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Right hemisphere capacities for word-finding: Bilateral modulation of event-related potentials in healthy adults and adults with aphasia

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Abstract

Language tasks are typically lateralized to the language dominant left hemisphere in healthy right-handed adults. Additionally, lesions in left frontotemporal areas typically result in a variety of language impairments called aphasia. Interestingly, increased activation in right cerebral regions homologous to left side lesions has been observed in patients with aphasia during word-finding tasks. The neural mechanism and the impact on word-finding remain unclear. There are two competing theories concerning compensatory right hemisphere activation. One view is that the right hemisphere plays a supportive role, taking over functions of the damaged left hemisphere. The other perspective is that rightward laterality is maladaptive and leads to some of the word-finding error patterns observed in aphasia. It may be possible to reconcile the discrepancy in the literature when considering a third view. I propose that while the right hemisphere may in fact be able to assist in language processes when the dominant left hemisphere is damaged, its capabilities are limited. Word-finding errors may result when this process is overgeneralized beyond the capacities of the right hemisphere. The aim of the present study is to examine how laterality is affected by word-finding difficulty in patients with chronic aphasia and in healthy adults. I used event-related potentials (ERP) to record neural activity that was time-locked to the cognitive events of interest among 10 participants with chronic aphasia secondary to single cerebrovascular accidents and 10, healthy age-matched control participants. Specifically, I compared ERP signatures between the two groups, during word-stem completion and picture naming. ERPs can reveal temporal dynamics and general spatial location of neural activity underlying word-finding processes. The outcomes of this study will provide key insights into the

qualitative and quantitative contributions of the right hemisphere for word-finding in both healthy adults and individuals with aphasia and may help inform intervention practices that aim to enhance or suppress bilateral activation.

Background

Language behaviors include verbal and written comprehension and expression, semantics or word meanings, and syntax or word order and structure. Brain regions associated with language are typically located in the left hemisphere. This cerebral asymmetry is also known as "lateralization." Speech production is thought to be exclusively lateralized to the left and numerous studies have demonstrated left hemisphere language dominance in healthy right-handed adults (reviewed in Buckner, Koutstall, Schacter, & Rosen, 2000; Chiarello, 1988; Gernsbacher & Kaschak, 2003; Thompson-Schill, D'Esposito, & Kan, 1999;). Additionally, lesions in left frontotemporal areas typically result in a variety of language impairments called aphasia. Regardless of aphasia sub-type, word-finding difficulty is a hallmark characteristic of aphasia.

Despite the superiority of the left hemisphere for many language functions, previous research has provided evidence of bilateral contributions for language comprehension and word finding. Specific semantic processes in the right hemisphere appear to be important for resolving ambiguity (words and sentences with more than one meaning), understanding non-literal and metaphorical language, and word comprehension and selection. Enhanced bilateral activation could also be a response to challenging language tasks that require more cognitive resource allocation.

Supportive Role

The right hemisphere may serve a supportive role during difficult language tasks in healthy adults (Heiss et al., 1997). The interhemispheric interaction hypothesis posits that challenging tasks require more effort and attention and therefore recruit bilateral activation. Banich (1998) found evidence of interhemispheric interaction across a variety of modalities including visual, auditory, and somatosensory processing. This body of research consistently demonstrates superior performance in interhemispheric conditions when compared to single hemisphere conditions for tasks that are more complex and cognitively demanding. Banich argues that "dividing processing across the hemispheres is useful when processing load is high because it allows information to be dispersed across a larger expanse of neural space" (Banich, 1998). While word generation was not explicitly studied, Banich describes attention as the cognitive mechanism that allow us to search and select from a wide range of sensory input and response output options. By that definition, we might assume that word generation under challenging conditions may rely on interhemispheric interactions.

These issues were explored in a transcranial Doppler sonography study that measure interhemispheric activation during a word generation task (Drager & Knecht, 2002). Healthy French speaking adults were divided into three groups and given twenty word beginnings each. The "easy condition" group was presented with single letter word beginnings and asked to generate a complete word. The "moderate condition" group was presented with two-letter and three-letter word beginnings, and the "difficult condition" group was presented with one-letter, three-letter, and five-letter word beginnings. Contrary to the hypothesis, they concluded that difficult word completions did not lead to additional activation in the subdominant right hemisphere. The results should be taken with caution, as they are only reliable if the classifications were truly “easy”, “moderate”, or “difficult.” Further research is indicated and should incorporate normative data and factors such as number of potential completions, dominant responses, and competition.

Semantic Processing

A study by Burgess and Simpson (1988) used a visual half-field paradigm to examine asymmetry in cerebral processing in response to ambiguous words that had both dominant and subdominant meanings. Central ambiguous primes were followed by target-words related to dominant or subordinate meanings. Targets were presented to the left or right visual field. Stimulus onset asynchronies (SOAs) of 35 and 750 ms were used for targets in both dominant meaning and subordinate meaning conditions. Responses to targets related to the dominant meaning were equally facilitated at both SOAs for right visual field/left hemisphere (RVF/LH) and left visual field/right hemisphere (LVF/RH). For subordinate meanings, however, the results reflected striking dissimilarities in the hemispheres. When targets related to the subordinate meaning of the prime were presented to the RVF/LH, facilitation occurred only at the 35 ms SOA, while in the LVF/RH, there was no facilitation at 35 ms and strong facilitation at 750 ms. Hence, responses to dominant meanings were processed more efficiently in the left hemisphere and subdominant meanings were processed longer in the right hemisphere. Burgess and Simpson attempted to explain their data in the context of a complimentary relationship between the hemispheres where the right has the role of ancillary processor of word meanings and the left attends to dominant meanings while suppressing subordinate meanings. This explanation is consistent with the coarse code hypothesis; the prevailing framework that describes the role of the right hemisphere for sematic processing.

The coarse code hypothesis suggests that semantic processing for language comprehension is broad but weak in the right hemisphere and strong but narrow in the left hemisphere (Jung-Beeman, 2005). In visual half-field studies, prime-target word pairs with varied semantic relatedness are presented to the left visual field/right hemisphere (LVF/RH) and the right visual field/left hemisphere (RVF/LH). The classic effect is that highly related words are quickly primed in the left hemisphere while weakly related words are slowly primed in the right hemisphere (Taylor & Regard, 2003). These complimentary functions may serve to allow the left hemisphere to concentrate on dominant targets while preserving alternative interpretations in the right hemisphere, should they be needed (Coney & Evans, 1999). Semantic flexibility may also be the key skill for understanding non-literal language such as metaphors, puns, and humor. Indeed, studies of individuals with right hemisphere damage have identified deficits in comprehension of jokes, metaphors, and figurative language (Brownell, Carroll, Rhak, &Wingfield, 1992; Kaplan, Brownell, Jacobs, & Gardner, 1990; Welyman, Brownell, Roman, & Gardner, 1989).

The coarse code hypothesis for language comprehension maps onto expressive language skills as well. Seger and colleagues (2000) used functional magnetic resonance imaging during a verb-generation task to explore hemisphere differences for language production. Participants were given concrete nouns and asked to generate either a closely related verb or an unusual verb. Results revealed stark contrasts in activation when semantic relatedness was close or distant. Areas of the left inferior frontal lobe were active when nouns and verbs were closely associated. Regions in the right frontal lobe were recruited when more distantly associated items were generated. This pattern of hemispheric asymmetry is consistent with the coarse code hypothesis for semantic processing for comprehension; with left hemisphere superiority for processing closely related words and the right hemisphere role for processing distant semantic relationships.

Lexical Competition

In addition to semantic relatedness, the number of potential options generated by left and right regions affects word selection. Chiarello et al. (2006) investigated laterality and verb generation while manipulating the number of possible responses. Findings point to a left hemisphere advantage for single response items only while the right hemisphere maintained a broader range of potential verb options. This account is consistent with similar findings of semantic priming research during word recognition tasks (Chiarello, 1991; Chiarello, 2003).

Chiarello and colleagues (2006) presented three letter word beginnings with one prepotent completion, two competing completions, or many potential completions without a dominant response centrally and to the RVF/LH and the LVF/RH. Participants were asked to generate a complete word beginning with the three letters. Results indicated that the right hemisphere responses reliably differed from those observed for left hemisphere and central presentation. For RVF/LH and centrally presented stimuli, reaction times were fastest with one dominant response, with significantly longer reactions for the two competing response condition and further slowing when there were many competing responses. In the LVF/RH however, there were no differences in reaction times in the two competitors versus one response condition. These findings suggest that the right hemisphere considers possible word options equally while the left hemisphere quickly and efficiently selects the most salient word, inhibiting other options. Further, when two options are equally dominant the competition is difficult for left hemisphere to resolve, resulting in slower processing speeds. If this account is accurate, it could explain the underling processes of stereotypical patterns of word finding errors observed in aphasia. For example, during a picture-naming task, a patient presented with an image of a knife may respond with a closely related word within a broader category (ex. “tool”) or with a similar feature (ex. “sharp”). However, when presented with the picture on a subsequent trial the same patient may name the object accurately (“knife”). We assume that if the patient is ever able to name the object accurately, then the word is not *lost*, but the *process* of accessing the word is impaired. When patients provide a close but inaccurate word, we may tend to believe they could not access “knife” so they gave “sharp” or “tool” instead. If our theory is correct, however, the right hemisphere is selecting targets at random from a pool of potential options that are all considered equally. Sometimes by chance it selects the prepotent response (“knife”) while at other times it selects a less salient but related competitor.

When combining interhemispheric interactions with the right hemisphere’s contributions for semantic processing, one can argue that right hemisphere can play a supportive role during challenging language tasks but can only help in specific ways.

Additionally, overactivation could push the right hemisphere beyond its functional capabilities resulting in more errors. Strategically exploiting these processes could lead to improved remediation approaches for patients with aphasia.

Right Hemisphere Activation in Aphasia

Research examining the relationship between increased right hemisphere activation and language recovery in patients with aphasia have produced conflicting results. One view suggests that increased right hemisphere activation represents a neuroplastic pattern and accounts for language recovery in the post-acute stage of vascular insults (Marchina, & Schlaug, 2012; Rosen et al., 2000; Thulborn, Carpenter, & Just, 1999; Zipse, Norton,). While the mechanism remains unclear, the lesion hypothesis describes reduced laterality as a consequence of tissue damage in the left hemisphere. Transcallosal disinhibition or failure to inhibit bilateral crosstalk, leads to activation and formation of new neural connections or "release" of previously suppressed language capable pathways in right frontotemporal regions. Thulborn et al. (1999) correlated recovery from aphasia in two patients with anatomic, physiologic changes using functional MRI. Rapid shifts in activation to homologous regions of the right hemisphere were observed in as early as three days post-stroke with increasing rightward lateralization six to nine months post-stroke. This phenomenon was referred to as "plasticity" which implies axon sprouting leading to reorganization by formation of new neural connections. However, observed changes in laterality, acutely and subacutely are inconsistent with the growth patterns needed to form new functional pathways (Murphy

& Corbett, 2009). Therefore, the current view favors suppression/release model versus the neuroplasticity explanation in early recovery.

Based on this idea, interventions such as Melodic Intonation Therapy (MIT) have been developed to facilitate more right hemisphere activity. MIT was designed to exploit the preserved ability to sing songs, a process believed to take place largely in the right hemisphere. By exaggerating the natural prosody of speech in a sing-song manner, the developers of MIT suggest engaging sensorimotor networks in right frontotemporal regions compensates for the damaged left hemisphere. Imaging studies using fMRI and DTI have found associations between functional improvement following MIT and changes in right frontal activation (Zipse et al., 2012) as well as increased volume and number of white matter fibers in the right arcuate fasciculus, the pathway connecting superior temporal lobe regions to interior frontal lobe regions (Schlaug et al., 2009).

Another group of functional imaging studies of chronic and partially recovered aphasics argue that right hemisphere lateralization is a maladaptive process that may account for characteristic speech errors and limit recovery (Blasi et al., 2002; Belin, Van Eeckhout, Zilbovicius, & Remy, 1996; Karbe et al., 1998). Recruitment of preserved left perilesional tissue, however, has been associated with improved language outcomes (Naeser et al., 2012). Behavioral therapy techniques such as Constraint Induced Therapy for Aphasia (CITA) have been developed based on this view. CITA was adapted from a physical therapy “constraint induced” paradigm for hemiplegia. The unaffected “strong side” is physically constrained or immobilized in order to force the weak limb to carry the burden of all activities and exercises. The mechanism underlying the treatment effect of CIT is based on strengthening neural connections in the damaged hemisphere through regular use. The rationale for CITA is based on the belief that therapy induced recruitment of perilesional tissue leads to better recovery. It assumes that right hemisphere language capacities are limited and that rightward lateralization leads to characteristic telegraphic utterances, agrammatism, and semantic errors. The intensive treatment protocol attempts to constrain the right hemisphere by increasing expressive language demands, ultimately forcing activation back to more capable left hemisphere language pathways. Richter, Milter, and Straube (2008) measured right hemisphere activation in chronic aphasics before (T1) and after CITA (T2) using fMRI. Findings indicate that participants with more right hemisphere activation at T1 demonstrated greater behavioral improvement. It is possible that right hemisphere overactivation predicts greater improvement potential as they shift from a sub-optimal to optimal process.

Perhaps the most convincing evidence supporting transcollosal disinhibition theory is the application of repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) as treatment interventions for aphasia (reviewed in Hamilton, Chrysikou, & Coslett, 2011). These interventions are based on the idea that right hemisphere overactivation is maladaptive and recruitment of left hemisphere perilesional tissue is beneficial. TMS is a non-invasive method that works by discharging an electromagnetic current generated by a simple circuit and copper coil held over the head. The current penetrates the scalp causing neurons to depolarize and produce action potentials. Manipulating the frequencies of the currents leads to either increased inhibitory (low frequencies) or excitatory (high frequency) activity. Low frequency rTMS has been used to treat non-fluent aphasia by targeting overactive right hemisphere language regions homologous to the left side lesion. Significant improvements in picture naming have been observed up to 43 months post stimulation (Naeser et al., 2005; Martin et al., 2009). Similarly, high frequency rTMS to the damaged left hemisphere is thought to induce direct reactivation of perilesional neurons. Dammenkens, Vanneste, Ost, and De Ridder (2014) used high frequency rTMS targeting the left inferior frontal gyrus (LIFG) in a 55-year-old woman with chronic non-fluent aphasia. Following the treatment, improved repetition, naming, and comprehension were associated with electrophysiological changes recorded with EEG. Activity in the right IFG decreased while it normalized in the LIFG indicating a shift in laterality back to the dominant albeit damaged left hemisphere. Transcranial direct current stimulation (tDCS) uses surface electrodes to deliver small currents, giving way to excitatory activity in cortical neurons. Studies using tDCS report similar findings as rTMS with enhanced left perilesional reactivation and reduced right hemisphere activation associated with improved language function (Monti et al., 2008).

A third view of reduced laterality is that it is neither maladaptive nor beneficial but rather reflects interhemispheric interaction, a phenomenon occurring in both healthy adults and aphasics and not a consequence of unilateral damage (Raboyeau et al., 2008). The functional recruitment hypothesis suggests that activation of right cortical regions is associated with language learning in healthy brains and not merely the result of a lesion and consequent aphasia. Blasi et al. (2002) employed fMRI during word-stem completion over multiple trials to compare patterns of learning in participants with aphasia and healthy controls. Both groups demonstrated similar RT decrements, fewer errors with learning, and similar rates of stereotypical responses. Both demonstrated reduced laterality and the aphasia group had greater activation in the right frontal cortex when compared to controls. Similarly, Raboyeau et at. (2008) used positron emission tomography (PET) to compared activation in the right inferior frontal cortex in patients recovering from aphasia and healthy controls during a picture naming task before and after training. Findings indicated comparable post-training performance and changes in regional cerebral blood flow in right hemisphere regions.

Variability in lesion size and location, individual differences in premorbid laterality and language processing, dynamic changes over time, comorbidities and other factors complicate matters further. Despite this complexity, patterns of activation across and within the cerebral hemispheres associated with language function are emerging. To date, imaging studies have dominated the aphasia literature and while they provide cortical locations responsible for language behaviors, the underlying processes are generally inferred from empirical outcomes of interventions or based largely on theories.

Electrophysiology

Explaining the temporal dynamics of neural activity is critical for gaining comprehensive understanding of language recovery in aphasia. Event related potentials (ERPs) are a method for measuring electrical activity in the cortex in response to a stimulus. ERPs record voltage fluctuations in the ongoing electroencephalogram (EEG) in response to time locked stimuli and response behaviors. Highly conductive silver chloride electrodes are placed on the surface of scalp and compare electrical changes to those measured at reference locations, such as the left and right mastoid processes. Voltages changes reflect post-synaptic potentials (PSPs) which occur when ion channels open and close in response to neurotransmitters binding with receptors on post-synaptic neuron membranes. In this way, ERPs are an indirect measure of neurotransmission of large numbers neurons that are lined up in the same orientation. The polarity of populations of neurons is arbitrary and not related to function. Electrical signals travel at light speed and are not affected by tissue or skull thickness. Therefore, ERPs capture neural voltage changes on the order of milliseconds resulting in electrical waveforms or “ERP signatures.” These waveforms can reveal temporal dynamics of specific cognitive behaviors with detailed precision (Luck & Kappenman, 2012). Within the waveform are “ERP components” which are defined by their latencies, or time point at which they occur, polarity, scalp location, and amplitude. All components are dipoles which have both positive and negative peaks at some place in the cortex. The strength of the amplitude, whether positive or negative, typically reflects the sensitivity to experimental conditions and indicate the brain has “reacted” to the stimulus (Kemmerer, 2015). When we observe changes in amplitudes and latencies of ERP components as a result of the stimuli manipulation we can form inferences about what behavioral operation the component represents. Components are denoted by their polarity (N for negative and P for positive) and their latency. ERP signatures overlap other signatures from roughly six to ten neurogenerators associated with separate processes occurring simultaneously in diverse areas of the brain. As such, the ERP waveform at a given electrode is the weighted sum of all the underlying components and will not reflect the activity of the only the cortical area directly under the electrode. The greater the electrode array, the easier it is to identify underlying neurogenerators (Kemmerer, 2015). However, spatial resolution is relatively poor, especially compared to ERPs outstanding temporal resolution. Additionally, the lateral spread of the electrical signal as it moves from more conductive subdural tissue to the less conductive scalp will "blur" the signal generator (Luck & Kappenman, 2012).

Language-related ERP components

Distinct cognitive behaviors generate characteristic waveforms and components, each with their own time course. Indefrey and Levelt (2004) conducted large scale meta-analysis of imaging literature for word production along with the available ERP data for time course of activations. Based on the analyses, they describe five distinct operations for picture naming in healthy adults beginning with conceptual preparation at 175 ms post-stimuli presentation and ending with word articulation onset at 600 ms post-stimuli presentation. The first operation is conceptualization which occurs at around 175ms post-stimuli onset. This behavior is associated with the left superior and middle temporal lobe region and can be described as "categorization" or deciding what the object is and then pre-activating potential target words (lemmas) within that category. The next operation is lemma selection which occurs around 250ms post-stimuli onset. This also takes place in the left superior and middle temporal region and describes the process of selecting the appropriate syntactic features of the target word such as the part of speech, tense, and grammatical structure. This process narrows the selection until the target word is selected but is prior to accessing the phonological representation of the target word. The next operation is phonological code selection which occurs between 320 and 350ms post stimuli presentation. This operation can be described as matching the lemma, or the morphological representation, to the phonological representation, or the way it sounds. Phonological coding is associated with inferior posterior region of the left frontal lobe.

The phonological code is then broken into smaller components, a process called “syllabification”, in preparation for motor programming. Syllabification occurs around 475ms post stimuli onset and is associated with the left posterior IFG. Finally, the phonetic code is sent to the supplemental motor area (SMA) and the premotor cortex for motor programming and planning and then to the primary motor cortex (M1) for motor execution. Verbal output time is measured by articulation or voice onset and typically occurs around 600ms post stimuli presentation.

The N400 is negative defection in the waveform peaking around 400 ms post stimuli onset. The N400 is associated with semantic access, or word meaning (Kutas & Federmeier, 2000). As sentences unfold, word by word, context and expectation allow for greater ease of lexical access. Therefor the N400 amplitude decreases as it becomes easier to fit words into plausible sentences. However, when the word expectation is violated the N400 amplitude dramatically increases. Another language-related component is the P600 which is sensitive to syntactic agreements such a verb tense, subject/pronoun agreement, and word order (reviewed in Hagoort, Brown, & Osterhout, 1999). Again, violations of such agreements elicits greater P600 amplitudes. While one is sensitive to semantic information and the other structural, the N400 and P600 both appear to be modulated by expectation and can be observed in behaviors beyond language including world knowledge (Hagoort, Hald, Bastiaansen, & Petersson, 2004), math (Nunez-Pena & Honrubia-Serrano, 2004), and music (Patel, Gibson, Ratner, Besson, & Holcomb, 1998). An earlier component, the “N2” is associated with nonselective and selective response inhibition and has more recently been described in competitive lexical selection (Shao, Roelofs, Acheson, & Meyer, 2014).

Top-down response inhibition is a hallmark of executive control and has been study extensively using non-linguistic tasks such as Go/NoGo tasks. Barry and Blasio (2014) describe ERPs associations for the N1 component as the start of the identification of the Go/NoGo stimulus, the frontal N2b as the subsequent categorization of NoGo stimuli, and the posterior N2c Go categorization. The amplitude of the N2b component is increased in NoGo trials when compared to Go trials (Sasaki, Gemba, Nambu, & Matsuzake, 1993). The NoGo N2b is followed by enhanced amplitude of a NoGo P3 component relative to the P3 signal elicited by Go trials (Kok, Ramautar, De Ruiter, Band, & Ridderinkhof, 2004).

Another common paradigm to examine inhibitory control is the stop-signal task where participants plan a go response but must suppress the response when a stop signal is presented (Vergruggen & Logan, 2008). The stop-signal is associated with the P3 component and requires greater inhibitory pressure on response-related processes because it involves withholding of a response that has already been triggered by the N2c Go reaction signal. Successful and unsuccessful stop-signaling is associated with differences in latencies between N2 and P3 components such that early P3 signals prevent concurrent activation processes while later P3 signals ineffectively suppress response activation (Kok et al., 2004). These findings are consistent with the horse race model proposed by Logan and Cowan (1984). The model describes action control as a race between an independent Go process that underlies an action and a separate NoGo process that inhibits the action. Responses are inhibited if the NoGo finishes before the Go process (Logan, Verbruggen, Van Zandt, Wagenmakers, 2014).

The Eriksen flanker task is a choice response task where participants choose a response to a central target stimulus, such as letters *H* and *S*, that is flanked by non-target stimuli (Eriksen & Eriksen, 1974). The task requires selective inhibition of responses competing with a target response. Trials are congruent if the target and distractors call for the same response (e.g. HHHHH or SSSSS) and incongruent when the target and distractors call for different responses (e.g. HHSHH or SSHSS). Larger frontal N2 amplitudes are elicited in response to incongruent flanker trials compared to congruent flanker trials (Purmann, Badde, Luna-Rodriguez, & Wendt, 2011). Based on the suggestion that inhibition plays an important role in lexical selection for language processing, de Zubicaray et al. (2001) adapted the Eriksen flanker task in a picture-word interference paradigm in an event related fMRI study. They reported hemodynamic responses associated with semantic inhibition in the left posterior and middle temporal gyri (MTG), and the left posterior superior temporal gyri (STG). These findings suggest that lexical response inhibition might occur at two time points described by Indefrey and Levelt (2004), first during conceptual selection and again during phonological code selection (de Zubicaray et al., 2001).

Shao et al. (2014) used ERPs to explore modulation of the N2 component in response to selective inhibition during a competitive lexical selection task. Participants were asked to name pictures with either high or low name agreement. Pictures with high name agreement had few lexical competitors. For example, a picture of a dog will be labeled “dog” by most participants. Pictures with low name agreement had several lexical competitors. For instance, a picture of a young person could be labeled “child”, “kid”, “baby” or “infant.” The N2 amplitude was enhanced in the low name agreement condition compared to the high name agreement condition, providing further evidence that the N2 component is associated with response inhibition during word selection tasks.

Few studies have used ERPs to investigate temporal dynamics in patients with aphasia. Depending of the aphasia sub-type we would expect divergences in ERP signatures at different time points, providing details about the specific process impaired. Laganaro, Morand, and Schnider (2009) examined this issue in patients with anomic aphasia who presented with either semantic errors (verbal paraphasias) or phonological errors (literal paraphasias) and found ERP abnormalities at different times; early for the semantic group (100-250 ms post-picture presentation) and later for the phonological group (300-450 ms post-picture presentation). Another study comparing emotional and neutral word processing in aphasics and healthy controls reported similar waveform patterns but differences in amplitude strength and latencies (Ofek et al., 2013). Hemisphere differences in ERP amplitudes and latencies in patients with aphasia compared to healthy adults has to yet to be explored. Certainly this information could provide key insights into qualitative and quantitative contributions of the left and right hemispheres, which could further inform intervention practices based on neurobiological principals of recovery.

Present Study

The aim of the present study was to examine how laterality and lexical selection are affected by word-finding difficulty in patients with chronic aphasia and in healthy adults. I used event-related potentials (ERP) to record neural activity that is time-locked to the cognitive events of interest. Specifically, I compared ERP signatures between the two groups, during word-stem completion and picture naming. Owing to their high temporal resolution, ERPs can reveal temporal dynamics and general spatial distribution of neural activity underlying word-finding processes. Word-stem completion is a gold standard task for studying word-generation and has also been used to examine the right hemisphere's ability for word-finding. Word-stem stimuli were divided into three conditions; easy: many completions/common words, difficult: few completions/uncommon words, and high frequency: 1-2 completions/common words. Picture naming stimuli will be divided into two conditions; easy: common objects, and difficult: unusual objects.

Predictions

I predicted differences in laterality and modulation of the N2 and N400 components between groups and conditions.

Primary Aim 1: Determine differences in laterality during easy and difficult word finding in aphasia and control groups. It was predicted that the control group would show a hemisphere difference in amplitude for the easy word finding condition, but not the difficult condition, and that the aphasia group would not show laterality effects in either condition

H_1: Controls will demonstrate hemisphere differences in amplitude for the easy word-finding condition with greater amplitudes in the left hemisphere but not the difficult condition and the aphasia group will not show laterality effects in either easy or difficult word-finding conditions. This will demonstrate 1.) previously observed patterns of decreased laterality in participants with aphasia during typical word-finding tasks, and 2.) that when word finding is difficult, control participants engage bilateral processes similar to aphasia participants. This finding will support the interhemispheric interaction hypothesis that reduced laterality observed in aphasia is a response to task difficult rather than a lesion effect.

Primary Aim 2: Determine the impact of lexical competitors on laterality in aphasics and healthy adults.

H_2: Controls will demonstrate hemisphere differences with greater N200 amplitudes in the left hemisphere during the high frequency word-finding condition compared the easy word-finding condition and that participants in the aphasia group will not demonstrate hemisphere differences in N200 amplitude in either condition. This will demonstrate that lexical response inhibition increases in trials with many response competitors when compared to trials with few competitors and is lateralized to the left hemisphere in healthy adults. This finding will provide further support the N200 component is associated with selective lexical response inhibition. This will also demonstrate that response inhibition is reduced in participants with aphasia, providing evidence for the more recent view that word-finding errors in aphasia are associated with poor inhibitory control as well as lexical search and selection processes associated with the right hemisphere.

Secondary Aim: Determine if word-finding accuracy is associated with laterality.

H_3: As left laterality decreases, accuracy in the difficult condition increases (negative correlation between laterality index and accuracy). This finding will provide evidence for a supportive role of the right hemisphere during difficult word-finding tasks.

Research Design Considerations

I have identified several important methodological design considerations related to this study and will provide a rationale for my decisions. Three potential areas of concern included aphasia participant inclusion/exclusion criterion, word-finding task selection, covert vs overt naming.

The first design consideration was whether to restrict inclusion criterion to a single aphasia sub-type, similar general site of lesion, and severity, or to expand criterion to include participants with diverse language errors, lesion sites and severities. While anterior lesions in the left perisylvian zone result in non-fluent, expressive aphasias and posterior lesions lead to fluent, comprehension aphasias, both sub-types include deficits in word-finding and naming. Similarly, both anterior and posterior lesions are associated with rightward laterality during expressive language tasks, the primary process of interest. Obtaining a homogenous sample of aphasic participants has logistic limitations such as lack of access to medical, radiology, and other imaging records, and challenges recruiting participants with chronic aphasia. Numerous studies measuring general patterns of anomia, reduced laterality, and recovery include participants with diverse types of aphasia and lesion sites (Laganaro et al., 2009; Ofek et al. 2013; Richter et al., 2008; Thulborn et al., 1999). The decision to include multiple aphasia subtypes allows for a larger sample size without compromising the predicted effects.

Another design consideration was word-finding task selection. Picture naming is a standard method for measuring word-finding and expressive language performance. Task instructions are simple and stimuli trials can be presented quickly, reducing completion time and fatigue in the aphasia group. Picture naming in the control group, on the other hand, will have a low ceiling effect. Picture stimuli were divided into “easy” and “difficult” conditions based on pilot data obtained from healthy participants. While there was reduced accuracy and increased reaction time in the “difficult” condition compared to the “easy” condition, the effects were likely due to participant’s unfamiliarity with the picture rather than difficulty thinking of the object name. In order to manipulate task difficulty in the control participants, I decided to use a word-generation task. Word-stem completion is the gold standard word-generation task and is sensitive to changes in task difficulty. The stem-completion task allowed me to capture true word-finding difficulty in healthy controls without concerns of ceiling effects or that they simply do not know the word.

Another consideration was using overt versus covert picture naming and stem-completion during ERP acquisition. Earlier EEG studies have used covert naming paradigms to reduce motor artifacts during speech articulation (Greenham, Stelmack, & Campbell, 2002; Wohlert, 1993). However, the word-finding processes of interest occur well before speech onset (Ganuschak, Christoffels, & Schiller, 2011). I analyzed the time window prior to the introduction of such motor artifacts. To reduce completion time, participants were encouraged to proceed to the next trial if word-generation is not completed within five seconds. Additionally, responses were recorded during ERP acquisition for picture naming only because the experiment was limited to 40 trials. Behavioral accuracy data, on the other hand, was collected from a word-stem task completed prior to ERP acquisition due to the larger number of stem trials (200).

Methods

Participants

A total of 20 adult subjects were recruited; 10 participants with chronic aphasia (> one year post-stroke) resulting from cerebrovascular accidents (CVAs) and 10 control subjects. Socio-demographic and clinical data for all participants are provided in Table 1. Participants in each group were matched based on age and years of education. All participants spoke English as their primary language and were right handed as determined by the Edinburgh Handedness Inventory (Oldfield, 1971). Participants with aphasia were recruited from the Eardly Speech Language and Hearing Clinic at Fontbonne University in St. Louis Missouri. Patient participants were selected based on the presence of expressive aphasia and anomia and ability to follow task directions. Exclusion criteria included more than one CVA, neoplasm, pre-morbid seizure disorder, progressive neurological disease, visual spatial deficits (hemi-anopsia, scotoma, or neglect), a history of traumatic brain injury with loss of consciousness greater than 30 minutes, or a Beck Depression Inventory- Second Edition (BDI-II) (Beck, Steer, & Brown, 1996) score greater than twenty. All participants with aphasia were receiving ongoing speech-language therapy services during the time of the study. The Clinical Dementia Rating (CDR) was used to screen for dementia in the patient group. Patient spouses or primary care-givers served as informants. All control participants were screened for dementia and excluded if they scored 0-4 on the Short Blessed Test (SBT) (Katzman et al., 1993). Other exclusion criteria included scores below two standard deviations of normative means on non-verbal intelligence and receptive vocabulary tests, or a BDI II score greater than twenty. This study had the approval of the University of Missouri – St Louis Institutional Review Board and signed informed consent statements were obtained prior to administering the self-report questionnaire. Participants were compensated at the rate of 20 dollars per hour for their time.

Standardized Measures

All participants completed the Test of Nonverbal Intelligence-4th Edition (TONI-4) (Brown, Sherbenou, & Johnsen, 1997) and the Peabody Picture Vocabulary Test- 3rd Edition (PPVT-3) (Dunn & Dunn, 2007) to determine non-verbal intelligence and receptive vocabulary respectively. Scores for both groups are provided in Table 2. These measures were selected based on their potential influence on experimental task performance. For example, if participants were identified as having below average non-verbal IQ or limited receptive language repertoire, poor accuracy on word-stem completion and picture naming tasks could reflect premorbid or concomitant cognitive deficits beyond aphasia in the patient population. Below average scores in the control group could reduce the contrasts in task performance when comparing the patient to control group.

Scores from the Western Aphasia Battery (WAB) (Kertesz, 1982) were used to characterized subjects based on aphasia subtype, severity, and aphasia quotient. Recent WAB scores (<6 months) were obtained from the patient’s clinical files.

Stimuli/Procedure

Word-Stem Task

Stimuli

A total of 200 three-letter word beginnings or word-stems were selected based on Kucera written frequencies (Kucera & Francis, 1967) and normative data from Shaw (1997). Three letter stems that could in fact be words (e.g. THE) were removed from the final list. Word-stems were then classified into three conditions; Easy (80), Difficult (80), and

High Frequency (40) based on stem-completion norms collected from the UMSL student population. Easy stems were defined as having multiple possible completions, many of which are common words (e.g. STA). Normative data confirmed that participants quickly and accurately completed Easy stems with a variety of word completions. Difficult stems were defined as having few completions, all of which are uncommon words (e.g., PTE). High-frequency stems were defined as those that have few completions but among them at least one or two common words (e.g. KNE).

All word-stem stimuli were presented in lowercase, black 18-point Courier New font on a white background using a 19-inch CRT monitor. E-Prime software (Psychology Software Tools, Pittsburgh, PA) was used to control experimental events and record behavioral responses. On each trial, a fixation cross appeared for (1,000 ms) to maintain participant focus and alert them to anticipating trial presentation, with a 1,000 ms inter-trial interval, during which participants were encouraged to blink. Each stem trial was presented in the center of the screen until a response was given. Stems were presented in random order of condition, in four blocks of fifty trials. Participants were encouraged to take brief breaks between blocks to rest their eyes and adjust in their seats.

Procedure

Participants were asked to generate a complete word, beginning with the three-letter stem. Reaction time for word retrieval was recorded with a button press and participants were instructed to press the button as soon as they had thought of a word to complete the stem. Examiners were experienced speech language pathologists or graduate students in speech language pathology. Twelve practice trials ensured that participants understood the task instructions, and were followed by the 200 experimental items. Responses were judged to be accurate if they were real words (not acronyms) in the English lexicon or socially accepted words in the vernacular. Slang and proper names were accepted as accurate responses if they met all other accuracy criteria. Misspellings, literal paraphasias, and phoneme errors secondary to dysarthria were not counted as errors if the intended word in fact started with the three-letter stem when spelled or articulated correctly.

Picture naming task

Stimuli

Forty black and white line drawings taken from the Boston Naming Test (BNT) (Kaplan, Goodlass, & Weintraub, 1983) were presented centrally on a 19-inch CRT monitor. Drawings in the easy condition (20) were derived from pictures 1-20 in the BNT. The Difficult condition (20) was derived from the last 20 imaged in the BNT. Normative data was collected from the university population to ensure that reaction time and accuracy were significantly different between the two conditions. Picture stimuli were presented in order of difficulty beginning with easy items and progressing to difficult items. E-Prime software was used to control experimental events and record reaction times.

Procedure

Participants were asked to press a button to record reaction time when they have mentally accessed the name of each line drawing. Next they provided the picture name verbally. The examiner recorded verbal responses phonetically for accurate analyses. Responses were judged accurate in accordance with BNT scoring criteria and if they are accessed within 5000 ms post-stimuli onset. To assess timing and accuracy of word finding specifically, I controlled for literal paraphasias and phonological errors secondary to dysarthria and they were not counted as errors in naming.

Electrophysiological recording

The electroencephalogram was amplified and continuously recorded from 16 scalp sites, using Ag/AgCl electrode channels placed in a nylon electrode placement cap according to the 10/20 International System (Active-Two; BioSemi, Amsterdam, Netherlands). Additional UltraFlat Active electrodes (BioSemi) were placed on the outer canthi and above and below the left eye. Vertical electro-oculogram (VEOG) and horizontal electro-oculogram (HEOG) was recorded to identify vertical and horizontal eye movements. UltraFlat Active electrodes were also placed on the left and right mastoid processes. Online recordings were referenced to electrodes placed on the mastoids. All recorded EEG voltages were relative to a common mode voltage based on common mode sense (CMS) and driven right leg (DRL) feedback loops (Active-Two). All signals were digitized with a sample rate of 256 Hz.

Offline, all scalp electrodes were referenced to an average of the left and right mastoid signals. Data was baseline corrected and then filtered using a linear finite 30 Hz band pass filter. Data was segmented in epochs from 100 ms prestimulus until 1,000 ms post-stimulus onset. Independent component analysis (ICA) was used to solve the blind source separation problem common in clinical populations (Jung et al, 2000). Trials containing eye blinks and other exogenous artifacts were rejected offline before averaging (<29% of trials were removed). Artifact rejection criteria was defined as minimum and maximum baseline-to-peak -75 to 75 mV.

ERP Analyses

Grand-average ERP waves were calculated for each group (aphasia/control) in each condition (easy/difficult/ and easy/high frequency). Analyses were performed for two time windows representing conceptual planning and word selection (N200: 100-320ms), and phonological encoding (N400: 350-500 ms) over a group of 4 electrode sites in the left hemisphere (F3, T7, C3, P3) and the right hemisphere (F4, T8, C4, P4).

Statistical Analysis

Primary Aim 1: Determine differences in laterality during easy and difficulty word finding in aphasia and control groups.

The first set of analyses explored differences between aphasics and healthy controls in laterality. Repeated measures ANOVAs were performed to investigate main effects of group (aphasia/control), condition (easy/difficult), and hemisphere (left/right). For these analyses, voltages were averaged over right hemisphere (F4, T8, C4, P4) and left hemisphere (F3, T7, C3, P3) sites. Repeated measures ANOVAs were also performed at individual electrode site pairs in each hemisphere (F3/F4, T7/T8, C3/C4, P3/P4) to investigate main effects of group, condition, and hemisphere in the frontal, temporal, central, and parietal regions specifically. Greenhouse-Geisser correction was used to offset sphericity violations common in ERP data. Separate analyses were performed for each task (picture naming and stem completion) and each time window (N200 and N400).

Crucially, it was predicted that the control group would show a hemisphere difference in amplitude for the easy word finding condition, but not the difficult condition, and that the aphasia group would not show laterality effects in either condition.

In order to investigate effects of difficulty on laterality in each group within each condition, paired samples t-tests were performed separately within control and aphasia groups. Hemisphere served as the independent variable and mean amplitude served as the dependent variable.

Primary Aim 2: Determine the impact of lexical competitors on laterality in aphasia and control groups.

The second set of analyses explored the impact of lexical competition on laterality in aphasics and healthy adults. These ANOVAs and paired samples t-tests were similar to those described above, but contrasted voltages between easy (many competitors) and high frequency (few competitors) stems.

Secondary Aim: Determine if word-finding accuracy is associated with laterality.

Finally, in order to determine if language performance is associated with laterality, Pearson product-moment correlation coefficients were used to examine relationships between word-finding accuracy (word-stem completion and picture naming) and laterality index. Laterality indices (LI) was calculated for the N400 component using the following formula:

$$\text{LI} = \frac{\text{N400 amplitude left} - \text{N400 amplitude right}}{\text{N400 amplitude left} + \text{N400 amplitude right}}$$

Laterality indices were calculated for each participant in the easy (Easy LI) and difficult (Difficult LI) stem completion conditions.

Power Analyses

Sample size (N=40) is based on an 84% power analysis, assuming a large effect size and significance set at $p < .05$. Ofek et al. (2013) examined differences in mean ERP amplitudes and scalp locations among aphasics and healthy controls during a word processing task and reported significant differences between groups and hemispheres (Cohen's d =.85). Inherent challenges in recruitment of clinical populations limited the final sample to 20 participants.

Results

Primary Aim 1: Differences in laterality during easy and difficult word finding

Stem Completion: Effects of Difficulty on N200 Laterality

To investigate group differences in effects of difficulty on N200 laterality, repeated measures ANOVAs were conducted with group (aphasic/control), condition (easy/difficult), and hemisphere (left, right) as independent variables. When combining electrodes in each hemisphere, there were no significant main or interaction effects. See Table 3. Analyses of individual electrode sites revealed a significant interaction between hemisphere and group in frontal (F3, F4) [$F(1,16) = 5.98$ ($p< .05$)] and parietal regions (P3, P4) [$F(1/15) = 5.02$ ($p<.05$)]. In the frontal region, there was a significant hemisphere difference in the aphasia group only ($p<.05$) with greater amplitude in the RH than the LH (Table 4.) There were no group differences within each hemisphere. In the parietal region, there was a significant hemisphere difference in the control group only

(p<.05) with greater amplitude in the RH than the LH. There were no group differences within each hemisphere.

When analyzing each group separately, there was a significant hemisphere difference among controls in the easy condition in the parietal region with greater amplitude in the RH (P4) than the LH (P3) ($t(7) = 2.33$, $p < .05$) . Hemisphere differences among controls in the easy condition within the frontal, temporal, and central electrodes were not significant (ts < 1.2). There was also a significant hemisphere difference among controls in the difficult condition in the frontal region with greater amplitude in the LH (F3) than the RH (F4) ($t(8) = 3.89$, $p<.01$). Hemisphere differences among controls in difficult condition within the temporal, central, and parietal regions were not significant (ts< 1.85). There were not significant hemisphere differences among the aphasia group in either condition at time 1 (ts < 1.73).

Stem Completion: Effects of Difficulty on N400 Laterality

To investigate group differences in effects of difficulty on N400 laterality, repeated measures ANOVAs were conducted with group (aphasia/control), condition (easy/difficult) and hemisphere (left/right) as independent variables. There was a significant main effect of hemisphere in the frontal region and when combining electrodes by hemisphere with greater amplitude in the LH than the RH [$F(1/15) = 6.44$ (p<.05), $F(1,13) = 11$ (p<.01)]. Main effects of condition and group were not significant. See Table 5. There was a significant interaction between hemisphere and group in the parietal region. However, simple effects were not significant.

When analyzing each group separately and combining electrodes by hemisphere, controls showed a significant difference in hemisphere within the easy condition with greater amplitude in the LH than in the RH ($t(7) = -3.08$, $p<.05$) (Table 6). There was also a significant difference in hemisphere among controls in the difficult condition but with greater amplitude in the RH than the LH ($t(8) = -3.29$, $p<.05$). Analyses of individual electrode sites in the easy condition revealed a significant hemisphere difference among controls in the temporal region with greater amplitude in the LH (T7) than the RH (T8) ($t(7) = -2.64$, $p <.05$). See Figure 1. Differences among controls in easy condition were not significant in the frontal, central, and parietal regions (*t*s< -1.79). Analyses of individual electrode sites among controls in the difficult condition revealed significant hemisphere differences within temporal, central, and parietal regions. There was significantly greater amplitude in the RH (T8) than the LH (T7) ($t(8) = -2.61$, $p<.05$), RH/C4 than LH/C3 ($t(8) = -2.56$, $p<.05$), and RH (P4) than LH (P3) [$t(8) = -2.65$ ($p<.05$)]. Differences among controls in the difficult condition were not significant in the frontal region ($t(8)= -.84$). See Figure 2. There were no significant hemisphere differences in the easy or difficult conditions in the aphasia group (*t*s< -1.97).

Picture Naming: Effects of Difficulty on N200 Laterality

To investigate group differences in effects of difficulty on N200 laterality, repeated measures ANOVAs were conducted with group (aphasia/control), condition (easy/difficult) and hemisphere (left/right) as independent variables. There was a significant main effect of hemisphere in the central [$F(1/17) = 7$ ($p<.05$)], and parietal regions [$F(1/17) = 6.39$ ($p<.05$)] and when electrodes were combined by hemisphere [$F(1/13) = 6.62$ ($p<.05$)] with greater amplitude in the RH than the LH. See Table 7.

There was also an interaction between hemisphere and difficulty over frontal electrodes [$F(1/16) = 6.02$ ($p<.05$)] with greater LH amplitude in the difficult condition ($p<.01$). There were no significant differences in the easy condition. Differences between easy and difficult naming in the LH trended towards significance ($p=.05$). Differences between easy and difficult naming in the RH were not significant.

Analyses of each group separately revealed significant hemisphere differences among the aphasia group. During difficult picture naming, there was a significant difference in frontal electrodes with greater amplitude in the LH (F3) than RH (F4) ($t(8) = -4.87$, $p<.001$) (Table 8). However, in parietal regions there was significantly greater amplitude in the RH (P4) than the LH (P3) ($t(8) = -2.26$, $p< .05$). Differences in the temporal and central regions were not significant in the aphasia group during difficult picture naming (ts< -1.94). There was not a significant hemisphere difference among the aphasia group in the easy condition ($t<-1.26$). There were no significant hemisphere differences among the control group in the easy or difficult conditions (ts<-1.58).

Picture Naming: Effects of Difficulty on N400 Laterality

To investigate group differences in effects of difficulty on N400 laterality, repeated measures ANOVAs were conducted with group (aphasia/control), condition (easy/difficult) and hemisphere (left/right) as independent variables (Table 9). There was a significant main effect of group in the frontal region [$F(1,17) = 6.07$ ($p< .05$)] with greater mean amplitude among the aphasia group than the control group. This effect was not significant in temporal, central, parietal, and combined electrode sites. Main effects of condition and hemisphere were not significant; however, there was a significant interaction between hemisphere and group in the frontal region [$F(1/17) = 6.84$ ($p<.05$)]

with greater amplitude in the LH than RH within the aphasia group ($p<.05$). There were not significant hemisphere differences within the control group. There was a significant group difference in the LH with greater amplitude in aphasia group compared to controls ($p<.01$) but there was not a significant group difference in the RH. Interaction effects were not significant in temporal, central, parietal, or combined electrode sites.

Analyses of each group separately showed a significant hemisphere difference among the control group. During easy picture naming, there was a significant difference in the temporal region with greater amplitude in the LH (T7) than the RH(T8) ($t(9) = 2.99$, $p<.01$). See Figure 3. There were no significant hemisphere differences in the frontal, central, or parietal regions among the control group in the easy condition (ts<1.75). There was not a significant hemisphere difference among the control group in the difficult condition ($t<-.7$). Finally, there were no significant hemisphere differences among the aphasia group in the easy or difficult conditions (ts<-2.02). See Table 10.

Primary Aim 2: Impact of lexical competitors

Stem Completion: Effects of Lexical Competitors on N200 Laterality

To investigate group differences in effects of lexical competitors on N200 laterality, repeated measures ANOVAs were conducted with group (aphasic/control), condition (easy/high frequency) and hemisphere (left/right) as independent variables (Table 11). There were no significant main effects of group, condition, or hemisphere. There was a significant interaction between hemisphere and group in the frontal region [$F(1,16) = 5.84$, $p< .05$)] with greater amplitude in the RH (F4) than LH (F3) within the aphasia group ($p<.05$). There were not significant hemisphere differences among the controls.

There were no differences between groups within each hemisphere. There was a significant interaction between condition and group when electrodes were combined by hemisphere [*F*(1/13) = 6.4 (*p*<.05)] but simple effects were not significant. There was a significant interaction between condition and group in the temporal region [*F*(1/14) = 5.18 (*p*<.05)] with greater amplitude in the easy condition among the control group (p<.05). There were no significant effects of condition in the aphasia group. There were no significant effects of group in either condition.

Analyses of each group separately showed a significant hemisphere difference among the control group in the high frequency condition in the frontal region with greater negative amplitude in the RH (F4) than the LH (F3) (t(8)=2.58, *p*<.05). See Table 12. There were no significant hemisphere differences among the control group in the high frequency condition in temporal, central, or parietal regions (*t*s<-1.69). There were no significant hemisphere differences in aphasia group in the easy or high frequency conditions (*t*s< -1.95).

Stem Completion: Effects of Lexical Competitors on N400 Laterality

To investigate group differences in effects of lexical competitors on N400 laterality, repeated measures ANOVAs were conducted with group (aphasia/control), condition (easy/high frequency) and hemisphere (left/right) as independent variables (Table 13). There was a significant main effect of hemisphere in the frontal region only [*F*(1/16) = 5.74 (*p*<.05)] with greater amplitude in the LH (F3) than the RH (F4). There was a significant interaction between hemisphere and group in the parietal region [*F*(1/16) = 5.26 (*p*<.05)] however, simple effects by group and hemisphere were not significant. There was also a significant interaction between condition and group in temporal and central regions [$F(1/15) = 6.78$ ($p<.05$), $F(1/17) = 7.42$ ($p<.05$)] with greater amplitude in the high frequency condition for the aphasia group ($p<.05$). Differences between conditions within the control group were not significant. There were no differences between groups based on condition. When electrodes were combined by hemisphere there was a significant interaction between condition and group [$F(1/13) = 14.23$ ($p<.01$)] with greater amplitude in the high frequency condition for the aphasia group ($p<.05$) but greater amplitude in the easy condition for the control group ($p<.05$). There were no differences between groups within each condition.

When analyzing each group separately and combining electrodes by hemisphere, controls showed a significant hemisphere difference in the high frequency condition with greater amplitude in the RH than the LH ($t(8) = -2.34$, $p< .05$) and within the easy condition with greater amplitude in the LH than in the RH ($t(7) = -3.08$, $p<.05$). See Table 14. Analyses of individual electrodes showed a significant hemisphere difference in the high frequency condition among the control group in the parietal region with greater amplitude in the RH (P4) than the LH (P3) ($t(8) = -3.36$, $p<.05$)]. See Figure 4. Within the high frequency condition, there were no significant differences in the frontal, temporal, or central areas (ts< 1.82). Analyses of individual electrode sites in the easy condition revealed a significant hemisphere difference among controls in the temporal region with greater amplitude in the LH (T7) than the RH (T8) ($t(7) = -2.64$, $p<.05$). Differences among controls in easy condition were not significant in the frontal, central, and parietal regions (ts<-1.79). There were no hemisphere differences in the easy or high frequency conditions among the aphasia group (ts<-1.89).

Secondary Aim: Relationship between performance and laterality

Picture Naming and Stem Completion Accuracy and Laterality

In order to determine if word-finding was associated with laterality, Pearson product-moment correlation coefficients were used to examine relationships between word-finding accuracy and laterality index. Laterality indices were calculated for each participant in difficult and easy stem completion conditions. See Table 15. There was significant positive correlation between LI in the difficult condition and accuracy in the difficult picture naming task for the control group ($r(10)=.69$, $p<.05$). There was not a significant correlation between difficult LI and difficult picture naming in the aphasia group ($r(10) =.12$). There were no significant correlations between easy LI and easy picture naming in the control group ($r(10) =.06$) or the aphasia group ($r(10) =.06$). There was not a significant correlation between difficult LI and difficult stem completion in the aphasia group ($r(10) = -.56$). There was not a significant correlation between easy LI and easy stem completion ($r(10) = .18$).

Behavioral Measures: Aphasia Group

In order to examine differences in performance based on task difficulty, paired samples t-tests were used to examine stem completion accuracy in each condition. There was a significant difference in accuracy between the easy and difficult stem completion condition ($t(8) =11.39$, $p<.001$) with greater accuracy in the easy condition (M = 86%) than the difficult condition (M = 46%). There was also a significant difference between accuracy in the difficult and high frequency condition ($t(8) = -6.28$, $p<.001$) with greater accuracy in the high frequency (M = 79%) condition than in the difficult condition. Accuracy differences between easy and high frequency stems were not significant (*t*(8)>.15). For picture naming, there was a significant difference in accuracy between the easy and difficult conditions (*t*(9) = 6.51, *p*<.001) with greater accuracy in the easy condition (*M* =61%) than the difficult condition (*M* = 21%). To determine if receptive vocabulary was associated with word-finding performance, Pearson product-moment correlation coefficients were used to explore relationships between PPVT-3 and accuracy scores for stem completion and picture naming. There were no significant relationships between PPVT-3 scores and easy picture naming accuracy (*r*(10) = .41) or difficult picture naming (*r*(10) = .55). There were no significant relationships between PPVT-3 scores and easy stem completion accuracy (*r*(10) = .64), or difficult stem completion accuracy (*r*(10) = .44).

Behavioral Measures: Control Group

In order to examine differences in performance based on task difficulty, a paired samples t-test was used to compare accuracy in difficult picture naming to easy picture naming. There was significant difference in accuracy (*t*(9)=4.92, p<.01) with greater accuracy in the easy condition (*M* = 99.5%) compared to the difficult condition (*M* = 76%). To determine if receptive vocabulary was associated with word-finding performance, Pearson product-moment correlation coefficients were used to explore relationships between PPVT-3 scores and picture naming accuracy. There was a significant positive correlation between PPVT-3 scores and accuracy in the difficult picture naming condition (*r*(10) =.64, *p*<.04). There was not a significant correlation between PPVT-3 scores and accuracy in easy picture naming condition (*r*(10) =.31).

Discussion

The present study measured changes in ERP amplitude in the left and right cerebral hemispheres of patients with chronic aphasia and aged matched healthy adults during word-finding tasks. Results revealed differences in laterality based on task difficulty. Specifically, during easy word-finding tasks, participants in the healthy control group demonstrated leftward laterality with greater N400 amplitude in the left hemisphere than the right hemisphere. The effect was evident in both picture naming and stem-completion tasks. Participants with chronic aphasia, however, did not demonstrate left hemisphere dominance during easy word finding. These findings are consistent with previous studies that reported decreased laterality in participants with aphasia during typical word-finding tasks (Silvestrini, Troisi, Matteis, Cupini, & Caltagirone, 1995; Thulborn et al., 1999; Weiller et al., 1995; Xing et al., 2016).

The role of the right hemisphere in aphasia has been debated in previous studies. Some argue that reduced laterality is a maladaptive process that may in part account for characteristic speech errors and may limit recovery (Belin et al., 1996; Blasi et al., 2002; Karbe et al., 1998). Yet others suggest increased right hemisphere activation represents a neuroplastic pattern and accounts for language recovery after vascular insults (Mohr et al., 2016; Rosen et al., 2000; Thulborn et al., 1999; Zipse et al., 2012). Based on the current data, I posit that language restitution in aphasia might be attributed to partial normalization of processes, which include strong left laterality balanced with complimentary right hemisphere support, whereas over or under reliance on right hemisphere processes could lead to errors. This account resolves conflicting findings of previous studies.

Hemisphere differences also emerged during difficult word-finding conditions. Beyond the prediction that control participants would demonstrate reduced laterality in difficult conditions, results showed consistent rightward dominance during the difficult stem completion task with greater N400 amplitudes in right temporal, central, and parietal regions. This finding not only supports the interhemispheric interaction hypothesis proposed by Banich and colleagues (1998) that bilateral activation is a response to task difficulty, it also provides evidence of a right hemisphere advantage during difficult word-finding.

Based on the coarse code hypothesis, semantic processing is strong but narrow in the left hemisphere and broad but weak in the right hemisphere (Jung-Beeman, 2005). In this context, word-finding difficulty may have led to broader semantic searches, thus, a right hemisphere advantage. When considering right hemisphere activation in aphasia, data suggest that reduced laterality is a response to task difficulty rather than a lesion effect. This account is consistent with Raboyeau and colleagues (2008) who argue that reduced laterality is neither maladaptive nor beneficial but rather reflects functional recruitment, a phenomenon occurring in both healthy adults and patients with aphasia. Further, aphasic participants were not sensitive to differences between easy and difficult tasks. A potential explanation is that all word-finding tasks are essentially “difficult” for individuals with aphasia. Therefore, consistent patterns of bilateral activation are observed.

Stem completion and picture naming accuracy data were obtained for the aphasia group. Fewer errors were made in easy conditions compared to difficult conditions. Accuracy data for the control group was only obtained from the picture naming task due to ceiling effects of the stem completion task. While control participants made more errors in the difficult picture naming condition than they did in the easy condition, as expected, they significantly outperformed the aphasia group in both easy and difficult conditions. Contrary to the hypothesis that decreased laterality would be associated with increased accuracy in the difficult conditions, laterality indices were positively correlated with picture naming accuracy in controls. Similar findings were reported in Mohr et al. (2016) who investigated therapy induced changes after intensive language therapy. Patients demonstrated increased left lateralization, which was positively correlated with improvement. While there are previous studies that are in line with these results, it is worthwhile to consider alterative explanations. First, laterality indices (LIs) were calculated based on stem completion rather than picture naming tasks. While both tasks require word-finding processes, picture naming and stem completion are fundamentally distinct language tasks. Picture naming is confrontational and highly constrained, whereas stem completion is generative and more flexible. For example, a picture of a unicorn will only lead to one accurate response (“unicorn”) while the word stem “UPH” could generate multiple accurate responses such as “uphill”, “uphold”, or “upholstery”. Therefore, it is possible that LI based on stem completion would not accurately predict picture naming performance. A second possible explanation is that participants who achieved higher accuracy scores for difficult picture naming could also have larger vocabularies. Indeed, receptive vocabulary, based on PPVT-3 scores, was significantly positively correlated with difficult picture naming accuracy. If rightward laterality occurs when word-finding is difficult, the lack of a negative correlation could indicate that control participants with high accuracy scores were not sensitive to difficult naming tasks because essentially all naming tasks were “easy”. Certainly the data show that when word-finding is difficult, the right hemisphere engages regardless of a lesion. Therefore, it appears self-evident that supportive right hemisphere contributions are part of healthy language processing. Finally, the positive correlation could have been due to a potential outlier. There was control participant with a strong right laterality index along with the lowest difficult picture naming accuracy. When the outlier was removed from the analysis, the correlation was not significant.

Within the aphasia group, however, there were no significant correlations between laterality and picture naming accuracy. Because accuracy scores in the difficult naming condition were significantly lower compared to the easy naming condition, it is possible that language demands exceeded the capacity of the right hemisphere and perilesional areas. Thus, laterality, left or right, did not predict performance. Moreover, while it did not reach statistical significance, there was a moderate negative correlation between difficult LI and difficult stem completion accuracy for the aphasia group. With a larger sample, it is likely that the negative relationship would be statistically significant. Stem completion accuracy in the difficult condition was also higher than accuracy in difficult picture naming. This could be due to the previously discussed distinctions between the two word-finding tasks with more flexibility in generative stem completion compared to constrained confrontational naming. Therefore, effects of reduced laterality on accuracy might only be apparent when tasks are challenging but still achievable.

The present data are consistent with previous findings that the number of lexical competitors impacts hemisphere differences in word-finding. Results support the hypothesis that control participants would demonstrate hemisphere differences in the high frequency word-stem condition due to response competition. Once again, not only was left laterality of the N400 reduced, control participants demonstrated right hemisphere dominance during word generation with few lexical competitors. Results are in line with the findings of Chiarello et al. (2006) which suggest that during semantic processing, the right hemisphere considers all targets with equal weight while the left selects the most salient word choice. Theoretically, when there are competing prepotent word options, the left hemisphere is more impacted by lexical competition and therefore less efficient. In contrast, the right hemisphere does not discriminate between word options which leads to greater ease of word selection. Complimentary roles of the left and right hemisphere contribute to language fluency, minimizing cognitive demands and errors. Participants in the aphasia group, however, did not demonstrate sensitivity to lexical competition in the few-competitor condition which could reflect pathological word selection processes. This type of deficient processing could account for some error patterns observed in expressive aphasia. For example, during naming tasks, patients often provide a semantically related but inaccurate word (“bang” for “hammer”). Rather than selecting the most accurate target word, targets are selected at random from a pool of potential options. Sometimes, by chance, the patient produces the accurate response (“hammer”), while at other times a less salient but related competitor is selected. This view also explains why patients are able to “find” a word in one trial but are unable to accurately name an object on a second trial. Thus, the word is not lost from their lexicon, but rather the search and selection process is impaired. Behavioral results were consistent with view. Differences in word generation accuracy between word stems with many or few lexical competitors were not significant within the aphasia group.

In addition to hemisphere differences based on task difficulty, contrasts between N200 and N400 effects emerged. To review, during typical word finding tasks the N200 represents conceptualization or deciding what an object is, and lemma selection. A lemma acts as a place holder for a target word and contains appropriate syntactic features of the target word (such as the part of speech, tense, and grammatical structure). The N200 is also associated with response inhibition during word selection (Purmann et al., 2011, Shao et al., 2014,). As such, I predicted that increased N200 amplitudes in the left temporal area would result from increased lexical competition. Interestingly, this effect modulated N400 amplitudes in the right hemisphere more than the N200 amplitudes in the left. De Zubicaray, Wilson, McMahon, and Muthiah (2001) also reported increased hemodynamic responses associated with semantic inhibition during phonological code selection and suggested that lexical response inhibition might occur at two time points. Although not expected, results could also indicate that conceptual planning and lemma selection occur more bilaterally when compared to strong lateralization of the N400 for phonological encoding. This view is further supported by the present data which demonstrate bilaterally distributed N200 effects in supplemental language areas outside of the temporal lobe. Overall, during picture naming there was greater N200 amplitude in the central and parietal regions of the right hemisphere and control participants demonstrated greater N200 amplitudes in the parietal region of the right hemisphere during the stem completion tasks with many competitors. Left laterality, on the other hand, was observed over frontal electrodes for both aphasia and control groups, particularly during difficult word finding tasks. These effects could also be associated with attention to task-relevant stimuli and inhibition of task-irrelevant stimuli (Eimer, Kiss, Press, & Sauter, 2009), and monitoring task demands and performance (De Zubicaray et al., 2001). Donkers and van Boxel (2004) describe yet another account based on a go/no go task where bilateral fronto-central N200 amplitudes were associated with conflict monitoring rather than response inhibition. These findings are in line with previous studies that report involvement of medial-frontal regions in conflict, competition, and inhibitory control of extrinsic and intrinsic interference stimuli (Barch, Braver, Sabb & Noll, 2000; Carter, Minton & Cohen, 1995).

Critically, similarities in N200 amplitudes between aphasia and control groups also suggest that early language processing within this patient sample were relatively normal. Instead, diversions in processing began during phonological encoding when lemmas are matched with what we think of as “words.” Unlike the lemma, phonological codes contain morphosyntactic, grammatical, and sound structure information. Clinically, these findings are in line with patient complaints and typical error patterns observed in aphasia. Patients frequently report that they know what they want to say but cannot access the word. This results in non-fluent speech with long pauses while individuals try to access words (Alexander, Naeser, & Palumbo, 1990). Additionally, word productions often contain grammatical, syntactic, and sound errors (Marshall, 2017; Martin, 2017; LaPointe, 2011). Patients with aphasia demonstrate particular difficulties with verb tense, pronouns, complex syntax, multi-syllabic words, and consonant blends. All of these features indicate deficits in phonological encoding. ERP methods used in this study were able to capture distinctions in language operations such as conceptual versus phonological processes. Methodologically, the results show how ERP can be used as a tool for identifying pathological processes that result in stereotypical aphasia errors. Creating more specific patient profiles could better identify individuals who would benefit from interventions that either promote or inhibit right hemisphere activation. Such specificity and individualized approaches could maximize recovery for patients with aphasia.

Limitations

A few limitations of this study should be acknowledged. First, behavioral performance was not measured during ERP recordings. Word retrieval and production for individuals with aphasia can take several seconds, increasing potential for movement artifacts along with electrical noise from other neural processes. Therefore, associations between laterality effects and accuracy were limited to correlations.

Second, it was inherently difficult to measure performance in the control group due to ceiling effects. Previous studies have used reaction time as an index of word finding efficiency (Taylor & Regard, 2003; Coney & Evans, 1999; Chiarello, Halderman, Robinson, & Kacinik, 2004) but even reaction time differences are on the order of milliseconds and not relevant during functional speech. Therefore, it was not possible to correlate laterality with behavioral outcomes of stem completion within the healthy control group.

Third, while participants in the aphasia group met all inclusion criteria, they ranged in severity and subtype. Some had stronger comprehension skills while others had better expressive skills. Phonological skills for reading and writing also varied among participants which could have impacted stem completion performance. A three-way interaction between group, condition, and hemisphere was not found, likely due to lack of power. Additionally, due to small within group sample sizes, moderate to strong correlations were not statistically significant. A more homogenous group, along with a larger sample size, could lead to more robust findings.

Finally, it is important to note that individual ERP components can be sustained over longer periods of time yet not reflected in the waveform because simultaneously occurring components of opposite polarity are cancelling them out. Therefore, the duration and amplitude of peaks in a waveform might be quite different than the duration and amplitude of the components themselves. In most experimental paradigms amplitudes and latencies are averaged over several trials, within the same subject (Luck & Kappenman, 2012). Each subject then contributes to possible statistical difference between groups/condition. However, averaging across trials can produce a "latency jitter" (Luck & Kappenman, 2012). Like many ERP studies, I reported grand averages or combined waveforms of a group as opposed to individual subjects. While this simplified data processing it may have also discounted significant variability among subjects such as differences in cognitive strategies and differences in cortical folding patterns.

Conclusions

The present study is the first to measure changes in ERP amplitude in the left and right cerebral hemispheres of patients with chronic aphasia and aged matched healthy adults during word-finding tasks. During easy word-finding, participants in the healthy control group demonstrated leftward laterality with greater N400 amplitude in the left hemisphere than the right hemisphere. Participants with chronic aphasia, however, did not demonstrate hemisphere dominance during easy word finding. These findings are consistent with previously observed patterns of decreased laterality in participants with aphasia during typical word-finding tasks. During difficult word-finding, results showed consistent rightward dominance during the difficult stem completion task in the control group, providing evidence of right hemisphere support. Thus, reduced laterality observed in aphasia could be a response to task difficulty rather than a lesion effect. With regards to word-competition, control participants demonstrated right hemisphere dominance during word generation with few lexical competitors. Participants in the aphasia group did not demonstrate sensitivity to lexical competition in the few-competitor condition which could reflect pathological search and selection processes. Methodologically, the results show that ERP can be a useful tool for identifying specific pathological profiles that could help determine who would benefit from interventions that either promote or inhibit right hemisphere activation.

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Table 1. *Socio-demographic data for all participants. Aphasia Quotient (AQ) and aphasia sub-type (AST) based on the Western Aphasia Battery is provided for patient participants.*

Patients							Controls				
Participant	Age	Sex	Years of Education	BDI	AQ	AST	Participant	Age	Sex	Years of education	BDI
1	80	M	18	4	49	Wernicke's	11	81	M	18	3
2	62	F	16	3	65	Mixed	12	67	F	16	3
3	53	M	16	3	70	Conduction	13	47	F	16	0
4	29	M	14	2	65	Conduction	14	32	F	14	1
5	71	M	18	3	77	Anomic	15	68	F	18	3
6	70	M	16	5	62	Conduction	16	70	M	16	4
7	55	F	16	2	75	Broca's	17	62	F	16	2
8	55	M	16	1	48	Broca's	18	51	F	16	1
9	66	M	16	4	66	Conduction	19	69	F	16	5
10	49	M	16	1	40	Mixed	20	44	M	16	1

Table 2. *Scores from the Test of Nonverbal Intelligence 4th-Edition (TONI-4) and the Peabody Picture Vocabulary Test- 3rd Edition (PPVT-3)*

Patients			Controls		
Participant	TONI-4	PPVT-3	Participant	TONI-4	PPVT-3
1	117	60	11	121	140
2	103	96	12	113	136
3	110	93	13	100	99
4	87	81	14	101	99
5	112	90	15	104	113
6	100	100	16	101	100
7	117	91	17	99	100
8	85	77	18	100	123
9	108	75	19	101	115
10	86	78	20	98	109

Table 3. *Stem Completion: Effects of Difficulty on N200 Laterality*. *F* values for main effects of hemisphere (Hemi), condition (Diff), and group, and interaction effects.

Location		Hemi	Diff	Group	Hemi*Group	Diff*Group	Hemi*Diff	Hemi*Diff*Group
Combined Electrode	*F*(1,13)	.15	.06	3.97	.92	2.58	1.14	.77
F3/F4	*F*(1,16)	.64	2.63	.13	5.98*	.54	.68	1.77
T7/T8	*F*(1,14)	1.9	.51	2.71	.06	2.07	.02	.24
C3/C4	*F*(1,16)	4.43*	.02	1.67	2.04	.74	.06	.18
P3/P4	*F*(1,15)	1.05	1.8	1.78	5.02*	.09	1.49	.39

Asterisks indicate statistical significance at *p*<.05.

Table 4. *Stem Completion: Effects of Difficulty on N200 Laterality*. Mean amplitudes at each electrode site and when combined by hemisphere for easy and difficult stems.

	Patients				Controls			
	Easy		Difficult		Easy		Difficult	
	M	SD	M	SD	M	SD	M	SD
F3	-.29	3.61	.93	4.95	-.03	7.34	1.01	6.12
F4	-.03	3.80	3.04	4.83	-.50	6.30	.09	6.40
T7	1.67	4.33	-.20	4.03	-1.88	2.81	-.78	4.74
T8	1.31	4.39	1.29	5.26	.50	5.49	-.17	2.32
C3	2.18	5.03	1.39	5.55	1.49	6.91	.45	3.7
C4	3.25	3.96	2.95	3.39	-.08	3.44	.64	3.65
P3	2.72	4.28	3.87	3.78	-.76	3.21	1.91	5.05
P4	2.61	3.95	2.27	2.61	1.16	2.20	3.37	4.97
Combined Left	.72	5.27	2.12	3.81	.51	6.15	-.35	3.14
Combined Right	2.07	3.27	1.80	2.82	-.56	2.85	.21	3.04

(F3:frontal left, F4:frontal right, T7:temporal left, T8:temporal right, C3:central left, C4:central right, P3:parietal left, P4:parietal right)

Table 5. *Stem Completion: Effects of Difficulty on N400 Laterality*. *F* values for main effects of hemisphere (Hemi), condition (Diff), and group, and interaction effects.

		Hemi	Diff	Group	Hemi*Group	Diff*Group	Hemi*Diff	Hemi*Diff*Group
Combined Electrodes	*F*(1,13)	11*	.00	.01	.25	2.83	.25	.00
F3/F4	*F*(1,15)	6.44*	3.06	.84	3.21	.58	.02	.06
T7/T8	*F*(1,15)	.35	.38	1.27	.93	2.97	.00	1.41
C3/C4	*F*(1,17)	3.23	.08	.07	.03	1.71	.00	.73
P3/P4	*F*(1,16)	.01	1.21	.02	7.39*	1.02	.00	2.55

Asterisks indicate statistical significance at $p<.05$.

Table 6. *Stem Completion: Effects of Difficulty on N400 Laterality*. Mean amplitudes at each electrode site and when combined by hemisphere for easy and difficult stems.

	Patients				Controls			
	Easy		Difficult		Easy		Difficult	
	M	SD	M	SD	M	SD	M	SD
F3	-4.17	5.21	-2.15	6.18	-.87	7.53	1.20	6.78
F4	-3.02	6.42	-.37	4.29	-.34	7.44	1.65	7.16
T7	3.38	7.70	-.05	7.79	-1.45	5.77	-1.06	6.23
T8	1.36	5.97	.68	8.83	-1.22	3.51	2.63	5.75
C3	-6.9	6.77	-1.35	5.12	-.87	7.70	.31	7.11
C4	.69	5.80	-.68	4.18	-.41	5.98	1.56	6.38
P3	1.95	6.53	2.51	5.30	-1.29	6.91	-.05	7.03
P4	.35	5.89	-.59	3.55	.31	5.00	2.54	5.16
Combined Left	.68	4.91	-.94	4.91	-1.12	6.65	.50	6.07
Combined Right	-.16	4.38	-.95	3.60	-1.27	4.68	2.10	5.83

(F3:frontal left, F4:frontal right, T7:temporal left, T8:temporal right, C3:central left, C4:central right, P3:parietal left, P4:parietal right)

Table 7. *Picture Naming: Effects of Difficulty on N200 Laterality*. *F* values for main effects of hemisphere (Hemi), condition (Diff), and group, and interaction effects.

		Hemi	Diff	Group	Hemi*Group	Diff*Group	Hemi*Diff	Hemi*Diff*Group
Combined Electrode	*F*(1,13)	6.62*	.44	.03	1.53	2.41	3.22	.03
F3/F4	*F*(1,16)	3.5	1.94	1.13	2.64	2.47	6.02*	1.82
T7/T8	*F*(1,16)	1.71	.25	.00	1.19	.22	.02	.54
C3/C4	*F*(1,17)	7*	2.69	2.63	4.32	1.01	1.84	.68
P3/P4	*F*(1,17)	6.39*	.03	.12	.2	.15	1.42	1.63

Asterisks indicate statistical significance at *p*<.05.

Table 8. *Picture Naming: Effects of Difficulty on N200 Laterality*. Mean amplitudes at each electrode site and when combined by hemisphere for easy and difficult pictures.

	Patients				Controls			
	Easy		Difficult		Easy		Difficult	
	M	SD	M	SD	M	SD	M	SD
F3	-1.56	6.63	-5.89	6.87	.50	4.41	.37	5.97
F4	-1.19	5.44	-5.21	11.46	1.29	7.33	.60	6.20
T7	-1.39	6.15	-1.33	4.84	.31	4.30	-.55	4.45
T8	.86	6.98	-2.92	10.86	-.16	4.00	1.10	4.37
C3	1.36	7.73	-5.48	8.66	2.85	7.39	1.78	3.88
C4	.91	5.62	-.31	4.88	1.51	6.35	2.40	3.70
P3	2.04	6.28	.12	6.20	1.41	6.55	2.40	4.18
P4	1.96	5.27	3.36	6.63	2.67	8.47	3.57	4.04
Combined Left	.11	5.17	-2.93	6.01	-.65	1.88	1.00	3.72
Combined Right	.63	5.22	-1.27	5.71	.52	5.01	1.53	3.38

(F3:frontal left, F4:frontal right, T7:temporal left, T8:temporal right, C3:central left, C4:central right, P3:parietal left, P4:parietal right)

Table 9. *Picture Naming: Effects of Difficulty on N400 Laterality*. *F* values for main effects of hemisphere (Hemi), condition (Diff), and group, and interaction effects.

		Hemi	Diff	Group	Hemi*Group	Diff*Group	Hemi*Diff	Hemi*Diff*Group
Combined Electrode	*F*(1,13)	1.74	.53	2.14	2.69	.83	2.79	.84
F3/F4	*F*(1,17)	.84	.7	6.07*	6.84*	.26	2.85	.14
T7/T8	*F*(1,17)	.33	1.29	2.27	4.23	.00	.3	2.86
C3/C4	*F*(1,16)	3.51	.4	3.2	4.01	1.52	1.73	.17
P3/P4	*F*(1,16)	1.16	.16	.68	.29	.78	.35	.1

Asterisks indicate statistical significance at $p<.05$.

Table 10. *Picture Naming: Effects of Difficulty on N400 Laterality*. Mean amplitudes at each electrode site and when combined by hemisphere for easy and difficult pictures.

	Patients				Controls			
	Easy		Difficult		Easy		Difficult	
	M	SD	M	SD	M	SD	M	SD
F3	-7.81	16.24	-12.72	11.40	5.25	12.39	3.5	5.41
F4	-5.84	13.96	-7.63	14.68	2.54	11.52	2.89	5.71
T7	-10.25	24.43	-5.04	9.50	6.45	13.88	.91	5.84
T8	-1.83	15.70	-3.11	11.22	2.39	11.36	1.47	5.76
C3	-3.07	10.02	-8.50	11.62	2.36	7.53	4.01	4.88
C4	-.41	10.29	-2.54	11.27	2.56	9.64	4.15	3.37
P3	2.81	10.30	.37	8.72	3.02	5.01	6.13	4.53
P4	2.92	9.39	3.62	11.23	5.62	9.35	6.49	3.81
Combined Left	-4.58	13.01	-6.16	9.47	3.03	7.78	3.64	4.04
Combined Right	-1.29	11.29	-2.04	10.50	3.20	9.72	3.68	3.51

(F3:frontal left, F4:frontal right, T7:temporal left, T8:temporal right, C3:central left, C4:central right, P3:parietal left, P4:parietal right)

Table 11. *Stem Completion: Effects of Lexical Competitors on N200 Laterality*. *F* values for main effects of hemisphere (Hemi), condition (Comp), and group, and interaction effects.

		Hemi	Comp	Group	Hemi*Group	Comp*Group	Hemi*Comp	Hemi*Comp*Group
Combined Electrode	*F*(1,13)	.75	.03	1.15	.02	6.4*	.26	1.52
F3/F4	*F*(1,16)	.57	.42	.05	5.84*	.14	.93	3.52
T7/T8	*F*(1,14)	.56	.32	.69	.00	5.18*	1.46	1.87
C3/C4	*F*(1,16)	2.09	.19	.74	3.71	2.49	.00	1.75
P3/P4	*F*(1,16)	.66	1.65	2.1	3.99	.05	.72	1.37

Asterisks indicate statistical significance at $p<.05$.

Table 12. *Stem Completion: Effects of Lexical Competitors on N200 Laterality*. Mean amplitudes at each electrode site and when combined by hemisphere for easy and high frequency (HF) stems.

	Patients				Controls			
	Easy		HF		Easy		HF	
	M	SD	M	SD	M	SD	M	SD
F3	-.29	3.61	-.56	4.52	-.03	7.34	.63	5.90
F4	-.03	3.80	2.77	6.41	-.50	6.30	-.63	5.43
T7	1.67	4.33	-2.72	5.42	-1.88	2.81	.24	3.23
T8	1.31	4.39	.30	4.35	.50	5.49	.97	4.29
C3	2.18	5.03	.11	5.98	1.49	6.91	2.29	5.44
C4	3.25	3.96	2.22	5.94	-.08	3.44	1.46	5.10
P3	2.72	4.28	4.27	5.47	-.76	3.21	1.82	4.04
P4	2.61	3.95	2.96	5.26	1.16	2.20	3.21	4.55
Combined Left	.72	5.27	.16	3.86	.51	6.15	1.24	4.52
Combined Right	2.07	3.27	1.72	4.65	-.56	2.85	1.25	4.74

(F3:frontal left, F4:frontal right, T7:temporal left, T8:temporal right, C3:central left, C4:central right, P3:parietal left, P4:parietal right)

Table 13. *Stem Completion: Effects of Lexical Competitors on N400 Laterality. F* values for main effects of hemisphere (Hemi), condition (Comp), and group, and interaction effects.

		Hemi	Comp	Group	Hemi*Group	Comp*Group	Hemi*Comp	Hemi*Comp*Group
Combined Electrode	*F*(1,13)	2.48	.09	.07	.18	14.23**	2.31	1.82
F3/F4	*F*(1,16)	.5.74*	4.00	.73	2.26	.06	1.81	1.19
T7/T8	*F*(1,15)	.14	.05	.15	.42	6.78*	1.01	.54
C3/C4	*F*(1,17)	3.22	.96	.19	1.1	7.42*	.12	.12
P3/P4	*F*(1,16)	.18	.00	.00	5.26*	4.14	1.42	.53

*indicate statistical significance at *p*<.05, **indicate statistical significance at *p*<.01.

Table 14. *Stem Completion: Effects of Lexical Competitors on N400 Laterality*. Mean amplitudes at each electrode site and when combined by hemisphere for each and high frequency (HF) stems.

	Patients				Controls			
	Easy		HF		Easy		HF	
	M	SD	M	SD	M	SD	M	SD
F3	-4.17	5.21	-2.24	6.33	-.87	7.53	.93	8.40
F4	-3.02	6.42	1.73	7.44	-.34	7.44	1.81	8.83
T7	3.38	7.70	-3.60	11.87	-1.45	5.77	.73	5.63
T8	1.36	5.97	-.49	5.51	-1.22	3.51	2.57	6.30
C3	-6.9	6.77	-3.59	6.89	-.87	7.70	.33	7.26
C4	.69	5.80	-1.49	5.59	-.41	5.98	.78	6.86
P3	1.95	6.53	-.08	5.89	-1.29	6.91	-.05	6.23
P4	.35	5.89	-.61	7.20	.31	5.00	1.89	4.91
Combined Left	.68	4.91	-2.73	5.65	-1.12	6.65	.49	6.51
Combined Right	-.16	4.38	-.47	4.82	-1.27	4.68	1.76	6.26

(F3:frontal left, F4:frontal right, T7:temporal left, T8:temporal right, C3:central left, C4:central right, P3:parietal left, P4:parietal right)

Table 15. *Laterality Index (LI) in easy and difficult stem-completion conditions for patients and controls. Positive values indicate left laterality.*

Patients			Controls		
Participant	LI EASY	LI DIFF	Participant	LI EASY	LI DIFF
1	-.29	-.03	11	.23	1.32
2	.41	1.17	12	.12	1.22
3	5.42	-20.13	13	.00	-.03
4	2.50	1.32	14	10.78	3.03
5	.08	-.45	15	.35	-.11
6	6.49	-1.00	17	.77	-7.44
7	-.67	-1.52	18	.30	.20
8	-.09	-.41	19	.27	.31
9	.35	.38	20	.24	.88
10	.14	.14			

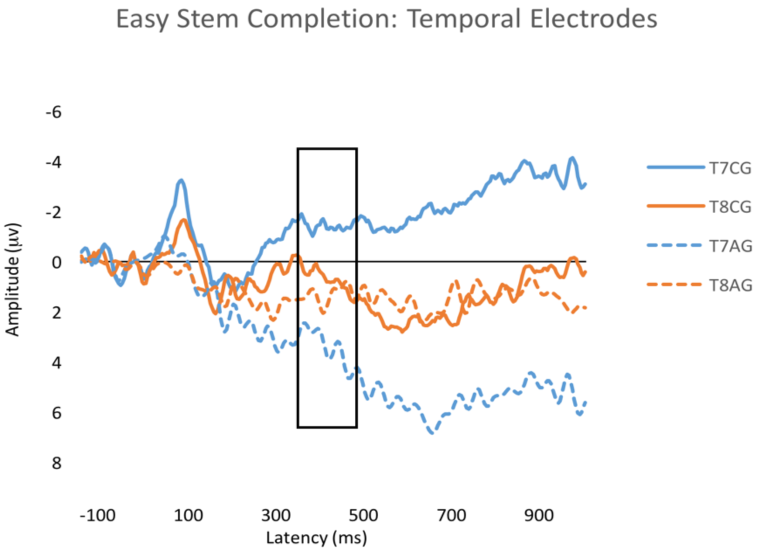

Figure 1. ERP waveforms elicited in response to easy stem completion. Grand averages of temporal electrodes in each hemisphere (T7(LH) and T8(RH)) in the control group (CG) and aphasia group (AG). Significant differences among the control group in the N400 time window (350-500ms) are highlighted.

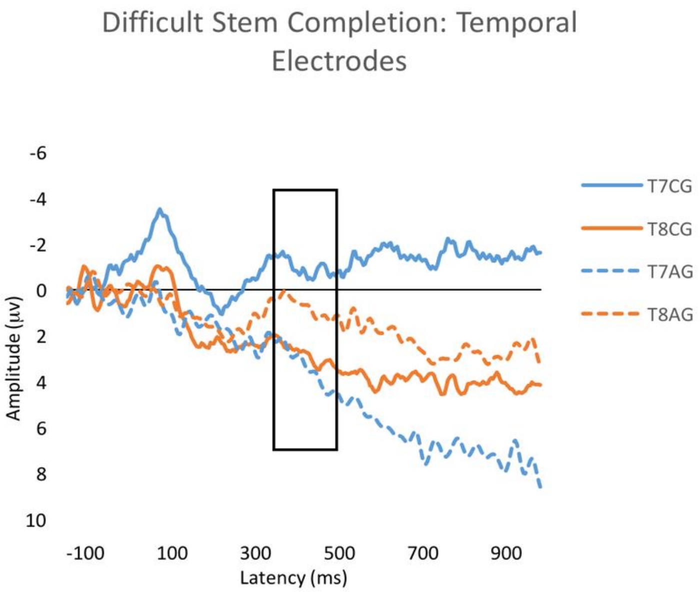

Figure 2. ERP waveforms elicited in response to difficult stem completion. Grand averages of temporal electrodes in each hemisphere (T7(LH) and T8(RH)) in the control group (CG) and aphasia group (AG). Significant differences among the control group in the N400 time window (350-500ms) are highlighted.

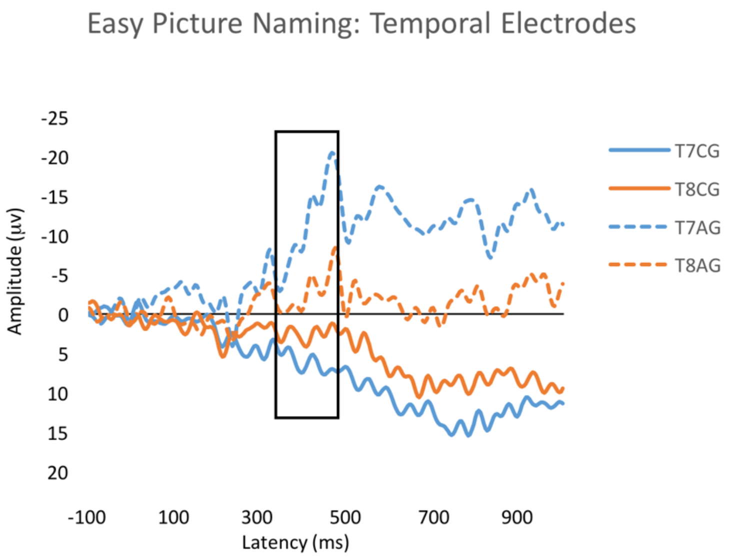

Figure 3. ERP waveforms elicited in response to easy picture naming. Grand averages of temporal electrodes in each hemisphere (T7(LH) and T8(RH)) in the control group (CG) and aphasia group (AG). Significant differences among the control group in the N400 time window (350-500ms) are highlighted.

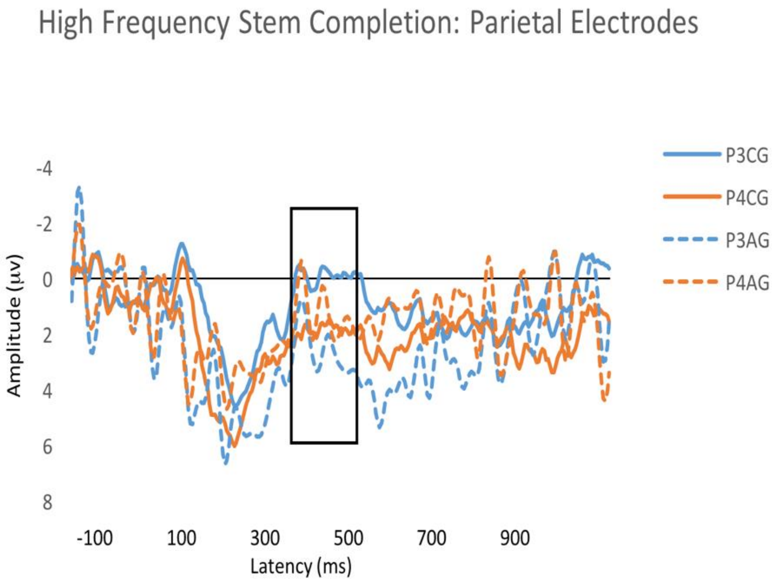

Figure 4. ERP waveforms elicited in response to high frequency stem completion. Grand averages of central electrodes in each hemisphere (P3(LH) and P4(RH)) in the control group (CG) and aphasia group (AG). Significant differences among the control group in the N400 time window (350-500ms) are highlighted.