were removed due to standard deviations being greater than 2.5 times an individual participant's mean. For the control group, 4.39% of the data was removed for the auditory ANT and 4.0% from the sentence picture matching task.

Results

Sentence-Picture Matching Task

Replicating previous work, main effects of sentence structure [stroke: F(1, 24)=5.99, *p*=.02; control: F(1, 19)=30.84, *p*<.001] and prosody [stroke: F(1, 24)=6.59, *p*=.02; control: F(1, 19)=73.31, *p*<.001] were observed in both the stroke and control groups with faster correct responses being observed for canonical sentence structures and sentences spoken with sentence prosody (Figure 7; Table 12); this indicates increased processing demands associated with non-canonical sentences and sentences spoken with list prosody. The interaction between sentence structure and prosody was not significant in either group [stroke: F(1, 24)= .23, *p*= .64; control: F(1, 19)=1.62, *p*=.22].

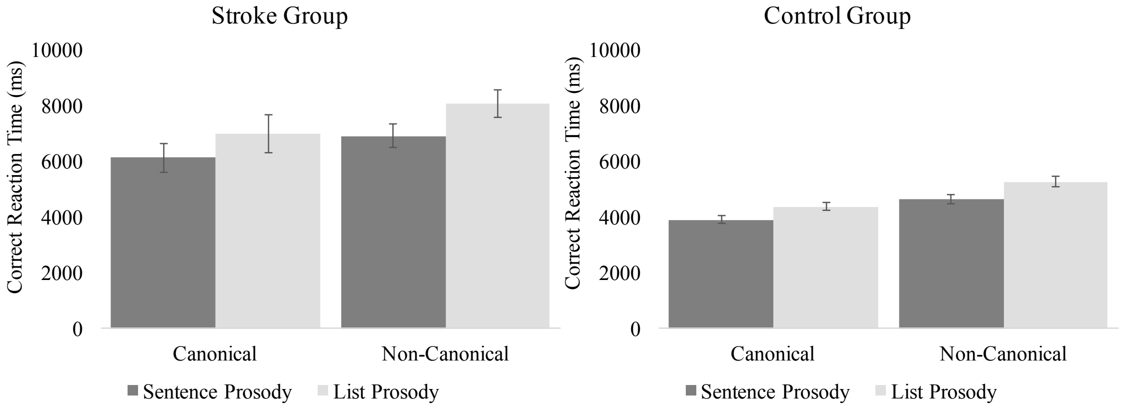

Figure 7. Mean reaction times (milliseconds) for the stroke group (left) and control group (right) for sentence structure separated by prosody. Error bars show SEM.

Table 12. Mean reaction times and standard deviations of the mean for canonical and non-canonical sentences spoken in sentence prosody and list prosody.

	Condition	Sentence Prosody Mean (sd)	List Prosody Mean (sd)
Control Group (n=20)	Canonical	3895.75 (637.60)	4355.56 (647.05)
	Non-Canonical	4618.34 (726.63)	5254.79 (833.28)
	RT Difference Score	786.60 (2189.26)	1059.43 (2628.75)
Stroke Group (n=25)	Canonical	6118.55 (2592.96)	6966.18 (3392.18)
	Non-Canonical	6905.15 (2173.53)	8042.40 (2460.26)
	RT Difference Score	722.60 (758.55)	899.24 (686.06)

Cognitive Measures Predicting Sentence Comprehension

Means and standard deviation of the means for each cognitive variable are reported in Table 13 for both groups. Separate multiple regression models were conducted for each group to determine the relationship between short-term memory (*RBANS* Immediate Memory index*)*, working memory (*WAIS-IV* Working Memory Index), and auditory attention (alerting, orienting, and executive control as measured by the auditory ANT and *RBANS* Attention index), and comprehension of non-canonical sentences spoken with sentence prosody and non-canonical sentences spoken with list prosody while accounting for the potential covariates [auditory single word comprehension, pure tone audiometry (500-4000 Hz better ear), age, education, time post-stroke].

Table 13. Means and standard deviations of the mean for each cognitive variable.

Cognitive Variable	Control Group Mean (sd)	Stroke Group Mean (sd)
Auditory Alerting	7.91 (44.28)	21.27 (209.35)
Auditory Orienting	-6.43 (44.75)	20.37 (119.24)
Auditory Executive Control	123.09 (56.77)	183.15 (232.22)

WAIS-IV Working Memory Index	108.15 (13.06)	70.96 (17.14)
RBANS Immediate Memory Index	96.59 (24.39)	65.24 (19.46)
RBANS Attention Index	102.25 (28.89)	64.12 (19.39)

Stroke group. Of the potential covariates, only auditory single-word comprehension significantly correlated with the dependent variables (Table 14). The overall regression model predicting non-canonical sentences spoken with sentence prosody was significant [R^2 =.55, F(7,17)=2.96, *p*=.03] with auditory single word comprehension (β=.61, *p*=.02) and auditory orienting attention (β= -.47, *p*=.04) being the significant predictors (Table 15). For non-canonical sentences spoken with list prosody, the overall regression model was significant [R^2 =.65, F(7,17)=4.44, *p*=.006] with the *RBANS* Immediate Memory index being the strongest significant predictor (β=.66, *p*=.008) followed by auditory executive control (β= -.37, *p*=.03) (Table 15).

Table 14. Bivariate correlations between potential covariates and the dependent variable for each group.

Non-Canonical - Canonical Sentences with Sentence Prosody RT		
Covariate	Stroke Group	Control Group
Age	*r*(23)= -.07, *p*=.75	*r*(18)= -.09, *p*=.70
Single Word Comprehension	*r*(23)= .58, *p*=.003*	*r*(18)= -.07, *p*=.77
Hearing Status	*r*(23)= -.08, *p*=.70	*r*(18)= .14, *p*=.57
Years of Education	*r*(23)= .03, *p*=.89	*r*(18)= .21, *p*=.37
Months Post Stroke	*r*(23)= -.26, *p*=.21	*n/a*
Non-Canonical - Canonical Sentences with List Prosody RT		
Age	*r*(23)= -.04, *p*=.84	*r*(18)= -.19, *p*=.43
Single Word Comprehension	*r*(23)= .41, *p*=.04*	*r*(18)= -.08, *p*=.74
Hearing Status	*r*(23)= .01, *p*=.97	*r*(18)= .09, *p*=.71
Years of Education	*r*(23)= -.26, *p*=.21	*r*(18)= .07, *p*=.78
Months Post Stroke	*r*(23)= -.26, *p*=.20	*n/a*
*significant at *p*<.05		

Table 15. Multiple regression models for stroke group.

Non-Canonical - Canonical Sentences with Sentence Prosody RT			
Predictors	β	*t*	*p*
Single Word Comprehension	.61	2.65	.02*
WAIS-IV Working Memory Index	-.60	-1.44	.17
RBANS Immediate Memory Index	.02	.07	.95
RBANS Attention Index	.42	1.04	.31
Alerting Attention	.28	1.31	.21
Orienting Attention	-.47	-2.19	.04*
Executive Control Attention	-.01	-.08	.94
Non-Canonical - Canonical Sentences with List Prosody RT			
Single Word Comprehension	.10	.47	.65
WAIS-IV Working Memory Index	-.67	-1.82	.09
RBANS Immediate Memory Index	.66	2.98	.008*
RBANS Attention Index	.63	1.76	.10
Alerting Attention	.37	1.95	.07
Orienting Attention	.03	.16	.88
Executive Control Attention	-.37	-2.30	.03*
*significant at *p*<.05			

Control group. There were no significant correlations between the potential covariates and the dependent variables for the control group (Table 14). The overall regression model predicting non-canonical sentences spoken with sentence prosody was significant [R^2=.59, F(6,13)=3.17, *p*=.04] with the *RBANS* Immediate Memory index (β= .69, *p*=.05) being the strongest significant predictor followed by auditory orienting attention (β= -.43, *p*=.04) (Table 16). For non-canonical sentences spoken with list prosody, the overall regression model was not significant [R^2=.45, F(6,13)=1.75, *p*=.19] (Table 16).

Table 16. Multiple regression models for control group.

Non-Canonical - Canonical Sentences with Sentence Prosody RT			
Predictors	β	*t*	*p*
WAIS-IV Working Memory Index	-.04	-.16	.87
RBANS Immediate Memory Index	.69	2.16	.05*
RBANS Attention Index	-.61	-1.95	.07
Alerting Attention	-.25	-1.14	.27
Orienting Attention	-.43	-2.23	.04*
Executive Control Attention	.28	1.40	.19
Non-Canonical - Canonical Sentences with List Prosody RT			
WAIS-IV Working Memory Index	-.38	-1.42	.18
RBANS Immediate Memory Index	.77	2.05	.06
RBANS Attention Index	-.64	-1.74	.11
Alerting Attention	.006	.03	.98
Orienting Attention	-.16	-.70	.50
Executive Control Attention	.28	1.19	.26
*significant at $p<.05$			

Discussion

The present experiment looked at the relationship between cognition (short-term memory, working memory, and auditory attention), prosody, and sentence comprehension in stroke participants and matched-controls. The findings indicate that in stroke participants, auditory orienting attention (i.e., being able to select specific information from a stimulus) predicts non-canonical sentence comprehension when sentences are spoken with sentence prosody. More specifically, stroke patients with relatively preserved auditory orienting attention demonstrated greater comprehension of sentences spoken with sentence prosody. Regarding list prosody, both auditory executive control and short-term memory predicted comprehension of non-canonical sentences spoken with list prosody. Interestingly, it was stroke participants with *poor* auditory executive control and/or short-term memory abilities that demonstrated *gains* in comprehension when sentences were spoken with list prosody. These results suggest that good auditory attention abilities are necessary to benefit from the cues characteristic of typical sentence prosody following a left hemisphere stroke. However, when stroke participants have cognitive deficits in auditory attention and/or short-term memory, they may not be able to capitalize on typical prosodic cues, and instead appear to benefit from the list prosody manipulation.

Attention and Sentence Prosody

As hypothesized, attention abilities significantly predicted comprehension of non-canonical sentences spoken with sentence prosody in the stroke participants. Of the four measures of attention entered in the model, orienting attention was the sole significant attention predictor indicating that stroke participants with relatively preserved orienting attention benefit when non-canonical sentences are spoken with sentence prosody. A similar pattern was observed in the control group: participants with better orienting attention demonstrated greater comprehension of sentences spoken with sentence prosody.

In the present experiment, attention was measured using Posner and Petersen's (1990) three measures of attention, alerting, orienting, and executive control, as well as the *RBANS* Attention index. Alerting measures the ability to maintain vigilance towards external stimuli, orienting attention is the ability to select specific information from a given stimulus, and executive control looks at the efficiency of obtaining a correct response when information conflicts within a stimulus (Fan & Posner, 2004; Posner &

Petersen, 1990). The *RBANS* Attention index is a measure of more basic attentional processes (i.e., sustained attention) and processing speed.

Given the intended underlying construct of each attentional process, it is not surprising that orienting attention was the strongest predictor of comprehension of non-canonical sentences spoken with sentence prosody. Sentence prosody contains meaningful pitch inflections and prosodic boundaries that are designed to direct listener attention towards important aspects of the sentence (Dahan, 2015; Schafer, 1997). Therefore, intact orienting attention resources are likely able to capitalize on the meaningful pitch inflections and prosodic boundaries as orienting attention is involved in selecting specific and relevant information from the stimulus (Fan & Posner, 2004; Posner & Petersen, 1990). This suggests that sentence prosody can engage relatively preserved orienting attention abilities in stroke patients to improve their comprehension of non-canonical sentences.

Basic attentional processes such as alerting attention may not be specifically recruited by sentence prosody (or list prosody) *per se*, but may instead be involved in more global aspects of speech comprehension more generally. Alerting attention is involved in the initial engagement following stimulus presentation as well as maintaining vigilance towards external stimuli (Fan et al., 2002; Posner & Petersen, 1990). This suggests that alerting attention is likely engaged by the initial onset of the sentence, but once engagement is established, it may not be crucial for sentence comprehension. Therefore, alerting attention is likely a necessary precursor for speech comprehension in general (single-word, sentence, discourse level, etc.) and not a prosody-specific attention function. The lack of a significant relationship between the *RBANS* Attention index and sentence prosody is likely explained similarly as the *RBANS* Attention index measures a more basic attentional process (i.e., sustained attention). The ability to sustain attention may also be a necessary precursor to sentence comprehension, regardless of prosody, and consequently, will not be specifically engaged by either sentence or list prosody.

Like alerting and sustained attention, executive control may also not be selectively engaged by a specific sentence structure or prosody manipulation. Executive control involves selecting relevant stimulus information while inhibiting irrelevant stimulus information (Fan & Posner, 2004; Posner & Petersen, 1990). In the present experiment, each single sentence only contained relevant information; this possibly equates executive control attentional demands across sentence structures and subsequently negates any potential executive control processing benefits non-canonical sentence structures may gain from sentence prosody. While good executive control abilities are not crucial in the present experiment for comprehending sentences spoken with sentence prosody, good executive control attention is likely necessary when potentially distracting information is presented simultaneously with the sentence as illustrated by (1) the cocktail-party effect, which simulates listening in a restaurant (i.e., a sentence is presented while multiple speakers talk in the background), and (2) sentences that contain semantic or syntactic ambiguities. Regarding the cocktail-party effect, good executive control abilities are likely necessary when participants need to selectively attend to the target stimulus (e.g., a sentence) while inhibiting the irrelevant background information (e.g., multiple background talkers) (Bronkhorst, 2000). Importantly, good executive control abilities have been linked to comprehension of sentences in noisy backgrounds (e.g., restaurants) (Bronkhorst, 2000, 2015). Similarly, good executive control abilities are likely necessary when sentences contain semantic and/or syntactic ambiguities as participants need to inhibit the alternative meaning to correctly select the intended meaning (January et al., 2009).

In addition to auditory orienting attention, the *RBANS* Immediate Memory Index additionally predicted comprehension of sentences spoken with sentence prosody in the control group. Interestingly though, it was control participants with *poor* short-term memory who demonstrated better comprehension of non-canonical sentences spoken with sentence prosody. It has been hypothesized that typical prosodic cues may facilitate sentence comprehension in neurotypical adults by reducing demands placed on cognitive resources during sentence comprehension (Cohen et al., 2001; Kjelgaard & Speer, 1999; Roncaglia-Denissen et al., 2013; Speer et al., 1996). Given this hypothesis, these findings indicate that in addition to directing listener attention to important aspects of the sentence, typical prosodic cues may also improve sentence comprehension by helping participants compensate for deficits in cognitive functions (e.g., short-term memory) that support complex sentence processing. For example, the exaggerated pitch inflections and prosodic boundaries characteristic of sentence prosody may provide participants with a clearer framework for how to group sentence-level information; this subsequently facilitates sentence comprehension by making information easier to maintain while higher-order comprehension processes occur (e.g., thematic role assignment, clause attachment). This function of prosody may be particularly important when the cognitive resources supporting complex sentence comprehension are damaged.

The identification of two predictors (with opposite directionalities) spanning multiple cognitive domains in control participants likely reflects some independence among cognitive resources such as memory and attention in neurotypical adults, and thus affects how each cognitive process relates to sentence prosody. This discrepancy in the directionality of the two predictors (i.e., good orienting attention and poor short-term memory being associated with sentence prosody) may reflect distinct changes in the neural resources supporting each cognitive function. Attention and working memory are at least partially supported by distinct functional networks; attention has been associated with a fronto-parietal network and working memory with the cingulo-opercular network (Wallis, Stokes, Cousijn, Woolrich, & Nobre, 2015). Therefore, changes to one of these networks, possibly due to age, may lead to a dissociation in the relationship between specific cognitive predictors and typical sentence prosody. However, future work is needed to better understand how the neural resources supporting sentence prosody change as a function of age.

Cognitive Deficits and List Prosody

Working memory, measured by the *WAIS-IV* Working Memory Index, did not significantly predict comprehension of non-canonical sentences spoken with list prosody for either group. Instead, auditory executive control and short-term memory (i.e., *RBANS* Immediate Memory index) both predicted comprehension of non-canonical sentences spoken with list prosody for the stroke group. In the control group, the overall regression model was not significant. However, the *RBANS* Immediate Memory subtest (i.e., short-term memory) trended (p=.06) towards significantly predicting comprehension of sentences spoken with list prosody.

Contrary to what was expected, stroke participants with *poor* auditory executive control demonstrated *better* comprehension of sentences spoken with list prosody.

Executive control is a measure of how well conflict can be consciously mitigated when competing information is presented and is largely supported by the dorsolateral prefrontal cortex (Cieslik et al., 2015; Domenech & Koechlin, 2015; January et al., 2009; Kane & Engle, 2002; MacDonald, Cohen, Stenger, & Carter, 2000), but also the parietal lobe (Cieslik et al., 2015; Rinne et al., 2013; Yin et al., 2012) and functional connections between these two regions (Dosenbach et al., 2007; Seeley et al., 2007). Typical sentence prosody has also been shown to be supported by the left dorsolateral prefrontal cortex, particularly Broca's area (den Ouden et al., 2016; Meyer et al., 2004). The similarities in the neural substrates supporting both sentence prosody and executive control attention make it likely that a stroke lesion affecting the dorsolateral prefrontal cortex could potentially result in a stroke patient having poor executive control abilities, as well as deficits in processing typical sentence prosody. Consequently, it is not surprising that persons with stroke with poor executive control attention demonstrate improved comprehension when sentences are spoken with list prosody; this is likely to be particularly true when attentional control abilities are reduced and therefore typical prosodic information cannot be utilized as attentional cues. However, future work is needed to better understand the neural resources supporting each type of prosody.

In addition to deficits in auditory executive control attention, stroke participants with *poor* short-term memory abilities also demonstrate *greater* comprehension of sentences spoken with list prosody. Speech processing relies on a combination of top-down and bottom-up processing mechanisms (de Heer, Huth, Griffiths, Gallant, & Theunissen, 2017). Top-down processes, including short-term memory and attention, likely facilitate sentence comprehension by using previous experiences with language (e.g., knowledge of how prosodic cues group sentence-level information) to parse the sentence's structure. Bottom-up processing mechanisms are used when linguistic information is absent or distorted as individuals are not able to draw upon their previous experiences with language to parse the sentence (Davis, Marslen-Wilson, & Gaskell, 2002). The consistent rhythm of list prosody disrupts the expected prosodic cues and, subsequently, knowledge of how to chunk sentence-level information; therefore, individuals may rely more on bottom-up processing mechanisms to comprehend sentences spoken with list prosody. This ability of list prosody to recruit bottom-up processing mechanisms may be particularly beneficial for individuals with cognitive deficits (e.g., attention, short-term memory) as these individuals are not able to use their previous experience with language (e.g., pitch inflections) to parse the sentence's structure, and may instead need to rely on alternative non-linguistic aspects of language (e.g., rhythm) to parse sentence-level information.

The consistent rhythm generated by list prosody may also facilitate non-canonical sentence comprehension by creating temporal expectancy effects that aid the chunking of information within damaged short-term memory resources. Rhythmic cueing prior to a stimulus has been shown to create temporal expectation and improve speech perception (Cason & Schön, 2012). The results from the present experiment suggest that temporal expectation can also be embedded within the speech stimulus itself and may be generated by the consistent rhythm associated with list prosody. Temporal expectancy may aid stroke patients in managing sentence-level information as having a clear expectation for when new information (e.g., words) will be added may help individuals compensate for deficits in the cognitive resources involved in chunking and the temporary storage of information. Importantly, previous work indicates that information is stored as chunks within short-term memory (Cowan, 2001; Miller, 1956). Therefore, the ability of list prosody's rhythm to generate temporal expectations may be particularly beneficial for individuals with deficits in the cognitive resources supporting the grouping and storage of information (e.g., short-term memory). However, further work is needed to better understand the relationship between list prosody, rhythm, and bottom-up processing mechanisms following a left hemisphere stroke.

As previously mentioned, the relationships between alerting attention and both sentence prosody and list prosody were non-significant. However, it should be noted that although non-significant, the relationship between list prosody and alerting attention was trending towards significance in the stroke group (p=.07). Similar to what was observed regarding auditory executive control, stroke participants with *poorer* auditory alerting abilities demonstrated *greater* gains in comprehension when sentences were spoken with list prosody. Alerting attention is involved in maintaining vigilance towards external stimuli (e.g., sentences) (Fan et al., 2002; Posner & Petersen, 1990) and is likely engaged by the initial onset of a sentence, regardless of prosody, indicating that alerting attention is a necessary precursor to speech comprehension in general. Yet, the relationship between alerting attention and list prosody may be stronger due to the structure of list prosody. List prosody is structured so that there are 20-milliseconds between each word. The structure of list prosody may lead to the re-engagement of alerting attention at the onset of each new word. Given this hypothesis, the trend towards persons with *poorer* alerting attention having *greater* comprehension when non-canonical sentences are spoken with list prosody is plausible as the structure of the list prosody (i.e., 20-

milleseconds of pausing between words) consistently re-engages alerting attention, helping patients to overcome potential deficits in alerting attention. Alternatively, the structure of sentence prosody (i.e., normally fluent prosody with natural pausing) does not afford a person with reduced alerting attention the same assistance as list prosody since sentence prosody solely engages alerting attention at the onset of the sentence. However, future work is needed to better understand the specific aspects of each prosody that recruit each type of attention.

Conclusion

The present study investigated the relationship between cognition, prosody, and sentence comprehension in stroke participants and matched-controls. Using measures of auditory alerting, orienting, and executive control attention, and verbal short-term and working memory, it was found that stroke participants with better auditory orienting attention demonstrated greater comprehension of sentences spoken with sentence prosody. Regarding list prosody, it was found that stroke participants with deficits in auditory executive control and/or short-term memory demonstrated greater comprehension of sentences spoken with list prosody. Overall, these findings indicate that following stroke, individuals need good auditory attention to benefit from the cues characteristic of typical sentence prosody. However, when cognitive deficits (e.g., auditory executive control, short-term memory) are present, stroke participants are not able to capitalize on typical prosodic cues, and instead benefit from the list prosody manipulation.

CHAPTER 6

EXPERIMENT 2B: NEURAL RESOURCES SUPPORTING PROSODY, COGNITION, AND SENTENCE COMPREHENSION POST-STROKE

Introduction

It is largely accepted that a left lateralized fronto-temporo-parietal network supports sentence comprehension and language more generally (Hickok & Poeppel, 2007). Classically, the suprasegmental aspects of speech, including prosody, are associated with the right hemisphere (Friederici & Alter, 2004; Gandour et al., 2004; Sammler, Grosbras, Anwander, Bestelmeyer, & Belin, 2015; Wildgruber et al., 2004; Wildgruber, Ethofer, Grandjean, & Kreifelts, 2009). Yet, more recent work indicates distinct contributions of each hemisphere to prosodic processing (Kreitewolf, Friederici, & von Kriegstein, 2014). More specifically, the left hemisphere is associated with processing linguistic prosody (i.e., prosody used to emphasize words/clauses or determine the form of an utterance) while the right hemisphere is more involved in affective or emotional prosody (Belyk & Brown, 2014; Wildgruber et al., 2004). Linguistic prosody (hereafter referred to as prosody) is of particular interest in aphasia research, as different prosodic manipulations have been shown to modulate specific neural resources within brain networks known to support sentence comprehension (den Ouden et al., 2016; Geiser et al., 2008; Humphries et al., 2005; Meyer et al., 2004), including the left inferior frontal gyrus (pars opercularis), left middle frontal gyrus, left posterior superior temporal gyrus, and left anterior temporal cortex (Belyk & Brown, 2014). This suggests that different types of prosody manipulations may be able to differentially engage relatively intact brain regions post-stroke to improve sentence comprehension. The purpose of this study was to investigate the relationship between unique prosodic patterns, lesion location, and sentence comprehension in chronic stroke patients.

In Experiment 2a, it was concluded that stroke participants with good auditory attention demonstrated better comprehension of sentences spoken with sentence prosody while stroke participants with deficits in auditory attention and/or short-term memory benefited when sentences were presented with list prosody. This post-stroke behavioral dissociation regarding cognition and prosody is likely driven in part by stroke lesion location suggesting that there may also be a unique relationship between prosody and lesion location. Importantly, previous work demonstrates specific brain regions to preferentially respond to specific types of prosody within neurotypical adults. For example, Humphries et al. (2005) identified list prosody (i.e., monotone prosody lacking pitch inflections and prosodic boundaries) to activate the left posterior superior temporal gyrus while typical sentence prosody activated the left anterior temporal lobe. Meyer et al. (2004) found flattened, monotone speech to activate bilateral posterior superior temporal gyri and inferior parietal lobe, left middle frontal gyrus, left superior parietal lobe, and right inferior frontal gyrus. A direct comparison of typical sentence prosody and monotone prosody revealed increased activation of the left superior frontal cortex, left anterior temporal lobe, left insula, left Heschl’s gyrus, and bilateral anterior cingulate cortex for sentence prosody compared to monotone prosody (den Ouden et al., 2016). These studies in neurotypical adults largely highlight the following pattern: left frontal and anterior temporal cortices respond preferentially to typical prosodic cues while left posterior temporal and inferior parietal cortices respond to irregular prosodic patterns such as monotone prosody and list prosody. Collectively, these results suggest that the brain regions involved in sentence processing may be modulated to some extent by prosody.

This preferential response of specific brain regions within the larger sentence comprehension network to unique types of prosody may be advantageous to improving sentence comprehension, particularly when a stroke lesion affects only part of the language network. Thus, the purpose of this study is to serve as a foundational step towards identifying the relationship between lesion location, prosody, and sentence comprehension post-stroke. It was hypothesized that (1) stroke patients with lesions sparing the left middle frontal gyrus and Broca's area (defined as the posterior two-thirds of the left inferior frontal gyrus; pars opercularis and triangularis) would demonstrate greater comprehension of non-canonical sentences spoken with sentence prosody (as sentence prosody should engage their relatively intact left frontal cortex), and (2) stroke patients with lesions sparing the left posterior superior temporal and inferior parietal cortices would demonstrate greater comprehension of sentences spoken with list prosody (as list prosody should engaged their relatively intact left posterior temporal and inferior parietal cortices). Additionally, the overall goal of Experiment 2 was to identify cognitive-neuroanatomical profiles associated with each type of prosody. Therefore, the results from Experiment 2a and 2b will be combined and interpreted together. It is hypothesized that (1) stroke patients with lesions sparing the left middle frontal gyrus and Broca's area and relatively preserved orienting attention will demonstrate greater comprehension of sentences spoken with sentence prosody, while (2) stroke patients with lesions sparing the left posterior temporal and inferior parietal cortices and poor auditory executive control and/or short-term memory will demonstrate improved comprehension when sentences are spoken with list prosody.

Method

Participants

Twenty-one participants (12 females) from Experiment 2a with MRI scans were included in the present study. Participants ranged in age from 28 to 80 years (*M* = 55, *sd* = 13.86) and met the same inclusion criteria as in Experiment 2a (Table 17; Figure 8).

Table 17. Stroke group demographics.

	Gender	Age	Months Post Stroke	Years of Education	Aphasia Diagnosis
AZ1001	Female	57	77	18	None
AZ1003	Female	48	110	19	Broca’s
AZ1006	Male	60	138	14	Broca’s
AZ1011	Female	73	53	16	Anomic
AZ1012	Male	77	85	16	Wernicke’s
AZ1016	Male	37	142	14	Broca’s
AZ1018	Female	43	29	14	Broca’s
AZ1022	Female	46	79	14	Broca’s
AZ1026	Male	70	50	16	None
AZ1028	Female	80	19	24	Wernicke’s
AZ1029	Female	34	174	14	None
AZ1030	Male	56	32	16	Broca’s
AZ1031	Female	40	63	20	Broca’s
AZ1032	Male	28	20	13	Anomic
AZ1033	Male	57	180; 60	14	Global
AZ1034	Female	59	110	15	Anomic
AZ1037	Male	57	13	16	Broca’s
AZ1038	Male	54	155	14	Broca’s
AZ1039	Female	66	48	14	Anomic
AZ1040	Female	54	45	14	Broca’s
AZ1041	Female	59	24	12	Anomic

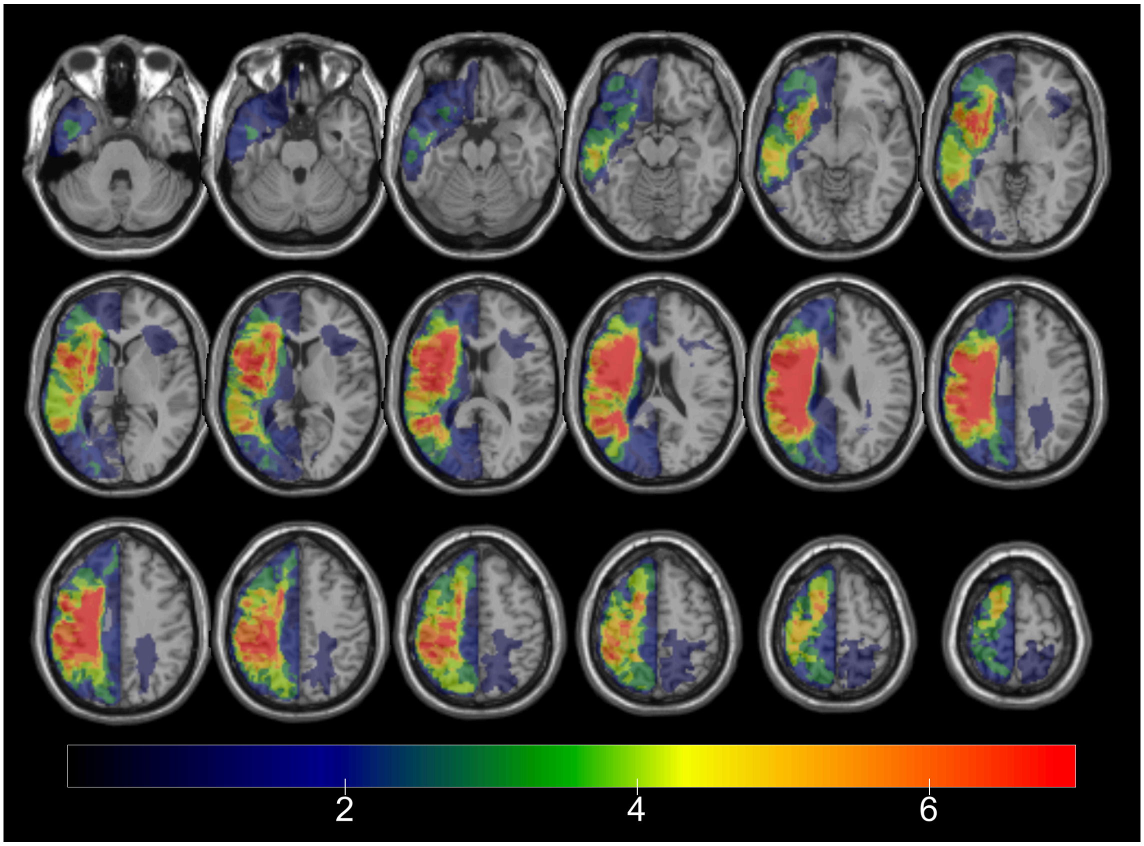

Figure 8. Lesion overlap map for all 21 stroke participants.

Experimental Design

Sentence-picture matching task. The sentence stimuli and sentence-picture matching task from Experiment 2a provided the measures of auditory sentence comprehension. As in Experiment 2a, the focus is on non-canonical sentence comprehension because patients with aphasia[10] have relatively specific deficits in comprehension of complex, non-canonical sentence structures (Bradley et al., 1980; Caramazza & Zurif, 1976). Therefore, the sentence comprehension dependent variables

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[10] Agrammatic comprehension (i.e., complexity-related sentence comprehension deficits) has primarily been reported in persons with Broca's aphasia, but this same phenomenon is also observed in conduction aphasia (Caramazza & Zurif, 1976).

were (1) non-canonical sentence reaction time – canonical sentence reaction time within sentence prosody (hereafter referred to as non-canonical sentences spoken with sentence prosody) and (2) non-canonical sentence reaction time – canonical sentence reaction time within list prosody (hereafter referred to as non-canonical sentences spoken with list prosody). Reaction time difference scores closer to zero reflect better sentence comprehension abilities.

Cognitive measures. The cognitive measures from Experiment 2a which significantly predicted comprehension of sentences spoken with sentence prosody and list prosody were included in the analyses to facilitate the development of cognitive-neuroanatomical profiles associated with comprehending each type of prosody. The cognitive measures included auditory alerting attention (reaction time difference for no cue – double cue trials), auditory orienting attention (reaction time difference for center cue – spatial cue trials), and auditory executive control (reaction time difference for incongruent – congruent trials) measured using the same auditory ANT from the previous experiments, and short-term memory (*RBANS* Immediate Memory index). Larger scores for auditory alerting, orienting, and short-term memory represented better cognitive abilities while scores closer to zero represented better auditory executive control abilities.

MRI data collection. Stroke participants underwent MRI scanning using a 3T Phillips Ingenia MRI scanner equipped with a 32 channel radiofrequency head coil located at the Keller Center for Imaging Innovation at the Barrow Neurological Institute in Phoenix, Arizona. Chronic stroke lesions were demarcated on a high-resolution anatomical T1 image (FOV = 270 X 252, TR = 6.7, flip angle = 9, voxel size = 1 x 1 x 1 mm) in MRIcron (Rorden & Brett, 2000).

Lesion identification and normalization. Lesion maps were smoothed with a 3mm full-width half maximum Gaussian kernel to remove jagged edges associated with manual drawing. Enantiomorphic normalization (Nachev et al., 2008) was conducted using SPM12 in accordance with procedures at the University of South Carolina (Rorden et al., 2012) (i.e., NiiStat's "nii_harvest"). First, a mirrored image of the T1 image (reflected across the midline) was co-registered to the native T1 image. Then, a chimeric image based on the native T1 image with the lesioned tissue replaced by tissue from the mirrored image (using the smoothed lesion map to modulate this blending, feathering the lesion edge) was created. SPM12's unified segmentation-normalization (Ashburner & Friston, 2005) was used to transform this chimeric image to standard space; the resulting spatial transformation was subsequently applied to the T1 image. The normalized lesion map was then binarized, using a 50% probability threshold.

Lesion symptom mapping. Lesion maps were parcellated into regions of interest using the JHU brain atlas, which uses structural-anatomical boundaries to define regions (Faria et al., 2012). From the 189 potential regions of interest defined by the JHU brain atlas, nine regions were chosen based on previous literature and *a priori* hypotheses detailing their involvement in either sentence comprehension and/or cognition (i.e., attention, short-term memory). Regions of interest extracted from the JHU atlas include the left dorsolateral prefrontal cortex (defined by the JHU atlas as the anterior half of the left middle and superior frontal gyri), the posterior half of the left middle frontal gyrus, Broca's area (pars opercularis), Broca's area (pars triangularis), left posterior superior temporal gyrus, left supramarginal gyrus, left angular gyrus, left superior parietal gyrus, and left anterior cingulate cortex (Figure 9). The percent of each region of interest that was intact was extracted from each patient's lesion map using an "in house" Matlab (MathWorks, Natick, MA) script.

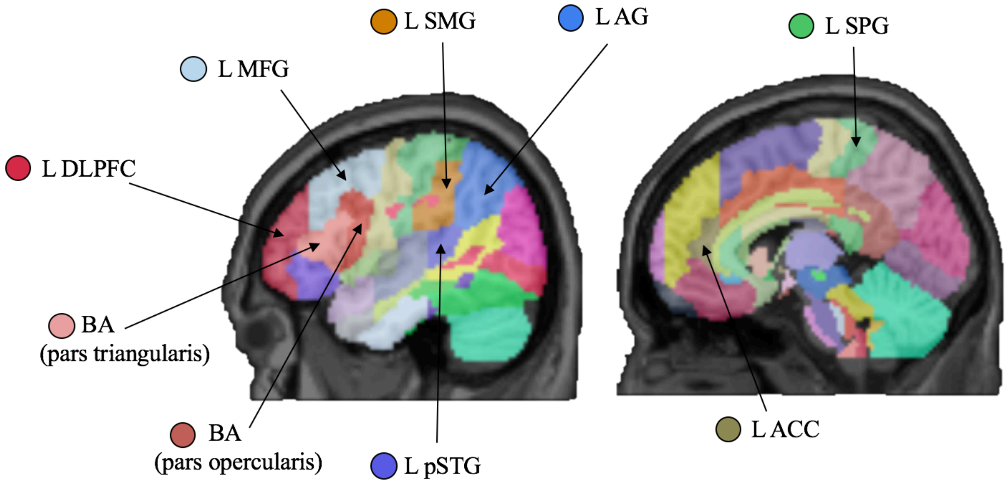

Figure 9. Sentence comprehension and cognitive anatomical regions of interest derived from the JHU atlas (Faria et al., 2012). Peak coordinates for each region of interest are as follows: L ACC (-6, 41, 7); BA pars triangularis (-43, 26, 10); BA pars opercularis (-45, 13, 15); L DLPFC (-35, 47, 12); L MFG (-36, 18, 38); L pSTG (-51, -34, 12); L SMG (-52, -29, 32); L AG (-42, -52, 38); L SPG (-24, -48, 51).

Key: L: left; ACC: anterior cingulate cortex; AG: angular gyrus; BA: Broca's area; DLPFC: dorsolateral prefrontal cortex (comprised of the left middle and superior frontal gyri); MFG: middle frontal gyrus; pSTG: posterior superior temporal gyrus; SMG: supramarginal gyrus; SPG: superior parietal gyrus.

Data Analysis

Sentence comprehension regions of interest.

Sentence comprehension brain regions predicting prosody. The sentence comprehension regions of interest included the left dorsolateral prefrontal cortex, left middle frontal gyrus, Broca's area (pars opercularis), Broca's area (pars triangularis), left posterior superior temporal gyrus, left angular gyrus, and left supramarginal gyrus (Figure 9). Of these seven sentence comprehension regions of interest, sentence prosody was expected to be associated with the left dorsolateral prefrontal cortex, the posterior half of the left middle frontal gyrus, and Broca's area (pars opercularis and triangularis). List prosody was hypothesized to be supported by left posterior temporal and inferior parietal cortices, specifically the left posterior superior temporal gyrus, left angular gyrus, and left supramarginal gyrus. Multiple regression analyses were used to predict comprehension of non-canonical sentences spoken with sentence prosody and non-canonical sentences spoken with list prosody from the percent of intact tissue in the seven regions of interest after controlling for the significant covariates in Experiment 2a. Of the potential covariates from Experiment 2a [auditory single word comprehension, pure tone audiometry (500-4000 Hz better ear), age, education, time post-stroke], only auditory single word comprehension significantly related to the sentence comprehension dependent variables (Experiment 2a, Table 10) and was therefore the only covariate included in the regression models.

Sentence comprehension brain regions predicting cognitive performance. Given our overall interest in identifying cognitive-neuroanatomical profiles supporting comprehension of sentences spoken with distinct prosodies, we also used multiple regression analyses to predict performance on the cognitive measures that significantly predicted sentence comprehension in Experiment 2a from the percent of intact tissue in each of the seven sentence comprehension regions of interest. As in the previous multiple regression analyses, significant covariates [auditory single word comprehension, pure tone audiometry (500-4000 Hz better ear), age, education, time post-stroke] were included in the model and the percent of intact tissue in each of the seven sentence comprehension regions of interest were the predictors. The cognitive measures (i.e., the significant cognitive tasks from Experiment 2a) included were the three measures within the auditory ANT (alerting, orienting, and executive control) and the *RBANS* Immediate Memory index (i.e., short-term memory)].

Cognitive regions of interest. While the neural resources supporting sentence comprehension and cognition largely overlap, at the resolution of standard MRI protocols, (Cieslik et al., 2015; January et al., 2009; Novick, Trueswell, & Thompson-Schill, 2010), some differences also are observed (Wallis et al., 2015). Regarding overlapping resources, sentence comprehension and cognition both recruit six of the seven sentence comprehension regions of interest previously discussed. Specifically, the left dorsolateral prefrontal cortex, left middle frontal gyrus (posterior portion), Broca's area (pars opercularis), Broca's area (pars triangularis), left supramarginal gyrus, and left angular gyrus (Cieslik et al., 2015; Domenech & Koechlin, 2015; Kane & Engle, 2002; MacDonald et al., 2000). In addition to these six regions of interest, three additional regions of interest more specific to cognition were identified including the left precuneus, left superior parietal gyrus, and the left anterior cingulate cortex; this resulted in a total of nine cognitive regions of interest (Figure 9).[11]

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[11] Several other left hemisphere brain regions other than the nine identified by this study are known to support cognitive processes including, but not limited to the left superior

The left precuneus, left superior parietal gyrus, and left anterior cingulate cortex are all consistently associated with the default mode network (Power et al., 2011; Yeo et al., 2011). In addition, sub-regions of the left precuneus and left superior parietal gyrus have also been associated with the more bilateral fronto-parietal network (Dosenbach et al., 2007). The dorsal portion of the anterior cingulate cortex has additionally been associated with the cingulo-opercular network (Dosenbach et al., 2007). The fronto-parietal and cingulo-opercular networks are both known to support cognitive control (Dosenbach et al., 2008, 2007; Marek & Dosenbach, 2018; Sheffield et al., 2015; Wallis et al., 2015), which is known to utilize both attention and short-term memory resources (D'Esposito & Postle, 2015; Mackie, Van Dam, & Fan, 2013; McCabe, Roediger, McDaniel, Balota, & Hambrick, 2010). But the two networks make different contributions: the fronto-parietal network plays a more prominent role in selective attention and the cingulo-opercular network the maintenance of task-relevant goals over time (Dosenbach et al., 2007; Sheffield et al., 2015; Yeo et al., 2011); this function of the cingulo-opercular network may implicate it in short-term memory (Gordon, Stollstorff, & Vaidya, 2012).

Cognitive brain regions predicting prosody. Multiple regression analyses were used to predict comprehension of non-canonical sentences spoken with sentence prosody and list prosody from the percent of intact tissue in the nine cognitive regions of interest after controlling for auditory single word comprehension.

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frontal lobe (prefrontal cortex), left posterior cingulate cortex, left posterior superior temporal gyrus, and thalamus. However, due to a small sample size resulting in a limited number of degrees of freedom, we are restricting our analyses to these nine prominent cognitive regions.

Cognitive brain regions predicting cognition. To further support the identification of cognitive-neuroanatomical profiles supporting comprehension of sentences spoken with unique prosodic patterns, multiple regression analyses were used to predict performance on the cognitive measures that significantly predicted sentence comprehension in Experiment 2a (auditory ANT, *RBANS* Immediate Memory index). Like the previous regression analyses, the predictors were the percent of intact tissue within each region of interest. Additionally, covariates which significantly correlated with the dependent variables were included in the models; the potential covariates included auditory single word comprehension, pure tone audiometry (500-4000 Hz better ear), age, education, and time post-stroke.

Results

Means and standard deviations of the mean for each sentence condition and cognitive variable are reported in Table 18.

Table 18. Means and standard deviations of the mean for each sentence condition and cognitive variable.

Cognitive Variable	Stroke Group Mean (sd)
RT Difference Score Sentence Prosody	817.32 (2383.78)
RT Difference Score List Prosody	1589.44 (1882.58)
Auditory Alerting	58.00 (173.37)
Auditory Orienting	36.97 (112.23)
Auditory Executive Control	187.29 (237.78)
RBANS Immediate Memory Index	67.05 (19.47)

Sentence Comprehension Regions of Interest

Sentence comprehension brain regions predicting prosody. The overall model predicting comprehension of non-canonical sentences spoken with sentence prosody was significant [R^2 =.77, F(8,12)=4.95, *p*=.007] with the anterior portion of the left dorsolateral prefrontal cortex (β= -1.00, *p*=.02), Broca's area (pars opercularis; β= -1.72, *p*=.006), and the left angular gyrus (β= -.93, *p*=.03)] being the significant predictors (Table 19). The overall model predicting comprehension of non-canonical sentences spoken with list prosody was also significant [R^2 =.78, F(8,12)=5.42, *p*=.005] with the left dorsolateral prefrontal cortex (β= -1.49, *p*=.001) being the sole significant predictor (Table 19).

Table 19. Multiple regression models for prosody predicted from sentence comprehension regions of interest.

Non-Canonical - Canonical Sentences with Sentence Prosody RT			
Predictors	β	*t*	*p*
Single Word Comprehension	.06	.17	.87
Left middle frontal gyrus	1.31	2.47	.03[a]
Left dorsolateral prefrontal cortex	-1.01	-2.70	.02*
Broca's area (pars opercularis)	-1.72	-3.29	.006*
Broca's area (pars triangularis)	1.67	3.18	.008[a]
Left supramarginal gyrus	.89	4.10	.001[a]
Left angular gyrus	-.93	-2.46	.03*
Left posterior superior temporal gyrus	.21	.61	.55
Non-Canonical - Canonical Sentences with List Prosody RT			
Single Word Comprehension	-.34	-1.03	.33
Left middle frontal gyrus	1.18	2.29	.04[a]
Left dorsolateral prefrontal cortex	-1.49	-4.13	.001*
Broca's area (pars opercularis)	-.96	-1.88	.09
Broca's area (pars triangularis)	.97	1.90	.08
Left supramarginal gyrus	.27	1.29	.22
Left angular gyrus	-.61	-1.65	.13
Left posterior superior temporal gyrus	.72	2.18	.05[a]
*significant at *p*<.05			

[a] Region of interest elicits a statistically significant finding in the unexpected direction (i.e., larger percent of intact tissue predicting worse performance). This is a common finding in lesion-symptom mapping and aphasia research due to lesion locations not being independent of one another, but should not be interpreted as intact tissue equaling impairment.

Sentence comprehension brain regions predicting cognitive performance. Of the potential covariates from Experiment 2a [auditory single word comprehension, pure tone audiometry (500-4000 Hz better ear), age, education, time post-stroke], only auditory single word comprehension significantly correlated with the *RBANS* Immediate Memory index ($r(19)= .57, p=.007$); no other predictor-covariate correlations were significant. The overall model predicting the *RBANS* Immediate Memory index was marginally significant [$R^2 =.65$, $F(8,12)=2.72, p=.058$] with the left posterior superior temporal gyrus being the sole significant predictor ($\beta= .93, p=.05$) (Table 20).

For auditory attention, the overall models predicting alerting [$R^2 =.17$, $F(7,13)=.37, p=.91$], orienting [$R^2 =.52$, $F(7,13)=2.00, p=.13$], and executive control [$R^2 =.26$, $F(7,13)=.66, p=.70$] were non-significant. However, given the trend towards significance for the orienting attention model, the findings from Experiment 2a implicating orienting attention in sentence comprehension, and my *a priori* hypotheses, I decided to cautiously explore the orienting attention model and found the left angular gyrus to be a significant predictor ($\beta= 1.13, p=.03$) (Table 20).

Table 20. Multiple regression models for cognitive performance predicted from sentence comprehension regions of interest.

Auditory Orienting Attention			
Predictors	β	*t*	*p*
Left middle frontal gyrus	-1.68	-2.67	.02[a]
Left dorsolateral prefrontal cortex	.77	1.57	.14
Broca's area (pars opercularis)	.98	1.56	.14
Broca's area (pars triangularis)	-.08	-.13	.90
Left supramarginal gyrus	-.61	-2.15	.05[a]
Left angular gyrus	1.13	2.49	.03*
Left posterior superior temporal gyrus	-.52	-1.84	.09
***RBANS* Immediate Memory Index (Short-term Memory)**			
Single Word Comprehension	-.37	-.86	.40
Left middle frontal gyrus	1.34	2.05	.06
Left dorsolateral prefrontal cortex	-1.09	-2.37	.04[a]
Broca's area (pars opercularis)	-1.07	-1.64	.13
Broca's area (pars triangularis)	1.05	1.62	.13
Left supramarginal gyrus	.15	.57	.58
Left angular gyrus	-.47	1.00	.34
Left posterior superior temporal gyrus	.93	2.21	.05*

*significant at $p<.05$

[a] Region of interest elicits a statistically significant finding in the unexpected direction (i.e., larger percent of intact tissue predicting worse performance). This is a common finding in lesion-symptom mapping and aphasia research due to lesion locations not being independent of one another, but should not be interpreted as intact tissue equaling impairment.

Cognitive Regions of Interest

Cognitive brain regions predicting prosody. The overall model predicting comprehension of non-canonical sentences spoken with sentence prosody was significant [R^2=.86, F(10,10)=6.05, p=.004] with Broca's area (pars opercularis; β= -1.33, p=.03) and the left anterior cingulate cortex (β= -.54, p=.05)] being the significant predictors (Table 20). The overall regression model predicting comprehension of non-canonical sentences spoken with list prosody was also significant [R^2=.81, F(10,10)=4.26, p=.02] with the left dorsolateral prefrontal cortex (β= -1.19, *p*=.03) being the sole significant predictor (Table 21).

Table 21. Multiple regression models for prosody predicted from cognitive regions of interest.

Non-Canonical - Canonical Sentences with Sentence Prosody RT			
Predictors	β	*t*	*p*
Single Word Comprehension	.06	.21	.84
Left middle frontal gyrus	1.13	3.01	.01[a]
Left dorsolateral prefrontal cortex	-.51	-1.27	.23
Broca's area (pars opercularis)	-1.33	-2.61	.03*
Broca's area (pars triangularis)	1.08	1.83	.10
Left anterior cingulate cortex	-.54	-2.26	.05*
Left superior parietal gyrus	.04	.08	.94
Left supramarginal gyrus	.70	2.62	.03[a]
Left angular gyrus	-.38	-.90	.39
Left precuneus	-.23	-.72	.47
Non-Canonical - Canonical Sentences with List Prosody RT			
Single Word Comprehension	-.13	-.39	.70
Left middle frontal gyrus	.73	1.69	.12
Left dorsolateral prefrontal cortex	-1.19	-2.54	.03*
Broca's area (pars opercularis)	-.74	-1.26	.24
Broca's area (pars triangularis)	.63	.93	.38
Left anterior cingulate cortex	-.34	-1.23	.25
Left superior parietal gyrus	-1.33	-2.05	.07
Left supramarginal gyrus	.51	1.65	.13
Left angular gyrus	.61	1.25	.24
Left precuneus	.59	1.62	.14

*significant at *p*<.05

[a] Region of interest elicits a statistically significant finding in the unexpected direction (i.e., larger percent of intact tissue predicting worse performance). This is a common finding in lesion-symptom mapping and aphasia research due to lesion locations not being independent of one another, but should not be interpreted as intact tissue equaling impairment.

Cognitive brain regions predicting cognitive performance. The overall models predicting the *RBANS* Immediate Memory index [R^2 =.63, F(10,10)=1.70, *p*=.21], auditory alerting attention [R^2 =.16, F(9,11)=.16, *p*=1.0], auditory orienting attention [R^2 =.62, F(9,11)=1.99, *p*=.14], and auditory executive control [R^2 =.42, F(9,11)=.88, *p*=.57] were non-significant.

Discussion

The purpose of Experiment 2b was to investigate the relationship between lesion location, prosody, and sentence comprehension. This relationship was explored in two sets of regions of interest: sentence comprehension and cognitive. As hypothesized, sentence prosody was associated with the left inferior and middle frontal regions in the sentence comprehension regions of interest: stroke participants with a larger proportion of the left dorsolateral prefrontal cortex and Broca's area (pars opercularis) intact demonstrated greater comprehension of non-canonical sentences spoken with sentence prosody. Additionally, a more intact left angular gyrus was also associated with better comprehension of non-canonical sentences spoken with sentence prosody. Within the cognitive regions of interest, greater comprehension of non-canonical sentences spoken with sentence prosody was associated with a larger proportion of Broca's area (pars opercularis) and the left anterior cingulate cortex being intact. Regarding list prosody, it was hypothesized that list prosody would be associated with the left posterior temporal and inferior parietal cortices. This hypothesis was not supported in either the sentence comprehension or cognitive regions of interest. Instead, within both sets of regions of interest, the regression models indicated that stroke participants with a more intact left dorsolateral prefrontal cortex demonstrated greater comprehension of non-canonical sentences spoken with list prosody.

The overall goal of Experiment 2 was to combine the results from Experiments 2a and 2b to identify cognitive-neuroanatomical profiles associated with comprehension of non-canonical sentences spoken with each prosody. Therefore, the intactness of the sentence comprehension and cognitive regions of interest were additionally used to predict performance on the significant cognitive predictors from Experiment 2a. Within the sentence comprehension regions of interest, a more intact left angular gyrus was associated with better auditory orienting attention, while having a larger proportion of the left posterior superior temporal gyrus intact was associated with better short-term memory (i.e., *RBANS* Immediate Memory Index). There were no significant predictors of auditory alerting, orienting, executive control, or short-term memory within the cognitive regions of interest.

Left Dorsolateral Prefrontal Cortex and Sentence Comprehension

Participants with larger proportions of the left dorsolateral prefrontal cortex (defined by the JHU atlas as the anterior half of the middle and superior frontal gyri) intact demonstrated better comprehension of non-canonical sentences spoken with both sentence prosody and list prosody. This finding suggests that the left dorsolateral prefrontal cortex likely supports sentence comprehension processes, regardless of prosody. It is widely accepted that the left dorsolateral prefrontal cortex is a domain-general resource known to support cognitive functions including attention, short-term memory, working memory, cognitive control, and executive functions (Cieslik et al., 2015; Fiez et al., 1996; Henson, Burgess, & Frith, 2000; January et al., 2009; Kane & Engle, 2002; MacDonald et al., 2000). The left dorsolateral prefrontal cortex has additionally been implicated in speech comprehension (Hickok & Poeppel, 2007).

Specifically, the left dorsolateral prefrontal cortex appears to be implicated in sentence comprehension because it supports cognitive resources such as working memory and cognitive control (Hagoort, 2013; Hsu, Jaeggi, & Novick, 2017; Klaus & Schutter, 2018). Collectively, these findings indicate that the left dorsolateral prefrontal cortex is likely recruited post-stroke to facilitate sentence comprehension because of its role in more general cognitive functions. However, it may also be that sentence prosody and list prosody are recruiting distinct sub-regions within the left dorsolateral prefrontal cortex. Future work is needed to more precisely characterize how prosody may be modulating the left dorsolateral prefrontal cortex's involvement in sentence comprehension, but this overall finding of involvement regardless of prosody type is in line with previous work implicating dorsolateral prefrontal cortex in almost any cognitive task.

Left Fronto-Parietal Network Supports Sentence Prosody

In addition to the left dorsolateral prefrontal cortex, participants having a larger proportion of the left pars opercularis, left anterior cingulate cortex, and left angular gyrus intact had better comprehension of sentences spoken with sentence prosody post-stroke. Previous work indicates that persons with unilateral left hemisphere lesions have specific deficits in processing linguistic prosody (Baum & Dwivedi, 2003; Baum & Pell, 1999; Pell, 1998), but that they also demonstrate gains in comprehension when sentences (Lasky et al., 1976) and paragraphs (Pashek & Brookshire, 1982) are spoken with an exaggerated linguistic stress. The results from the present study expand upon this previous work by indicating that a left fronto-parietal network, which not only includes the domain-general left dorsolateral prefrontal cortex but also the anterior portion of Broca's area (pars opercularis), anterior cingulate cortex, and angular gyrus, appears to be engaged in processing typical sentence prosody post-stroke and that persons with aphasia with these brain regions preserved may benefit from exaggerated prosodic cues.[12]

Typical sentence prosody has been hypothesized to facilitate sentence comprehension by reducing demands placed on cognitive resources (Kjelgaard & Speer, 1999; Roncaglia-Denissen et al., 2013; Speer et al., 1996). Behaviorally, the use of sentence prosody is associated with greater accuracy and decreased response times. However, within the brain, sentence prosody appears to recruit a more disperse cognitive-linguistic network, which includes brain regions implicated in both non-canonical sentence comprehension (Broca's area) and attention (anterior cingulate cortex, angular gyrus). This suggests that sentence prosody is primarily beneficial if it can engage this extended network of cognitive-linguistic resources. However, if these resources are lesioned, then sentence prosody may not be helpful and could possibly, even be distracting.

Two prominent features of sentence prosody are pitch inflections and prosodic boundaries, both of which are considered to be linguistic elements of prosody (Rosen, 1992). Pitch inflections and prosodic boundaries are proposed to facilitate sentence comprehension by directing listener attention towards important sentential information (Schafer, 1997). Attention is commonly associated with a bilateral fronto-parietal network (Dosenbach et al., 2008; Petersen & Posner, 2012; Wallis et al., 2015), including the left dorsolateral prefrontal cortex, Broca's area (pars opercularis), and left angular

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[12] The sentence prosody manipulation utilized in the sentence prosody is exaggerated in that the pitch inflections and prosodic boundaries are over emphasized, but still perceived to be within the range of normal.

gyrus. The anterior cingulate cortex is part of the well-studied cingulo-opercular network (Dosenbach et al., 2007). While the fronto-parietal network is frequently implicated in selective attention, the cingulo-opercular network is thought to be more involved in sustained attention (i.e., tonic alertness) (Petersen & Posner, 2012) and the maintenance of task-relevant goals over time (Dosenbach et al., 2007). Therefore, the pitch inflections and prosodic boundaries characteristic of sentence prosody may additionally engage sustained attention, which is a necessary precursor of higher order attention and linguistic processes.

Collectively, this evidence suggests that sentence prosody may recruit two separate neural networks to facilitate sentence comprehension post-stroke. Sentence prosody may facilitate sentence comprehension by engaging the cingulo-opercular network to support more basic attentional processes, i.e., sustained attention, and the left fronto-parietal network to preemptively direct the listener's *attention* to important clauses, i.e., selective attention. However, future work is needed to parse apart the specific functions of each aspect of sentence prosody (e.g., pitch inflections, prosodic boundaries, word stress, etc.) and how they individually relate to sentence comprehension and the supporting neural correlates.

Left Dorsolateral Prefrontal Cortex and List Prosody

The left dorsolateral prefrontal cortex was the sole region associated with comprehension of non-canonical sentences spoken with list prosody. Beyond being involved in comprehending sentences spoken with list prosody because of basic sentence comprehension processes discussed above, the left dorsolateral prefrontal cortex may also be associated with list prosody due to its rhythm. List prosody is generated by inserting

20-milisecond intervals between each word; this procedure creates a consistent beat, which subsequently makes rhythm a prominent linguistic feature of list prosody. The ability to process speech rhythms has previously been linked to the left dorsolateral prefrontal cortex (Grahn, 2012). Therefore, list prosody may be improving sentence comprehension post-stroke by recruiting the rhythm processing abilities of the intact left dorsolateral prefrontal cortex.

The consistent rhythm of list prosody disrupts the expected structure of the sentence. This disruption may force individuals to draw upon bottom-up processing mechanisms to chunk sentence-level information since typical prosodic cues are unavailable to help parse the sentence. This ability of list prosody to recruit bottom-up processing mechanisms may be particularly important for individuals with stroke lesion patterns which disrupt the left lateralized fronto-parietal network shown to support sentence prosody as these individuals may not be able to capitalize on the typical prosodic cues characteristic of sentence prosody (e.g., pitch inflections), and may instead need to rely on the more rhythmic aspects of language. This suggests that patients with relatively preserved rhythm processing abilities post-stroke may be benefitting from the list prosody manipulation since both rhythm and list prosody are supported, at least in part, by the left dorsolateral prefrontal cortex.

In addition to the left dorsolateral prefrontal cortex, the basal ganglia have additionally been associated with processing linguistic rhythm (Grahn, 2012). There were no specific hypotheses regarding the relationship between prosody and the basal ganglia in the present experiment, however, an exploratory analysis (Table 22) indicates that a more intact left globus pallidus predicts better comprehension of non-canonical sentences spoken with list prosody. Importantly, the overall model predicting comprehension of non-canonical sentences spoken with sentence prosody from the nuclei of the left basal ganglia was not significant. This relationship between brain structures known to process speech rhythm and those associated with list prosody further suggests that rhythm is a critical feature of list prosody and necessary for improving comprehension. Thus, individuals with intact rhythm abilities may experience gains in comprehension when list prosody is used as list prosody may facilitate the chunking of information within cognitive resources specialized for processing speech rhythm (e.g., the left dorsolateral prefrontal cortex and basal ganglia).

Table 22. Predicting sentence comprehension from the left basal ganglia. The overall model predicting sentence prosody was not significant [R^2 =.47, F(5,15)=2.64, *p*=.07]. The overall model predicting list prosody was significant [R^2 =.66, F(5,15)=5.83, *p*=.003].

Non-Canonical - Canonical Sentences with Sentence Prosody RT			
Predictors	β	*t*	*p*
Single Word Comprehension	.36	1.23	.24
Left Caudate	-.67	-1.46	.17
Left Putamen	-.05	-.12	.90
Left Globus Pallidus	.51	1.27	.22
Left Thalamus	.22	.75	.47
Non-Canonical - Canonical Sentences with List Prosody RT			
Single Word Comprehension	.68	2.91	.01*
Left Caudate	.45	1.21	.24
Left Putamen	.02	.05	.96
Left Globus Pallidus	-1.18	-3.72	.002*
Left Thalamus	.18	.76	.46
*significant at *p*<.05			

The fact that list prosody solely recruited the left dorsolateral prefrontal cortex in both the sentence comprehension and cognitive regions of interest indicates that more bilateral brain regions may be involved in processing sentences spoken with list prosody. The right hemisphere demonstrates a preferential response to slower temporal information (Poeppel, 2003). While the fine-grained pitch changes associated with sentence prosody rely more on neural resources within the left hemisphere, the longer temporal duration associated with the overall sentence is likely processed, at least partially, by right hemisphere resources. Therefore, list prosody may additionally be improving sentence comprehension post-stroke by recruiting right hemisphere resources. Interestingly, in terms of speech production, rhythmic tapping of the left-hand is a prominent feature of Melodic Intonation Therapy (Albert, Sparks, & Helm, 1973; Norton, Zipse, Marchina, & Schlaug, 2009) and shown to improve speech production independent of melodic intoning (Boucher, Garcia, Fleurant, & Paradis, 2001; Laughlin, Naeser, & Gordon, 1979; Stahl, Kotz, Henseler, Turner, & Geyer, 2011). Given rhythm's ability to improve speech production, it is also likely that rhythm is able to improve speech comprehension independent of pitch. However, future work is needed to parse apart the specific aspects of list prosody (e.g., rhythm, stress, pitch, etc.) that may be improving comprehension as well as the neural resources supporting each aspect of list prosody.

As previously mentioned, list prosody disrupts the expected structure of the sentence, which may bias participants towards utilizing bottom-up processing mechanisms to comprehend sentences spoken with list prosody. Bottom-up processing mechanisms are typically used during speech comprehension when linguistic information is absent or distorted (Davis et al., 2002); in the present study, typical sentence prosody is distorted to create list prosody. The neural resources associated with bottom-up processing of speech primarily include bilateral anterior-medial auditory cortices (de Heer et al., 2017). From primary auditory cortex, speech processing moves into the bilateral posterior temporal-inferior parietal cortices before recruiting more top-down regions in the frontal cortex, including prefrontal cortices (de Heer et al., 2017). In neurotypical adults, irregular prosodic patterns such as list prosody and monotone prosody have been associated with left posterior superior temporal and inferior parietal regions (Humphries et al., 2005; Meyer et al., 2004). Together, this evidence suggests that list prosody may first recruit bottom-up neural resources including the left posterior-inferior parietal cortices prior to engaging the left dorsolateral prefrontal cortex to improve sentence comprehension. Although not quite significant, the present study does observe a relationship between the left angular gyrus and list prosody: stroke participants with a more intact left angular gyrus demonstrated greater comprehension of sentences spoken with list prosody (p=.13).

Collectively, these findings demonstrate that list prosody may recruit a multifaceted network of neural resources, including subcortical and right hemisphere regions, to improve sentence comprehension. This ability of list prosody to engage a broader neural network may be advantageous to improving sentence comprehension post-stroke as individuals with a wider range of stroke lesion patterns may be able to benefit from it. However, the structural intactness of a given brain region is not the sole measure of brain function. Therefore, future work is needed to investigate both structural and functional connectivity among different brains regions, in order to better understand the contributions of specific neural networks to comprehension of sentences spoken with both sentence and list prosody.

Cognitive-Neuroanatomical Profiles Predicting Non-Canonical Sentence Comprehension

The overall goal of Experiment 2 was to identify cognitive-neuroanatomical profiles predicting comprehension of non-canonical sentences spoken with sentence prosody and list prosody. Therefore, I also investigated the relationship between the brain regions of interest and auditory attention and short-term memory; the two cognitive measures from Experiment 2a associated with better comprehension of sentences spoken with sentence and list prosody, respectively. The cognitive regression models in Experiment 2b were non-significant, nonetheless I decided to explore potential neural predictors for orienting attention and short-term memory given the models trend towards significance, the findings from Experiment 2a, and my *a priori* hypotheses. This exploration identified an intact left posterior superior temporal gyrus to be associated with better short-term memory while an intact left angular gyrus was linked to better orienting attention. Attention, and to a lesser extent short-term memory, are largely supported by a bilateral fronto-parietal network (Corbetta & Shulman, 2002; Marek & Dosenbach, 2018; Posner & Petersen, 1990; Ungerleider & Haxby, 1994; Vossel et al., 2014; Wallis et al., 2015). This bilateral organization of attention and short-term memory may allow stroke patients to compensate for damage to left hemisphere regions by relying more on their right hemisphere homologues to support cognitive functions post-stroke, and subsequently language performance too. However, future work is needed to better understand how neural resources, particularly in the right hemisphere, adapt post-stroke to support both cognition, language, and their interaction.

In Experiment 2a, a unique behavioral relationship was identified between specific cognitive functions and prosody manipulations. Specifically, participants with intact attentional control (i.e., orienting) resources benefited from sentence prosody while participants with deficits in attentional control (i.e., alerting, executive control) and short-term memory benefited from list prosody. From these results, it was concluded that the pitch inflections and prosodic boundaries characteristic of sentence prosody likely facilitated non-canonical sentence comprehension by directing listener attention towards important aspects of the sentence. However, for list prosody, it was concluded that the consistent rhythm generated by list prosody created temporal expectations that facilitated the chunking of information when typical prosodic cues could not be perceived. This unique relationship between specific aspects of auditory attention and prosodic manipulations suggests that depending on an individual's attentional strengths and weakness, unique prosodic patterns can be used to improve sentence comprehension post-stroke.

Experiment 2b provides a neuroanatomical basis for this post-stroke behavioral dissociation regarding specific aspects of attention and the effects of prosody on sentence comprehension observed in Experiment 2a. In Experiment 2b, attention, specifically orienting attention which was found in Experiment 2a to be linked to improved sentence comprehension when sentences were spoken with sentence prosody, was associated with the left angular gyrus; this region is a node within the larger well-studied bilateral fronto-parietal network that supports several aspects of attention (Cieslik et al., 2015; Domenech

& Koechlin, 2015). Alternatively, deficits in short-term memory, which were found in Experiment 2a to be linked to improved sentence comprehension when sentences were spoken with list prosody, was associated with the left posterior superior temporal gyrus. The posterior superior temporal gyrus as well as the adjacent left inferior parietal lobe have previously been implicated in verbal short-term memory in both control subjects and stroke patients (Beeson, Bayles, Rubens, & Kaszniak, 1993; Buchsbaum et al., 2011; Gläscher et al., 2009; Leff et al., 2009).

Regarding prosody, previous work demonstrates specific brain regions to preferentially respond to specific types of prosody within neurotypical adults. For instance, sentence prosody is frequently associated with the left frontal and anterior temporal cortices and list prosody with left posterior temporal and inferior parietal cortices (den Ouden et al., 2016; Humphries et al., 2005; Meyer et al., 2004). My own work using the present experiment's sentence and list prosody manipulations identifies a similar pattern of dissociation in neurotypical adults: sentence prosody recruits the left middle frontal gyrus and list prosody the bilateral posterior superior temporal gyrus and inferior parietal cortex (LaCroix et al., in prep). While Experiment 2b confirms and extends these findings in terms of sentence prosody,[13] it failed to identify a similar prosodic dissociation for list prosody, likely due at least in part to insufficient power provided by the sample size; however, a more intact left angular gyrus trended towards significantly predicting comprehension of non-canonical sentences spoken with list prosody and an exploratory analysis also details an association between the left globus

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[13] Sentence prosody was associated with a more intact left dorsolateral prefrontal cortex, left anterior cingulate cortex, Broca's area (pars opercularis), and left angular gyrus.

pallidus and list prosody. Collectively, this evidence indicates that the brain regions involved in sentence processing may be modulated to some extent by prosody to improve sentence comprehension post-stroke.

Overall, the results from Experiment 2b indicate that the brain regions supporting prosody may dissociate similarly to the brain regions supporting attention and short-term memory. Specifically, attention is supported by a left fronto-parietal network and sentence prosody was found to also be associated with similar regions. The relationship is not as clear for short-term memory and list prosody, yet, short-term memory was associated with a more intact left posterior superior temporal gyrus and list prosody with a more intact left angular gyrus (p=.13), suggesting more posterior temporal and inferior parietal regions may be important for comprehending sentences spoken with list prosody. Collectively, this evidence suggests that cognitive-neuroanatomical profiles may exist that relate to better comprehension of sentences spoken with each prosody manipulation. More specifically, stroke patients with relatively preserved orienting attention (i.e., selective attention) and a more intact left frontal-parietal network (i.e., left dorsolateral prefrontal cortex, the pars opercularis of Broca's area, and left angular gyrus) appear to benefit when complex non-canonical sentences are spoken with sentence prosody. For list prosody, stroke patients with deficits in auditory executive control attention and/or short-term memory, who also have a larger proportion of the left posterior superior temporal gyrus and left angular gyrus intact, appear to benefit when complex non-canonical sentences are spoken with list prosody. Since the neuroanatomical relationship for list prosody appears to be mixed, possibly due to its ability to recruit more right hemisphere and subcortical resources, I further propose a second cognitive-neuroanatomical profile for list prosody: stroke patients who may have good rhythm perception, and an intact left dorsolateral prefrontal cortex and/or left basal ganglia may also benefit when non-canonical sentences are spoken with list prosody. However, future work is needed to better understand the cognitive-neuroanatomical relationship between attention, memory, lesion location, and list prosody.

Conclusion

The present study investigated the relationship between stroke lesion location, prosody, and sentence comprehension post-stroke. Using the sentence comprehension regions of interest, the left dorsolateral prefrontal cortex was identified to support comprehension of sentences spoken with both sentence prosody and list prosody; likely due to the left dorsolateral prefrontal cortex's role in supporting basic sentence comprehension via more domain-general cognitive processes. A left fronto-parietal network including the left dorsolateral prefrontal cortex, Broca's area (pars opercularis), and left angular gyrus was further identified to support sentence prosody. Regarding list prosody, the left dorsolateral prefrontal cortex was the sole significant predictor for list prosody, however, the left angular gyrus trended towards significance and an additional exploratory analysis indicates that the left globus pallidus may also be implicated in comprehending sentences spoken with list prosody. This evidence suggests that different prosodic patterns may be used to improve sentence comprehension post-stroke by engaging distinct brain regions. Overall, the findings from Experiment 2 indicate that unique prosodic patterns may be able to improve non-canonical sentence comprehension post-stroke through their association with distinct cognitive resources and their corresponding neural correlates.

CHAPTER 7

GENERAL CONCLUSION

The purpose of this dissertation was twofold: (1) determine the interaction between three components of attention (alerting, orienting, and executive control) and presentation modality in persons with aphasia and matched-controls, and (2) whether distinct prosodic manipulations can be used to improve auditory sentence comprehension post-stroke by recruiting relatively preserved cognitive functions (including components of attention and working memory) and non-lesioned brain regions. To this end, persons with aphasia and matched-controls completed matched-versions of the Attention Network Test (ANT) in the visual and auditory modalities in Experiment 1. The results from Experiment 1a indicate that while the aphasia group was slower overall in both modalities, the two groups did not differ in any of the three components in either modality. Furthermore, the three components did not significantly correlate between the auditory and visual modalities in the control group; for the aphasia group, the only significant between-modality correlation was the alerting component. These findings from Experiment 1a indicate that visual and auditory attention measures are poor predictors of one another. In Experiment 1b, lesion-symptom mapping methodologies extended the understanding of the neural resources supporting visual and auditory attention and revealed visual executive control abilities to be associated with a more intact left angular gyrus, auditory alerting to be associated with the left supramarginal gyrus, and auditory orienting attention to be associated with Broca's area (pars opercularis). Overall, the findings from Experiment 1b indicate that auditory and visual attention are supported in part by distinct neural resources. Collectively, the results from Experiment 1 indicate the need to separately assess all three components of attention in all perceptual modalities of interest to gain a complete picture of an individual's attention abilities. Assessing visual and auditory attention separately post-stroke is particularly important as stroke lesion patterns likely impact the neural resources supporting each type of attention differently.

The second goal of this dissertation was to identify the relationship between prosody, cognition, stroke lesion patterns, and auditory sentence comprehension. Therefore, in Experiment 2, chronic stroke participants and matched-controls completed a cognitive-linguistic battery that assessed auditory attention using the auditory ANT from Experiment 1, working memory, short-term memory, and comprehension of sentences spoken with sentence prosody and list prosody. The results from Experiment 2a indicate that stroke participants and matched-controls with better auditory orienting attention had better comprehension of sentences spoken with sentence prosody while stroke participants with poor auditory executive control and/or short-term memory abilities demonstrate better comprehension of sentences spoken with list prosody. Experiment 2b extended the results from Experiment 2a by identifying stroke lesion patterns associated with better comprehension of sentences spoken with each prosody. Overall, Experiment 2b demonstrated that while the left dorsolateral prefrontal cortex supports auditory sentence comprehension in general, a left fronto-parietal network which includes the left anterior cingulate cortex, Broca's area (pars opercularis), and left angular gyrus particularly supports the comprehension of sentences spoken with sentence prosody. The relationship between lesion location and list prosody was not as clear, however, a more intact left angular gyrus and basal ganglia (globus pallidus) were associated with better comprehension of sentences spoken with list prosody. Collectively, the results from

Experiment 2 indicate unique cognitive-neuroanatomical profiles to support comprehension of sentences spoken with sentence prosody and list prosody. More specifically, chronic stroke patients with relatively preserved auditory orienting attention and a larger proportion of the left fronto-parietal network intact, which includes the left anterior cingulate cortex, Broca's area (pars opercularis), and left angular gyrus, demonstrate better comprehension of sentences spoken with sentence prosody. Alternatively, chronic stroke patients with deficits in auditory executive control and short-term memory, who likely have lesions affecting the fronto-parietal network identified to support sentence prosody, may benefit from sentences spoken with list prosody, especially when they have a larger proportion of the left inferior parietal cortex (i.e., left angular gyrus) and/or left basal ganglia intact.

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APPENDIX A

RAW DATA FOR CONTROL PARTICIPANTS

APPENDIX A

Table A1. Raw data for control participants.

Participant	Age	Gender	Hearing Status (500-4000 Hz, better ear)	Education (Years)	Auditory Single Word Comp (BDAE-III)	Canonical (Sentence Prosody)	Canonical (List Prosody)	Non-Canonical (Sentence Prosody)	Non-Canonical (List Prosody)	RT Difference Score (Sentence Prosody)	RT Difference Score (List Prosody)	Auditory Alerting	Auditory Orienting	Auditory Executive Control (Incongruent - Neutral RT)	Auditory Executive Control (Incongruent - Congruent RT)	Visual Alerting	Visual Orienting	Visual Executive Control (Incongruent - Neutral RT)	Visual Executive Control (Incongruent - Congruent RT)	RBANS Immediate Memory Index	RBANS Attention Index	WAIS-IV Working Memory Index
PROC1001	51	Female	8.75	16	1	3167.4	4250.88	6503.71	6332.22	3336.31	2081.35	-57.22	-136.21	192.39	266.83	109.68	45.61	114.94	89.94	94	82	86
PROC1002	43	Female	6.25	16	0.94	4230.6	5063.9	5319.7	5312.9	1089.1	249	9.05	42.22	143.01	177.32	1.98	75.53	79.87	99.45	90	112	117
PROC1003	49	Female	8.75	14	1	4744.4	4882.1	4651.33	5333.11	-93.07	451.01	-30.3	-0.48	89.45	130.09	8.76	11.77	97.66	75.91	90	106	102
PROC1004	51	Female	12.5	16	1	3248.9	3410.6	3920.88	4513	671.98	1102.4	-14.65	29.48	33.68	51.92	47.38	38.2	108.07	101.05	148	132	136
PROC1005	44	Female	11.25	16	1	4709.8	5124.8	4652.5	5522.3	-57.3	397.5	13.39	-52.39	155.38	118.39	10.44	14.9	81.45	81.01	94	125	102
PROC1007	50	Female	10	18	0.94	3148.5	3698.5	3802.7	4339.3	654.2	640.8	37.52	-2.66	97.99	130.69	61.97	21.37	84.58	83.46	114	115	117
PROC1008	64	Male	11.25	16	1	4026	4691.8	4021.89	4485.9	-4.11	-205.9	1.36	-20.12	103.65	189.85	-70.75	-69.44	142.65	169.45	87	122	111
PROC1009	65	Female	12.5	12	1	4553.7	5192.2	5204.33	7159.3	650.63	1967.1	8.6	-6	136.57	295.92	12.63	-30.35	160.99	122.99	94	109	97
PROC1010	66	Female	12.5	14	1	4108.9	4573.5	4031.3	4705.5	-77.6	132	10.67	71.06	144.91	76.24	72.62	83.36	122.84	144.18	90	112	97
PROC1011	79	Female	32.5	12	1	4830.3	5016.44	5230.8	5188.63	400.5	172.18	-19.63	-5.06	139.52	195.9	42.54	74.39	112.81	98.39	103	91	119
PROC1012	52	Female	6.25	14	1	4358.4	4912.7	4796.8	5538.7	438.4	626	80.61	13.8	194.38	312.11	41.71	18.17	146.33	128.31	94	88	111
PROC1013	68	Male	42.5	20	1	3644.4	4170.6	4978.2	5519	1333.8	1348.4	-19.05	-55.89	181.29	218.5	69.11	102.39	54.1	62.46	97	106	108
PROC1014	44	Female	5	15	1	4551.1	4951.1	4769.25	6621.3	218.15	1670.2	41.04	-22.12	103.26	149.77	27.26	47.08	115.07	126.3	85	91	95
PROC1015	47	Male	10	15	1	4286.2	4719.6	4886.44	5300.89	600.24	581.29	20.77	16.27	168.72	187.23	66.39	17.6	141.38	129.25	100	112	102
PROC1016	31	Female	6.25	16	1	3634.3	4400.4	4393.2	5086.33	758.9	685.93	26.49	-2.52	78.5	61.97	105.05	40.18	95.99	82.15	103	106	122
PROC1017	31	Male	18.75	16	0.94	3731.6	3900.22	5194.11	6027	1462.51	2126.78	-114.22	47.35	131.74	148.21	55.39	9.54	139.32	115.71	94	75	83
PROC1018	41	Male	10	16	1	3710.5	3596.9	4522.4	5068.5	811.9	1471.6	80.92	21.74	165.72	181.85	53.85	55.37	80.9	60.32	109	122	125
PROC1019	61	Female	16.25	12	1	3476.9	3909.3	4473.44	5116.78	996.54	1207.48	40.7	-48.19	181.99	193.05	-4.8	-4.35	64.1	85.34	109	138	111
PROC1020	56	Female	13.75	12	1	3112.2	3354.9	3876.9	3967.6	764.7	612.7	25.59	-1.65	9.87	-0.46	-6.95	18.45	87.32	74.59	123	100	108
PROC1021	35	Male	13.75	18	1	2640.8	3290.7	3137	3957.6	496.2	666.9	16.6	-17.31	9.87	96.36	28.69	25.88	73.27	64.14	83	100	114

APPENDIX B

RAW DATA FOR STROKE PARTICIPANTS

APPENDIX B

Table B1. Raw data for stroke participants.

Participant	Age	Gender	Hearing Status (500-4000 Hz, better ear)	Education (Years)	Time Post-Stroke (Months)	Auditory Single Word Comp (BDAE-III)	Canonical (Sentence Prosody)	Canonical (List Prosody)	Non-Canonical (Sentence Prosody)	Non-Canonical (List Prosody)	RT Difference Score (Sentence Prosody)	RT Difference Score (List Prosody)	Auditory Alerting	Auditory Orienting	Auditory Executive Control (Incongruent - Neutral RT)	Auditory Executive Control (Incongruent - Congruent RT)	Visual Alerting	Visual Orienting	Visual Executive Control (Incongruent - Neutral RT)	Visual Executive Control (Incongruent - Congruent RT)	RBANS Immediate Memory Index	RBANS Attention Index	WAIS-IV Working Memory Index
AZ1001	57	Female	5	18	77	1	3934.56	4940	5509	6265.44	1574.44	1325.44	-27.42	17.37	130.22	194.93	32.24	-9.84	106.89	107.69	89	97	92
AZ1003	48	Female	15	19	110	1	3718	4276.2	4748.43	6056.33	1030.43	1780.13	4.21	30.96	33.49	125.15	42.71	-20.33	113.07	119.54	61	72	77
AZ1006	60	Male	26.25	14	138	0.88	8239	8316.3	9304.83	9124	1065.83	807.7	701.65	307.5	123.88	39.7	680.81	-18.67	478.13	276.7	40	40	50
AZ1011	73	Female	18.75	16	53	1	5576.6	5826.38	7291.22	10581.1	1714.62	4754.73	15.32	-82.81	224.56	358.8	38.94	117.07	69.36	49.94	94	82	83
AZ1012	77	Male	53.75	16	85	0.63	9190	9526.67	11610	9488.33	2420	-38.33	159.12	27.9	51.96	42.29	104.27	57.92	380.65	255.24	40	46	50
AZ1013	47	Female	-3.75	17	258	0.69	8118.8	21029.86	7957.33	12584	-161.47	-8445.86	-614.01	-263.44	513.96	415.1	34.17	156.47	246.66	-228.63	40	40	53
AZ1016	37	Male	-2.5	14	142	1	6399.7	7861.9	11095	15238.83	4695.3	7376.93	-18.84	-53	-44.58	-42.76	21.28	39.98	75.29	115.04	83	75	71
AZ1018	43	Female	16.25	14	29	0.94	4382.8	4381.63	4831.2	6008.86	448.4	1627.23	-5.4	-163.5	109.21	187.05	97.5	-3.6	99.27	99.1	69	64	66
AZ1022	46	Female	10	14	79	0.94	5877.7	6458	5860	6957.6	-17.7	499.6	92.78	-67.94	450.13	404.8	49.63	149.92	199.04	233.86	53	64	63
AZ1026	70	Male	22.5	16	50	1	4069.7	4471.9	4722.13	5225.6	652.43	753.7	-22.28	-7.91	623.49	564.05	-14.63	49.15	132.94	95.48	100	112	122
AZ1028	80	Female	21.25	24	19	0.88	10093.67	10713	10451.33	9382.5	357.67	-1330.5	242.58	71.9	616.08	628.87	129.78	-39.6	729.09	1043.43	49	53	53
AZ1029	34	Female	-5	14	174	1	3246	3771.9	4577.33	4670.25	1331.33	898.35	3.68	-42.77	76.89	109.45	79.29	108.42	260.62	274.12	44	43	60
AZ1030	56	Male	23.75	16	32	1	7363.44	7071.22	5788.67	7282.43	-1574.78	211.21	-194.85	160.6	4.63	-226.17	5.43	274.35	170.75	215	61	85	83
AZ1031	40	Female	21.25	20	63	1	4732	5410.78	5519.9	6601.67	787.9	1190.89	41.76	16.94	37.18	55.93	43.39	-28.81	117.64	115.1	76	79	100
AZ1032	28	Male	5	13	20	0.94	5399.4	6068.2	6549.13	6665	1149.73	596.8	41.57	-78.3	45.31	193.26	300.22	7.68	120.01	52.34	83	40	63
AZ1033	57	Male	20	14	180	0.5	15231.6	7596.5	7434.75	9766.63	-7796.85	1750.67	44.2	209.86	37.6	-194.43	-335.36	-129.04	957.89	664.15	40	40	55
AZ1034	59	Female	8.75	15	110	1	6247.11	6251.4	7854.38	10591.38	1607.26	4339.98	-45.7	144.32	466.74	597.7	-20.63	98.97	184.09	37.29	87	72	71
AZ1035	41	Female	6.25	17	72	0.94	3717.22	5271.56	4863.67	5961.11	1146.44	689.56	23.34	-17.98	-27.23	11.27	58.68	69.68	85.87	104.04	78	53	63
AZ1036	65	Male	12.5	15	158	0.94	4628.1	5512.22	5297.67	6346.83	669.57	834.61	20.17	-17.15	226.46	295.38	23.53	21.65	119.61	129.32	65	72	83
AZ1037	57	Male	16.25	16	13	1	6386.67	7610	10632.17	8723.29	4245.5	1113.29	36.57	-46.15	92.23	124.35	137.3	-33.17	153.57	66.55	49	64	71
AZ1038	54	Male	12.5	14	155	1	5020.44	5987.1	5633	6825	612.56	837.9	-73.23	152.48	402.41	430.97	38.32	30.55	45.17	47.71	83	64	77
AZ1039	66	Female	13.75	14	48	1	4519.7	4914	5039.63	6030.2	519.93	1116.2	49.11	19	233.8	250.97	0.85	27.91	199.96	188.61	61	79	83
AZ1040	54	Female	15	14	45	1	5036.11	6301.43	5744	8986.8	707.89	2685.37	173.75	92.79	-229.09	26.89	-7.17	21.12	144.35	142.87	85	49	63
AZ1041	59	Female	35	12	24	0.94	5183.9	5917.8	6815.67	6998.71	1631.77	1080.91	-0.53	67.1	51.8	61.34	45.95	-12.72	216.12	249.72	61	75	69
AZ1042	55	Male	18.75	14	37	0.81	6651.63	8668.67	7498.33	8698	846.71	29.33	-115.91	31.63	-214.47	-76.06	-1.17	101.21	137.65	87.06	40	43	53