INHIBITORY DEFICITS IN APHASIA: ROLE OF NEUROVISCERAL INTEGRATION

by

BIJOYAA MOHAPATRA

(Under the Direction of Rebecca Shisler Marshall)

ABSTRACT

People with Aphasia (PWA) often demonstrate deficits in higher order cognitive functions such as attention, executive function, and working memory that significantly interfere with their linguistic abilities. It is suggested that the basic cognitive function that underlies all other cognitive processes is inhibition, and it is defined as the potential to suppress pre-potent responses and select more optimal responses to perform efficiently in a challenging environment. The use of heart rate variability (HRV) to index inhibitory behavior in PWA has not yet been studied. HRV is a tool that represents the balance between the sympathetic and parasympathetic branches of the Autonomic Nervous System and reflects the change in cardiovascular activity as a response to increase in cognitive load. The goal of the present study is to determine whether inhibition can be physiologically indexed by HRV in PWA, and whether working memory (WM) is related to inhibitory behavior in PWA. Twelve PWA and 12 healthy age and education matched controls were assessed on two computerized experimental tests: 1) Continuous Performance Test-3 with greater inhibitory demands and 2) Continuous Performance Test-X with lower inhibitory demands. Physiological activity (time and frequency domain measures of HRV) was continuously recorded in five conditions: 1) baseline-10

minute rest, 2) first experimental test, 3) 10-minute between-task rest, 4) second experimental test, and 5) recovery-10 minute rest. N- back task was used as a measure of WM. On all the tests, PWA performance was significantly reduced (less sensitivity and greater response times) in comparison to healthy controls. Both participant groups demonstrated significant decrease in HRV indices with increase in inhibitory demands. This indicates that increase in inhibitory demands decreases parasympathetic activity to produce low HRV. Also, there is suppression of HRV during the experimental tasks compared to the baseline and recovery conditions in both groups. PWA demonstrate prolonged HRV recovery compared to healthy controls. Also, WM ability is associated with behavioral and physiological inhibitory performance in PWA. The results are consistent with Thayer and Lane's Neurovisceral Integration model and suggest that HRV can potentially be used as an index inhibitory behavior in PWA.

INDEX WORDS: Aphasia, Inhibition, Heart Rate Variability, Neurovisceral Integration, Working Memory

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by

BIJOYAA MOHAPATRA

B.Sc., University of Calcutta, India, 2008

M.Sc., University of Mysore, India, 2010

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BIJOYAA MOHAPATRA

Major Professor:	Rebecca Shisler Marshall
Committee:	Anne K. Marcotte
	Liang Chen
	Laura L. Murray

Electronic Version Approved:

Suzanne Barbour
Dean of the Graduate School
The University of Georgia
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DEDICATION

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TABLE OF CONTENTS

LIST OF TABLES

Page

LIST OF FIGURES

Page

CHAPTER 1

INTRODUCTION

The ability to suppress pre-potent responses is an important characteristic of a healthy and mature human being and is often referred to as '*inhibition*'. It requires selection of optimal responses from the set of behavioral repository and suppression of less functional responses. Inhibition has the ability to channel 'excitatory neural function to produce context appropriate responses' (Thayer, Hansen, Saus-Rose, & Johnsen, 2009). The process of inhibition is frequently associated with intact prefrontal cortex. Attentional regulation and the ability to inhibit pre-potent responses are essential for many tasks that include cognitive functions such as working memory (WM), executive functions, behavioral inhibition, and sustained attention. These functions are all associated with prefrontal cortical activity. There is a common inhibitory network associated with these cognitive and affective processes, and pathways that connect the prefrontal cortex to the inhibitory action of the medullary cardio-acceleratory circuits. This network has been explained by a 'neurovisceral integration model' (Thayer & Lane, 2000, 2009), which is described as integrating cognitive, affective and physiologic regulation in the service of a goal-directed behavior, and it has been linked to vagally mediated cardiac function (Porges, 1992) indexed by heart rate variability (HRV). While high HRV is linked to high functional prefrontal inhibitory action that enables us to have control over emotional states and cognitive responses, low HRV is associated with decrease in prefrontal inhibitory control.

Deficits to any of these cognitive functions are associated with prefrontal cortical damage, such as in aphasia. Due to the neurological damage, people with aphasia (PWA) often demonstrate diminished inhibitory control on tasks that require significant involvement of attentional resources and interference in their process of communication (Hula & McNeil, 2008; Murray, 2012). However, the field of aphasiology still lacks a clear understanding of inhibitory control in PWA, and whether current trends in accuracy and latency measurements are accurate indicators of inhibitory ability. Therefore, the current study will determine inhibitory performance in PWA through physiological measurements, such as the HRV.

This study will further examine the relation between inhibitory control and WM ability in aphasia and healthy participants. Results obtained will be discussed with relation to the neurovisceral integration model (Thayer & Lane, 2000, 2009) that integrates autonomic regulation and cognitive functioning into a functional and structural cortical-subcortical network.

CHAPTER 2

REVIEW OF LITERATURE

Inhibition and Attention Resource Allocation- Theoretical Foundations

In cognitive science, 'resources' are described as the capacity of the WM system to hold and allow manipulation of information in immediate awareness, or in simple terms, something that characterizes as a maximum rate of processing. Kahneman introduced the advanced idea of perceptual and cognitive operations that utilize a restricted pool of attentional resources. He described these resources in terms of attentional capacity that functions as a limited resource and must be allocated among concurrent perceptual and mental activities (Kahneman, 1973).

Inhibition requires and consumes attentional resources, and the availability of these resources varies across individuals. Grandjean and Collette, 2011 attributed individual differences in inhibitory function to the availability of attentional resources for WM. The association between limited attentional resources and inhibition has been demonstrated through different experimental research. In one of the earliest studies, Nakagawa (1991) demonstrated that inhibition occurred on a lexical-decision task only when the target item was presented to the left-hemisphere. With the introduction of a simultaneous shadowing task, participants did not show any evidence of inhibition when items were presented directly to the left hemisphere. Engle and colleagues provided similar evidence that negative priming decreases as workload (attentional resource

activity) increases suggesting that the ability to inhibit may result from individual differences in controlled resource allocation and not because of an inefficient inhibitory mechanism (Engle, Conway, Tuholski, & Shisler, 1995). Such differences in availability of attentional resources are assumed to originate from developmental and individual differences (Conway, 1996). These authors further argued that if inhibition is dependent on attentional resources, then drawing on those resources with another attention-demanding task would decrease an individual's ability to inhibit irrelevant stimuli. They also found that individuals with low working memory span do not have adequate attentional resources necessary to inhibit irrelevant information. Thus, these findings suggest that inhibition is a resource demanding process and when the required resources are no longer available, inhibition is hindered.

The 'limited capacity resources model' proposed that mental capacity is divided between processing space and storage space (Case, Kurland, & Goldberg, 1982). Case and colleagues argued that the aggregate sum of mental spaces or resources accessible to perform cognitive functions stays steady all through childhood. There is an increase in cognitive performance during childhood primarily due to progressive increase in efficient processing of cognitive tasks. Thus, with efficient processing, less space is needed to complete a given task, which in turn allows extra space to be available for relevant processing or storage of a subsequent or secondary task (Case, 1985). The limited capacity theory also addresses the phenomenon of 'inhibition' (or 'cognitive inhibition') that is responsible for the suppression of previously activated or interfering content (Bjorklund & Harnishfeger, 1990; Harnishfeger, 1995; Harnishfeger & Bjorklund, 1993). Individuals with efficient inhibitory abilities are able to dismiss previously activated

information from WM not relevant to task performance, thereby reducing the processing space and allowing extra space for storage. Although the inhibitory process does not occur consciously, often it is an active process. Overall it is suggested that efficient inhibition of a function, action or cognitive process is a resource consuming process. Thus an increase in attentional resource activity on a task, might result in difficulty in inhibiting irrelevant information (Ferraro, Park, Ronald, Hage, & Palm, 2010). There is evidence for such phenomenon from the negative priming experiments (Banks, Roberts, & Ciranni, 1995; Engle et al., 1995; Tipper, Weaver, Cameron, Brehaut, & Bastedo, 1991). Tipper et al. (1991) provided evidence for the nature of inhibition through negative priming experiments with respect to various types of disruption and intervening events. They suggested that in the presence of an unexpected event, inhibitory ability gets disrupted because resources become limited when attention is oriented towards the processing of an unexpected event. Thus, *competition* for limited attentional resources when processing of multiple tasks, events, or stimuli is the central theme of the resource allocation theory (Erickson, Goldinger, & LaPointe, 1996).

Another theory by Engle, Conway, Tuholski, and Shisler (1995) proposed the 'resource-dependent model of inhibition'. They found that individuals with high WM capacity have more resources that assist in task performance (such as, inhibition of irrelevant information) than individuals with low WM capacity and has been demonstrated on tasks that require controlled attention. Such difference in task performance between high and low WM capacity individuals have been indicated on tasks requiring inhibitory control, such as the paired-associates task (Rosen & Engle, 1998), a negative priming task (Engle et al., 1995), fan-effect in fact-retrieval task

(Cantor & Engle, 1993; Conway & Engle, 1994), and the cocktail party phenomenon (Conway, Cowan, & Bunting, 2001). With all of the above information, it could be concluded that inhibition is an effortful and resource demanding process and is influenced by individual differences in WM capacity (Conway & Engle, 1994; Engle et al., 1995; Redick, Heitz, & Engle, 2007).

In summary, when numerous and/or conflicting inputs are present, the human brain utilizes attentional resources to process the intended target and inhibit the irrelevant non-target inputs. Alternatively it can be explained that attention is the required resource that enhances the activation of target items while dampening the processing of distracting items (Conway & Engle, 1994; Engle et al., 1995; Hasher & Zacks, 1988; Kane & Engle, 2003; Miyake et al., 2000).

Following this theoretical foundation, a subsequent question arises- what happens to inhibitory functions in the case of brain damage leading to aphasia? Why do PWA demonstrate differences in inhibitory deficits? Is there a connection between their inhibitory performances and limited resource allocation? The next section will address these questions.

Inhibition and Aphasia

One primary theory that addresses the concept of the limited capacity resources is Hasher and Zacks's Working Memory Approach (1988). This theory associates inefficient inhibition with cognitive changes in older healthy individuals. It proposes that WM is a limited capacity resource and that there is competition between the processes (storage and processing) for this capacity (Baddeley & Hitch, 1974; Hasher & Zacks,

1988). Similar to Case et al.'s (1982) limited capacity *resources model* (described previously), Hasher and Zack theorized that irrelevant information in WM takes up limited resources, thereby restricting the available resources for processing and storage of task relevant information. They stated that, "a person with reduced inhibitory functioning can be expected to show more distractibility, to make more inappropriate responses and/or to take longer to make competing appropriate responses, and finally, to be more forgetful than others" (p. 215). Their work has primarily focused on WM storage, and performance in older adults in comparison to the younger adults (Connelly, Hasher, & Zacks, 1991; Zacks & Hasher, 1993), particularly expanding the discussion to integrate the relation between presence of irrelevant information in WM to poorer encoding, retrieval, and comprehension in older adults. It also includes discussion on prediction of WM performance from individual's age and inhibitory control, suggesting that older adults' diminished capacity is not the result of a reduced capacity size but primarily due to the inability to inhibit irrelevant information (Schelstraete & Hupet, 2002). On the other hand, younger adults are able to inhibit irrelevant information readily that allows WM capacity to be available for relevant information processing. Thus, inadequate inhibition of irrelevant information in WM may lead to slowing of the overall WM system and limit the storage and processing systems. Inferences made from Hasher and Zack's theory suggest that if WM capacity engages inhibitory control and if older adults have decreased inhibition then it is likely that PWA may have decreased processing partially due to a decrease in their inhibitory control (Wright & Shisler, 2005).

Attention allocation and Inhibition in Aphasia. Several researchers have theorized that inhibition is an important phenomenon to consider in PWA and have estimated diminished attentional systems in them (Erickson et al., 1996; Glosser & Goodglass, 1990; Murray, Holland, & Beeson, 1997b). The attentional systems are arguably 'limited' in aphasia and significantly interfere with the process of building linguistic representations (Hula & McNeil, 2008; Murray, 2012; Tseng, McNeil, & Milenkovic, 1993). Inhibitory difficulties particularly affect word retrieval, auditory comprehension, spoken word production, and attentional control in PWA (McNeil et al., 2010; Murray, 2000; Murray, Holland, & Beeson, 1997a; Tseng et al., 1993).

Several other WM models such as Baddeley's WM model (2000) and Norman and Shallice's (1986) model also include components, such as the central executive and supervisory attentional system (SAS) that centralize its function on attention allocation. Particularly, Baddeley's WM model proposed that the central executive subsystem functions as a limited capacity system, responsible for allocating resources between the other sub components of WM (phonological and visuospatial sketchpad) for processing of auditory and visual information. The central executive, as explained by Baddeley, plays an important role during dual task execution by coordinating performance between tasks and appropriately allocating attentional resources between the primary and secondary tasks. It is responsible for resource allocation by providing storage and work space for both these tasks. Baddeley has associated the central executive to Norman and Shallice's SAS system (Baddeley, 1993; Norman & Shallice, 1986) and stressed the role that the central executive plays in allocating attentional resources. The SAS is assumed to be a limited capacity system, functionally dependent on the prefrontal cortex (Burgess &

Shallice, 1996; Shallice, 1982). It assigns or inhibits activation of attentional resources by executing automatic and unintentional control and building several different parallel action schemes depending on the task demands. With respect to the above models, attention is viewed as a mental resource that fuels cognitive activities, and inhibition is considered to play a major role in the attentional process by hindering activation of unnecessary stimuli irrelevant to that goal.

Attention is speculated to enhance the activation of relevant information and actively inhibit irrelevant information, and its resources are allocated according to the task demands and the context of the surrounding environment (Cohen, Dunbar, & McClelland, 1990; Conway & Engle, 1994; Houghton, Tipper, Weaver, & Shore, 1996; Kane & Engle, 2003; Miyake et al., 2000). Consequently, if attention is misallocated or diminished, relevant inputs may not be activated, and at the same time irrelevant and interfering inputs may not be suppressed, thereby impeding the process of building target language processes (Hula & McNeil, 2008; Murray, 2012; Pompon, McNeil, Spencer, & Kendall, 2015; Tseng et al., 1993); McNeil, Hula & Sung, 2010). In addition, events/occurrences with strong activation pathways are presumed to require less attention and activate more automatically than events that follow weaker pathways (Cohen et al., 1990). In the presence of an interfering task (such as sound discrimination task), PWA's reaction time increases on a picture-naming task, and is significantly impaired in comparison to the healthy individuals (Lim, McNeil, Dickey, Doyle, & Hula, 2012; Martin & Allen, 2008; Murray et al., 1997b). This presence of exaggerated interference in PWA is arguably indicative of a reduced capacity to inhibit irrelevant information and

a poorly controlled allocation of attention (Hamilton & Martin, 2005; Wiener, Tabor Connor, & Obler, 2004).

Further support comes from the selective inhibition hypothesis (Fox, 1995) regarding the strong (automatic) and weak (less automatic) activation pathways (Cohen et al., 1990) between primary versus secondary and target versus non-target stimuli. The hypothesis empathizes that initially all visual stimuli are activated, but due to competition for dominance between stimuli, inhibitory processes are employed to reduce activation on secondary or non-target stimuli. As a result, the primary or target stimuli are more activated for further storage and processing. Thus the role of inhibition in this hypothesis is particularly important when applied to aphasia because researchers have speculated that PWA have reduced attentional mechanisms and decreased attention allocation and processing (Erickson et al., 1996; Glosser & Goodglass, 1990; L. Murray et al., 1997b; Wiener et al., 2004).

Inhibitory deficits in Aphasia. PWA manifest with difficulties in allocating attention resources required for language and cognitive processing (Erickson et al., 1996; Hula, McNeil, & Sung, 2007; Murray et al., 1997b; Murray, 1999; Tseng et al., 1993). With increase in task demands, PWA find it difficult to allocate the existing resources to attention-demanding tasks and therefore encounter problems in language comprehension and expression (Hula et al., 2007; Murray, 2000; Murray et al., 1997b; Tseng et al., 1993). Various studies have analyzed the effect of interference and speculated decreased working memory (Caspari, Parkinson, LaPointe, & Katz, 1998; Christensen & Wright, 2010; Friedmann & Gvion, 2003; Wright & Shisler, 2005) and attention (Erickson et al.,

1996; Murray, 2012; Murray, 2002; Murray, Keeton, & Karcher, 2006; Tseng et al., 1993) in aphasia. Behavioral and physiologic studies conducted in aphasia have also indicated deficits in orientation of attention in PWA (Hunting-Pompon, Kendall, & Bacon Moore, 2011; Peach, Rubin, & Newhoff, 1994; Petry, Crosson, Rothi, Bauer, & Schauer, 1994). Research has supported the presence of deficits in attention allocation in PWA and impaired inhibition has been indicated as an explanation to these deficiencies. With this background, (Wiener et al., 2004) investigated the inhibitory ability of PWA on a modified Stroop task to determine the cognitive mechanisms affecting resource allocation. They hypothesized that PWA would present with greater difficulty than their healthier counterparts in inhibiting irrelevant information, as evidenced by slower task reaction times. Five PWA and 12 control participants were tested on a modified Stroop task that involved presentation of Arabic numbers in congruent, incongruent and neutral conditions. Participants with aphasia demonstrated significantly lower identification scores than the non-brain injured controls when the tasks required them to suppress or inhibit information during incongruent and neutral conditions. However, on tasks not requiring inhibition, there were no significant differences between the groups. Authors established that such differences in attentional deficits in PWA are not solely a result of aging, but are the result of a restricted attentional processing system. They suggested that these deficits may be due to a decreased ability to allocate attentional resources. Therefore, PWA exhibit reduced ability to distinguish between conflicting stimuli and demonstrate impaired inhibitory mechanisms.

Results obtained from these studies indicate that in the presence of interfering distractions, PWA exhibit significantly lower and less precise target responses than the

control participants. Thus, these studies hypothesized that due to decreased attentional resources it becomes difficult for PWA to allocate resources to manage interference and inhibit unnecessary distractions. In these conditions, active distractors prevent the processing of intended target items by consuming the attentional resources allocated to them. Such decreased and misallocation of attentional resources is observed during linguistic processes in PWA, in the form of word finding difficulties during conversations, comprehension and word retrieval tasks (Lim et al., 2012; McNeil et al., 2010; Murray, 2000; Murray et al., 1997b; Tseng et al., 1993). Other researchers have also indicated diminished inhibitory control due to reduced attentional resources in PWA (Hula & McNeil, 2008; McNeil, Odell, & Tseng, 1991; Murray, 2012).

Given the connection of language and attention, it is important to address the issue of allocation of resources in PWA in order to avoid inaccurate assessment of language impairments that may have resulted from an attention deficit. This will help further determine the connection between attentional resources and how PWA engage these resources to perform efficiently on language as well as higher cognitive processes such as working memory and executive function.

Effect of inhibitory deficits on language processing in Aphasia. During sentence comprehension, executive processes are also used to monitor and select judiciously among competing sentence representations. Conflict inhibition[1] plays a major role in this process and allows for a coherent interpretation of the sentence. Adults with poor comprehension skills are likely to demonstrate deficient inhibition and suppression

[1] Conflict inhibition arises during simultaneous activation of incompatible response tendencies (i.e., competition between the execution and the inhibition of a single response).

of competing representations. With respect to syntactically ambiguous sentences, the speaker's ability to control conflicts is confounded by the linguistic elements and format of complex sentence structures (Novick, Trueswell, & Thompson-Schill, 2005). However, executive processes such as error detection and cognitive monitoring trigger control mechanisms to resolve conflicts and aid in better comprehension (Ye & Zhou, 2009). Similarly, conflict control in word production is contributed by executive processes such as, inhibition of prepotent responses, controlled access to lexical items in semantic memory, and attention control to resolve competitions among lexical representations (Badre & Wagner, 2007; Thompson-Schill, Bedny, & Goldberg, 2005). With such emphasis on the importance of inhibition to PWA, it is imperative to understand how inhibitory deficits are critical to language processing in PWA. In other words, if attentional resources are limited and allocated inadequately in PWA, then language processes such as word finding during speech production may get strained due to the presence and processing of interfering distractions.

A number of recent studies in aphasia have investigated the nature of cognitive processing deficits during speech production (Biegler, Crowther, & Martin, 2006; Biegler, Crowther, & Martin, 2008; Crowther, 2007; Dell, Schwartz, Martin, Saffran, & Gagnon, 1997; Ilshire & McCarthy, 2002; Jefferies, Patterson, & Ralph, 2008). All of these deficits fall into one of these categories- exaggerated inhibitory mechanisms on naming tasks (McCarthy & Kartsounis, 2000), inability to control active representations within the lexical system (Ilshire & McCarthy, 2002), interferences in selection of word due to damage in syntactic control processes (Schwartz & Hodgson, 2002), and decreased inhibitory function in semantic short-term-memory (STM; Freedman, Martin, & Biegler,

2004). Studies have shown that PWA demonstrate increased naming latencies on the semantically blocked items than semantically unrelated items (Ilshire & McCarthy, 2002; McCarthy & Kartsounis, 2000) and this effect is exaggerated when the repetitions are presented at a faster rate. McCarthy and Kartsounis (2000) attributed such semantic blocking effect to excessive/exaggerated inhibition of lexical representations. In another study by Biegler and colleagues (2008), fluent and nonfluent aphasia participants were assessed on picture-naming and word-picture matching tasks. Non-fluent participants showed semantic blocking effects in both tasks, and the effects were more prominent on the naming task. The authors thus postulate that non-fluent speech production in (non-fluent) aphasia is a result of the prolonged activation of lexical representations due to post selection inhibition (Biegler et al., 2008). Research has also shown that the inability to retain semantic information in case of persons with limited STM (e.g., PWA) may be due to inhibitory deficits in executive function (Martin & Ayala, 2004; Martin, Saffran, & Dell, 2000; Martin & Allen, 2008). In an experiment conducted by Martin and colleagues, PWA with semantic STM deficit showed difficulty in inhibiting distractor words. Authors explained this phenomenon by associating it to the inability to inhibit lexical-semantic representations. Also in PWA, conversational deficits can sometimes be attributed to impaired inhibition, such as, the presence of perseverations in verbal output proposed to be indicative of deficits in response inhibition (Frankel, Penn, & Ormond-Brown, 2007).

The previous research suggests that monitoring cognitive resources and selective allocation of attention to cognitively demanding activity can be resource-consuming in PWA. For instance, in the case of damage to the attention system, as in aphasia, cognitive

resources available to the individual may be insufficient, thus manifesting itself in the form of a reduction in the overall capacity and also the allocation process (McNeil et al., 1991). However, the concept of "resources" is quite abstract and lacks a direct measurement. Therefore, researchers have explained the availability (and utilization) of "resources" in PWA by analyzing different indirect measures, such as, amount of effort invested based on task demands (Clark & Robin, 1995; Lapointe & Erickson, 1991; Murray et al., 1997a), divided attention utilized in dual task paradigms, (Erickson et al., 1996; Lapointe & Erickson, 1991; Murray et al., 1997a), inhibitory control during inhibition tasks (Wiener et al., 2004), and performance during task switching paradigms (Mecklinger, Yves von Cramon, Springer, & Matthes-von Cramon, 1999).

Based on the literature reviewed in the previous paragraphs, inhibitory control is arguably a powerful influence in linguistic processing for PWA. Most of these studies have examined the inhibitory deficits during behavioral performances in cognitive or linguistic tasks through accuracy or reaction time (latency) measures. A significant challenge present in these studies is that participants are required to comprehend, perform, and/or respond to inherent linguistic demands imposed by the structure of the task. Linguistic demands are often present in the form of reading load or interpretation of task items or instructions and often require semantic, syntactic, or phonologically loaded information processing for successful completion. Owing to such demands, attentional resources get distributed between the primary task (inhibitory processing) and not significant secondary task (linguistic processing). It has been established that PWA have linguistic difficulties (Erickson et al., 1996; Freedman et al., 2004; Ilshire & McCarthy, 2002; McCarthy & Kartsounis, 2000; McNeil et al., 1991; Murray et al., 1997a, 1997b;

Schwartz & Hodgson, 2002); therefore processing linguistics items (during cognitive tasks) consumes a lot of resources leaving very modest resources for the actual inhibitory task processing. As a result, it remains uncertain how cognitive resources are allocated effectively between tasks and whether behavioral performance (e.g., accuracy, latency) is an accurate judgment of inhibitory ability in PWA. The combination of these factors provides a new push to expand the understanding to 'alternative determinants' of inhibitory performance in PWA. While there are several physiological measurements of cognitive behavior, such as cardiovascular activity, respiratory rate, salivary cortisol levels, and blood pressure, the current research will explore the potential of heart rate variability as a measure of inhibitory deficits in PWA; this study will also address the neurophysiological process associated with inhibitory control.

Few studies in aphasia have used physiological assessments to understand the underlying nature of aphasia. Salivary cortisol measures have been used in stress research in various clinical populations, including aphasia. Laures-Gore and colleagues have conducted a series of studies using salivary cortisol to measure physiological stress during cognitive and linguistic tasks (Laures-Gore, Hamilton, & Matheny, 2006; Laures-Gore, Heim, & Hsu, 2007; Laures-Gore, 2012). Stress is generally explained as an involuntary response to a situation that poses as a threat to the individual. In such situations, the individual experiences adaptive behavioral and physical changes including psychosocial alterations, lack of control and unpredictability, inadequate coping resources (Bohnen, Nicolson, Sulon, & Jolles, 1991; Dickerson & Kemeny, 2004; Elenkov & Chrousos, 2005). Salivary cortisol has been indicated as biomarker in stress research (Dickerson & Kemeny, 2004; Hellhammer, Wüst, & Kudielka, 2009;

Kirschbaum & Hellhammer, 1989; Takai et al., 2004) and a reliable measure of hypothalamus—pituitary—adrenal axis (HPA) mechanism to stress (Gozansky, Lynn, Laudenslager, & Kohrt, 2005; Hellhammer et al., 2009; Schommer, Hellhammer, & Kirschbaum, 2003). Laures-Gore et al. (2007) evaluated PWA on the effort perceived by them while processing verbal and non-verbal tasks. They used salivary cortisol measures to estimate the stress invested by them on each of these tasks. Results from the study revealed that PWA perceived more stress than the healthy participants on the verbal task opposed to the non-verbal task evident from the salivary cortisol. Another study by Laures-Gore and colleagues (2010) determined the stress responses from salivary cortisol measures in relationship to word productivity and error frequency performances by participants with aphasia (Laures-Gore, DuBay, Duff, & Buchanan, 2010). Although salivary cortisol changes to physiological stress have been demonstrated in PWA, it has been suggested by various researchers that salivary cortisol is a slow responding measure of stress (Backs & Seljos, 1994; Everly & Sobelman, 1987) and the HPA axis mechanism involved in the production of cortisol is impaired in people with brain injury (Franceschini, Tenconi, Zoppoli, & Barreca, 2001; Johansson, Ahren, Näsman, Carlström, & Olsson, 2000). Moreover, production of cortisol in the bloodstream takes time, so the use of salivary cortisol to detect changes in stress may not be as effective since experimental tasks used with PWA are often of shorter durations. In addition, cortisol is typically used in tasks that have high social-evaluative threat; there is a need for a more sensitive objective measure, such as cardiovascular activity. In fact, Laures-Gore et al. (2007) suggested that cardiovascular measures, such as blood pressure, heart rate (HR), heart rate variability (HRV) can be used as alternatives to cortisol responses

during cognitive/linguistic tasks. Laures-Gore and colleagues (2003) also explored the changes in blood pressure between aphasia participants and healthy controls on baseline and vigilance tasks. The participants with aphasia performed more poorly than the controls but significant results were not obtained on the magnitude of difference in blood pressure between baseline and vigilance tasks (Laures, Odell, & Coe, 2003). Although blood pressure measurements show promise, there is need for a more sensitive, objective measure, such as HRV, that reflects change in a cardiovascular activity as a response to an increase in mental workload during cognitive tasks and also reflects the effort allocated to those tasks (Backs & Seljos, 1994; Capa, Audiffren, & Ragot, 2008; Hansen, Johnsen, & Thayer, 2003; Kalsbeek, 1971; Porges, 1992; Veltman & Gaillard, 1993).

With the development of the field of psychophysiology, more and more research is being conducted to understand how physiological activities provide information about an individual's vital signs and overall health. There is an increasing interest among researchers to explore the interactions between the mind and the body, i.e. the mental and physiological processes (Bates, Buckman, & Miller, 2013; Thayer, Åhs, Fredrikson, Sollers, & Wager, 2012; Thayer et al., 2009; Thayer & Lane, 2009; Wager et al., 2009). The autonomic nervous system (ANS) has been the focus area in research studies exploring the interaction of the mental and physiological processes. The ANS controls the actions of all visceral organs of the human body, involving circulation, respiration, and digestion. The ANS is divided into three systems: the sympathetic nervous system (SNS), the parasympathetic nervous system (PNS) and the enteric nervous system. The SNS becomes active during stress; responses otherwise known as 'fight' or 'flight.' It increases heart rate and secretion of sweat glands, speeds up breathing and increases

adrenaline and blood sugar to prepare the body for action. In contrast, the activation of the PNS produces an inhibitive action on the increased activity in the target organs. This antagonistic action of the parasympathetic system helps the body to naturally recover from stress by slowing down the heart rate and breathing, and reducing brain and body activity. The fight and flight (due to sympathetic activity) are now counterbalanced by 'rest' and 'renew' (due to parasympathetic activity). Different physiological measures such as respiratory rate, respiratory sinus arrhythmia (HF-HRV), HR, HRV, blood pressure, and galvanic skin response have served to explain psychophysiological connections and the functioning of the ANS. Among them, HR and HRV are the commonly used cardiovascular measures.

Heart beat or the rhythmic contractions of the heart occur 'spontaneously' due to the initiation of the sinoatrial (SA) node which also acts as the natural pacemaker of the body. However, physiologic events mediated by the sympathetic and parasympathetic systems also influence the cardiac functions and cause changes in the cardiovascular system (e.g., HR, HRV, blood pressure). Due to this involvement of ANS (both SNS and PNS) in cardiac changes, HR and HRV are considered as the most common physiological measures. The following two sections discuss the ANS's role in HR and HRV and how it correlates with cognitive inhibition.

Neurovisceral Integration Model and Heart Rate Variability

Thayer and Lane (2000, 2009) proposed the Neurovisceral Integration Model (NIVM) that integrates a neuronal network involved in the regulation of the autonomic nervous system, emotional and cognitive processing and affective regulation. They

identified multiple areas (see details below; see Thayer & Lane, 2009 for a review) in the brain that influence the activity of the autonomic nervous system, and areas involved with emotion and attention. Specifically, Thayer and Lane posit that HRV, defined as the beat-to-beat fluctuations between heartbeats, is a reliable and valid measure of emotion regulation and overall physical health.

As described in the previous paragraphs, the ANS is comprised of the excitatory SNS and the inhibitory PNS that often interact antagonistically. The SNS is responsible for increases in HR and pupil dilatation and is mostly associated with subcortical brain areas. In contrast, the PNS is responsible for decreases in HR and pupil constriction. While the SNS is controlled by the subcortical areas of the brain, the PNS is associated with the cortical areas. Together the cortical and subcortical brain areas are responsible for regulating the ANS and therefore the visceral organs including the heart; and also emotions, thoughts, and behaviors (Thayer et al., 2012). The heart is under tonic inhibitory control via the vagus nerve (primary parasympathetic nerve), such that the PNS exerts a dominating action on the SNS at rest condition to ensure that the body is in a healthy state; this state is referred to as '*autonomic balance'* (Thayer & Lane, 2000). Thus, autonomic imbalance, suggestive of low PNS activity, has also been shown to be a marker of cerebrovascular disorders (Thayer & Lane, 2007).

In particular, Thayer and Lane (2000) suggested that the cortical and sub-cortical areas of the brain within the central nervous system (CNS) are responsible for goal directed behavior form a network called the central autonomic network (CAN; Benarroch, 1993). The CAN incudes functional units such as the anterior cingulate, insular, orbitofrontal, and ventromedial prefrontal cortices, and subcortical brain areas

such as the amygdala and insular cortex (Thayer et al., 2009). These structures are reciprocally interconnected to allow bidirectional flow of information (top-down and bottom-up) between the higher and lower levels of the CNS. The CAN is mediated through the sympathetic preganglionic neurons passing through the stellate ganglia (responsible for cardiac sympathetic innervation), and the parasympathetic preganglionic neurons that innervate the heart via the vagus nerve (responsible for cardiac parasympathetic innervation). Therefore the activity of these pathways in the CAN determine the functions of the SA node (the natural pacemaker of the heart) in modulating the healthy HR time series. While sympathoexcitatory activity increases the HR, parasympathoinhibitory activity is responsible for decreasing the HR. In addition, the CAN is under tonic inhibitory control via GABAergic (gamma-aminobutryic acid; an inhibitory neurotransmitter within the CNS) interneurons in the nucleus of the solitary tract (NTS). Disruption of this pathway leads to disinhibition of the sympathoexcitatory circuits within the CAN.

In fact, the prefrontal cortical areas (orbitofrontal and medial prefrontal cortex) of the brain (through the cingulate and insular cortices) form a bidirectional communication with the subcortical regions such as the amygdala, and tonically inhibit the amygdala via the prefrontal vagal pathways. Activation of the central nucleus of the amygdala (CeA) may lead to increased HR and decreased HRV (sympathetic activation and parasympathetic suppression). This occurs through three primary pathways identified within the system (1) activation (disinhibition) of the CeA inhibit the NTS which in turn inhibits the inhibitory caudal ventrolateral medullary (CVLM) inputs to the rostral ventrolateral medulla (RVLM) leading to a net *increase in sympathetic activity*, (2)

inhibition of neurons in the NTS leads to inhibition of tonically active nucleus ambiguus (NA) and dorsal vagal motor nucleus (DVN) neurons leading to a net *decrease of parasympathetic activity*; and (3) direct activation of sympathoexcitatory RVLM[2] neurons lead to a net *increase in sympathetic activity*. Therefore, 'decreased activation of the prefrontal cortex would lead to disinhibition of the tonically inhibited CeA further leading to a simultaneous disinhibition of sympathoexcitatory neurons in the RVLM (pathway one) and an inhibition of parasympathoexcitatory neurons (pathway two). Both these events would lead to a net increase in HR, and a concomitant decrease of vagally mediated HRV' (Thayer & Lane, 2009).

ANS influences the cardiac activity to a great extent via the sympathetic and parasympathetic (vagal) branches innervating the heart. Though the natural pacemaker of the heart, SA node (action potential is generated from its firing) is responsible for causing the rhythmic beating of the heart (at a rate of approximately 60 to 70 beats per minute for a resting heart), the sympathetic and parasympathetic fibers are in fact responsible for regulating the HR by exerting excitatory and inhibitory influences on the SA node by increasing or decreasing it (HR). In other words, the PNS and ANS act antagonistically to monitor the time intervals between consecutive heart beats, with slower HR corresponding to longer interbeat intervals (HRV), and vice versa. The influences of the parasympathetic branch, are however predominant at rest conditions, and serves to maintain the resting HR well below the SA node-generated HRs. Therefore, at rest, vagally mediated HRV serves as an index of parasympathetic activity as the 'sympathetic

[2] This route is a minor pathway associated with only a small percentage of the fibers connecting the CeA with the medullary ANS outputs.

influences on the heart is too slow to produce beat to beat changes' (Thayer et al., 2012). Taken together, HRV is a marker of vagus nerve, or PNS activity, such that an individual with higher HRV reflects a healthy and adaptive organism (Thayer & Lane, 2000) and 'reflects the degree to which cardiac activity can be modulated to meet changing situational demands" (Appelhans & Luecken, 2006).

In conclusion, the neurovisceral integration model (Thayer & Lane, 2000, 2009) emphasizes the role of the cortical and subcortical regions of the brain (collectively identified as the CAN) that serve as the neuroanatomical link between the ANS and higher order cognitive functions localized in the prefrontal cortex. All the structures in the CAN are reciprocally interconnected in the form of a circuit, allowing the prefrontal cortex to exert tonic inhibitory influence on sympathoexcitatory sub- cortical structures to monitor behavioral, cognitive, emotional, and physiological responses that are critical for self-regulation and adaptability. The primary output of the CAN (mediated through the sympathetic and parasympathetic neurons) extends to the heart and controls the autonomic input to it by innervating the SA node, which generates the HR time series. Therefore, increased HRV (an indication of greater vagal tone) at rest is the product of a network of structures (CAN) in which "the prefrontal cortex exerts inhibitory control over subcortical circuits thus allowing the organism to respond to environmental challenges in a controlled and adaptive manner when needed. For this reason, examining the parasympathetic influence on the heart via HRV can provide an index of an individual's (self-regulatory) capacity to effectively function in a complex and challenging environment" (Gillie & Thayer, 2014).

Heart rate variability (HRV). HRV is measured as the time intervals (distance) between two consecutive cardiac beats and is regulated by the autonomic nervous system. The electrical signal originating from the heart is registered in the form of a continuous electrocardiogram (ECG) trace. The most distinct feature of the ECG recording is the QRS complex. It consists of three closely related Q, R and S waves originating as result of the depolarization of the heart ventricles (R wave is the largest of the three waves and is easy to identify). The time between two successive QRS complexes is recorded as the duration between the peak of one R wave to the peak of the next R wave (also called the R-R interval). The R-R interval therefore represents the distance (in milliseconds) between the interbeat intervals (IBI), commonly referred to as the HRV (see Figure 1). In a continuous ECG recording, the interval between adjacent normal QRS complexes resulting from sinus node depolarization (and not due to abnormal beats occurring from atrial or ventricular arrhythmias) is called the normal-to-normal (NN) interval or normal R-R intervals (Appelhans & Luecken, 2006; Billman, 2011; Karim, Hasan, & Ali, 2011).

A major portion of these changes in HR occur simultaneously with respiration. During inspiration HR rate increases (R–R interval shortens) and during expiration HR decreases (R–R interval prolongs). This rhythmic oscillation in the HR is referred to as the respiratory sinus arrhythmia (HF-HRV). HF-HRV is mediated through inhibitory parasympathetic fibers to the SA node and reflects changes in cardiac autonomic regulation. HRV and HF-HRV are often used synonymously, but ideally HF-HRV represents the high frequency (HF) component[3] of the spectral band of the HRV

[3] Spectral analysis of the HRV usually reveals three distinct frequency components: 1) a low frequency (LF) band (located in the 0.02-0.06Hz range), 2) a mid-frequency (MF) band (0.07-0.14Hz), and 3) a high-frequency (HF) band (0.10-0.50Hz) (Cardiology, 1996; Jorna, 1992)

associated with respiration (Cardiology, 1996). While parasympathetic activity increases HRV (HR decreases, HF-HRV increases), sympathetic activity decreases HRV (HR increases, HF-HRV decreases).

HRV has been suggested as an objective measure of mental and cognitive workloads (Backs & Seljos, 1994; Hansen et al., 2003; Hansen, Johnsen, & Thayer, 2009; Porges, 1992; Veltman & Gaillard, 1993). While performing on cognitively demanding tasks there is a drop in HRV from baseline (at rest) to task (during performance on task) conditions (Kalsbeek, 1971) indicating a decrease in parasympathetic activity. Normally the parasympathetic system works towards slowing down the heart rate (also, indicative of increased HRV) that has been excited by the sympathetic system. However, during cognitively demanding tasks, the parasympathetic activity is inhibited (Thayer & Lane, 2000, 2009). In the absence of parasympathetic action, the antagonistic action to sympathetic activities is lost, resulting in an increase in HR and drop in the HRV. This decrease in HRV is further indicative of diminished cognitive resources to cognitively challenging tasks.

Association between heart rate variability and inhibition. As mentioned in the previous sections, HRV is associated with activity of the prefrontal cortex. In the following section, it will be established that HRV is also related to performance on tasks that are mediated in the prefrontal cortex.

Cognitive control (also referred to as attention control, executive attention, or executive functioning (McCabe, Roediger III, McDaniel, Balota, & Hambrick, 2010; Wessel, Overwijk, Verwoerd, & de Vrieze, 2008) refers to the mental processes required

to keep goal-relevant information active and inhibit the processing of irrelevant information (Braver, 2012; Miyake et al., 2000). Successful cognitive control is ensured by a*ctive maintenance of patterns* of neural *activity* in the prefrontal cortical areas (E. K. Miller & Cohen, 2001), and the extent of functional connectivity with other networks. Since, resting HRV is associated with activity in the prefrontal cortex, it is important to identify that individual differences in HRV reflects one's cognitive control ability. Miyake et al. (2000) identified three primary functions that underline cognitive control: updating of working memory, set-shifting and inhibition. However, inhibition is the basic function that underlies all other cognitive control functions, such as working memory and attentional set-shifting (Miyake & Friedman, 2012; Thayer & Lane, 2009). Also HRV is largely an index of inhibitory control, therefore individual differences in HRV would potentially reflect the extent to which these inhibitory processes are effective (Thayer, 2006).

The ability to inhibit pre-potent responses has been associated with the availability of attentional resources towards a task/activity. Most activities in our day-to-day life involve cognitive functions such as memory, sustained attention, inhibition, and mental flexibility, for survival. All of these cognitive functions are associated with pre-frontal cortical activity. Decline in any of these cognitive functions may be caused due to one of the various reasons, such as aging, illness, neurological and clinical disorders, and negative affective states.

Autonomic dysregulation may also affect attention and cognitive performance. The association between autonomic dysregulation and cognitive performance has been demonstrated in different research studies. More often in the literature, HRV has been

used as a measure of reactivity[4] to attentional tasks by behaving as a dependent variable. Recent studies have utilized HRV as an independent variable in predicting performance on cognitive tasks (Hansen et al., 2003). A growing body of research shows that, individuals with higher levels of HRV at rest demonstrate enhanced cognitive performance on tasks that require processing of working memory, attentional control, and inhibition. Hansen and colleagues (2003) examined the effect of vagal tone (through HR and HRV measures) on two cognitive tasks, a continuous performance test (for sustained attention) and a working memory test in young adult male sailors. Authors of the study observed that participants in the high HRV group demonstrated better responses than the low HRV group on both the tasks. Faster reaction times, more correct responses and fewer errors in the high HRV group was suggestive of the fact that high HRV was associated with improved performance on executive function tasks. In a similar study, Hansen, Johnsen and Thayer (2009) demonstrated the relationship between resting HRV and cognitive functions by adding a threat of shock condition during cognitive task processing. In the presence of a threat shock condition, task performance was significantly poorer in the low HRV group. High HRV group was more tolerant to threat conditions. High HRV participants showed better performance on cognitive tasks than the low HRV participants in a stressful environment suggesting that high HRV individuals maintained enhanced WM capacity independent of threat conditions (Hansen et al., 2009). Further support for the causal relationship between WM capacity and

[4] Vagally-mediated cardiac tone is sensitive to cognitive task changes (such as varying inter-stimulus intervals for temporal demands, increasing number of target items to be counted, or manipulating the difficulty of the task). Performances on such task changes also result in concomitant changes in HRV. Therefore, HRV is regarded as a measure of reactivity to cognitive tasks.

individual differences in HRV came from the (Hansen, Johnsen, Sollers III, Stenvik, & Thayer, 2004) study in which aerobic training/detraining produced concomitant changes in WM performance and HRV. Participants in the training group (continued aerobic raining over a 4-week period) demonstrated higher levels of resting HRV and faster reaction times and more true positive responses on the post-test relative to the detraining group participants (who discontinued from aerobic exercise).

Resting HRV has also been associated with tasks that are associated with attention control. A study by Johnsen et al. (2003) investigated the attentional bias in dental phobic patients by using an emotional Stroop paradigm. Participants were presented with color congruent and color-incongruent words, and with neutral words and dental-related threat words (e.g., cavity, drill). Low HRV participants demonstrated decreased attentional performance than those with high HRV on both stimuli colored words and threat words. The results of the study suggested that low HRV group had decreased ability to organize resources to meet demands during attention tasks, and therefore represented a low degree of neurovisceral integration (Johnsen et al., 2003). Park et al. (2012) also found that individuals with low levels of HRV were less able to inhibit their attention to affectively significant cues such as locations where fearful faces were previously presented (Park, Van Bavel, Vasey, & Thayer, 2012). In a later study authors examined the relationship between HRV and selective attention under load. In high load conditions (attention task with one target letter and five non-target letters), individuals with high HRV were faster in trials with neutral distractors than fearful distractors Findings from the study suggest that ‘cardiac vagal tone is associated with successful control of selective attention critical for goal-directed behavior, and its impact is greater when fewer cognitive resources are

available' (Park, Vasey, Van Bavel, & Thayer, 2013). Mathewson and colleagues reported similar findings where enhanced performance on an executive component of a maze learning task was closely associated with the autonomic regulation of cardiac control. were reported by (Mathewson, Dywan, Snyder, Tays, & Segalowitz, 2011) Healthy young and old adults completed a maze learning task of increasing difficulty levels (i.e., increasing demands). Older adults demonstrated higher error rates and rated the task as more challenging than their younger counterparts. The older group also showed a markedly reduced autonomic cardiac control indexed by respiratory sinus arrhythmia. With this trend of results in older versus younger groups, authors suggested that autonomic measures could possibly predict maze performance accuracy.

Consistent with findings on working memory and attention control tasks, studies have also found association between resting HRV and performances on tasks that require inhibitory control. (Krypotos, Jahfari, van Ast, Kindt, & Forstmann, 2011) have found that in an emotional stop-signal task (negative vs. non-emotional stimuli) individuals with higher HRV activated and inhibited their responses faster than those with lower HRV in the presence of negative stimuli, suggesting that in the presence of interfering emotional stimuli, HRV is affected. In a recent study by Hovland et al. (2012), patients with panic disorder showed that higher levels of resting HRV were correlated significantly with better performance on measures of Wisconsin Card Sorting Task and the Color-Word Interference Task respectively. The findings of the study corroborates the idea that resting HRV is related to activity in the prefrontal cortex, and predicts general performance on executive function tasks but it is most strongly associated with aspects of the tasks that reflected inhibitory control (Gillie & Thayer, 2014; Krypotos et al., 2011).

Therefore, autonomic regulation (indexed by HRV) is an essential contributor of attentional (inhibitory) control, and individuals with higher cardiac vagal tone demonstrate 'successful' inhibitory ability mediated by cortical inhibitory mechanisms. While attention to external stimuli slows the HR (and increases HRV), attention to internal stimuli (i.e., cognitive work) contributes to increased HR and decreased HRV (Lacey, Kagan, Lacey, & Moss, 1963). In young adults, higher baseline HRV has been shown to relate to enhanced WM and attentional control. In summary, HRV is influenced by parasympathetic branch of the ANS. 'Taken together, these results support the usage of HRV to index efficient allocation of attentional and cognitive resources needed for efficient functioning in a challenging environment in which delayed responding and behavioral inhibition are key' (Thayer & Friedman, 2004).

Heart Rate Variability in People with Aphasia

HRV is considered to be a valid physiological measure of most cognitive processes that are difficult to reliably assess in PWA, including memory (Hansen et al., 2003), attentional resources (Porges, 1992), and mental effort or workload (Althaus, Mulder, Mulder, Van Roon, & Minderaa, 1998; Backs & Seljos, 1994; Hansen et al., 2003) . A cognitive inhibitory task usually elicits a stress reaction that is measured as a decrease in HRV from baseline to task conditions (Kalsbeek, 1971). Normally, the parasympathetic nervous system decreases heart rate as an antagonistic response to the sympathetic nervous system that increases heart rate. However, during a cognitively challenging task, the functions of the parasympathetic system are inhibited (Kalsbeek, 1971; Thayer & Lane, 2000, 2009). This decrease in HRV provides an objective physiological measure for attentional allocation to cognitive challenging tasks. This

happens due to responses from the parasympathetic system that works in opposition to the sympathetic system to slow the heart.

Researchers from other disciplines have recommended the use of HRV as a physiological measure to understand the linguistic and cognitive performance in healthy and disordered populations. But very few studies in aphasiology have actually explored the effects of linguistic and cognitive performances on HRV. Christensen and Wright (2014) investigated HRV as a measure of effort allocated to verbal and spatial WM tasks of increasing levels of difficulty. Eight PWA and 19 neurologically intact control participants were assessed on verbal and spatial n-back (working memory) tasks (Christensen & Wright, 2014). Effort allocation was measured as the difference in HRV (at mid frequency range, 0.07–0.14 Hz) during the WM tasks and the HRV during post task baseline conditions. While results of the study suggest that both participant groups allocated some effort to the verbal and spatial tasks, PWA did not exhibit significant changes in HRV to task difficulties thereby suggesting that they did not allocate effort appropriately when it was needed. Additionally, PWA demonstrated non-significant relationships between change in HRV in the mid frequency (.07-.14 Hz) range and task types (verbal, spatial) suggesting that the difference is not specific to verbal stimuli. In a prior study with 13 PWA and 21 control participants, Christensen (2012) reported that PWA demonstrated an increased stress response (a drop in HRV), but the correlations between task difficulty and HRV change was non-significant for both the verbal and spatial tasks (Christensen, 2012). She associated this increased stress response to allocation of effort on tasks but the extent to which task difficulty ratings may reflect allocation of effort is still of debate. Results further revealed that PWA differed only on

verbal tasks and not on spatial tasks, suggesting that they have an intact central executive component of working memory. This could be attributed to Baddeley's WM model (2000), which suggests that both verbal and spatial components of WM share a common central executive component, and intact processing on either of the spatial or verbal tasks would still signify an intact central executive component of WM. Christensen concluded that WM deficits in PWA are primarily a result of their linguistic deficit and that PWA may incorrectly assess the task demands for both verbal and spatial tasks.

Both the studies provide a rich context with which to compare and contrast the results of the present study and determine the use of HRV in PWA. However, there are certain limitations in their study that may have confounded identifying significant HRV outcomes. First, 'inhibition' is the basic process that underlies all other cognitive control functions, such as WM and attentional set-shifting (Miyake & Friedman, 2012; Thayer & Lane, 2009). Although the studies revolve around the idea that there is increased cardiovascular response to rising WM demands, they do not discuss the importance of inhibitory processing/ inhibitory ability as the primary function that participants might engage in while performing WM tasks. Second, inhibitory processing is associated with high frequency HRV (.15-.40 Hz) (Cardiology, 1996) During cardiovascular activity the ANS increases sympathetic outflow to the SA node that causes a concurrent inhibition of vagal tone, which is also an indicator of parasympathetic activity. Therefore, parasympathetic activity (vagal influence) is an important phenomenon to be addressed in research involving inhibition and HRV. While high frequency HRV (.15-.40 Hz) is a marker of parasympathetic activity, it was not explored in either of Christensen's studies. Thus, there remains a need to examine cardiovascular activity in the high frequency band

of the HRV spectrum and its relation to inhibitory control in PWA. Third, both the studies did not exclude participants on cardiovascular medications or who had hypertension. Participants on anticholinergic, antipsychotics, angiotensin-converting enzyme (ACE) inhibitors, statins, or beta-blocker medications potentially affect the cardiac functions by decreasing the sympathetic input and diminishing the predictive value of HRV. Other limitations are: small sample size, wide range of age and gender distribution of participants, and insufficient statistical power leading to non-significant differences in task difficulty and effort allocation. Also, both the studies report the WAB-R-AQ scores for PWA participants, however they did not investigate the potential impact of aphasia severity on WM task performance.

In another study in PWA, Chih (2011) investigated the physiological correlates of word retrieval. Seven PWA and 38 healthy controls participated on a picture-naming task in four experimental conditions (i.e., stress, counting, low frequency word, high frequency word) during simultaneous measurement of their cardiac (HR, HRV) and respiratory activity (respiratory rate). PWA exhibited significant differences in HR, and high and low frequency power of HRV during linguistic tasks. However no change in respiratory rate was observed. Difficulty and stress ratings were obtained from the participants in all conditions. With respect to perceived level of stress (from subjective ratings) and physiological responses, similar findings were reported, suggesting that participants perceived increased stress on tasks when they could not handle the task better. In other words, naming performance decreased when PWA reported perceiving an increase in stress. Overall these findings suggest that there is some amount of SNS arousal while PWA are performing speech and language tasks (Chih, 2011). Two

limitations, however, were identified in this research study. Chih recorded significant changes in HRV during linguistic processing in PWA and controls, but did not include any firsthand cognitive parameter/task in the study design. It is possible that 'inhibition' is the primary process controlling for the word retrieval behaviors, such as naming accuracy, naming latency, and word frequency, in the participants and exploring the participants' inhibitory behavior would have provided additional information about their linguistic processing abilities. Additionally, this study did not explore changes in the time domain variables of HRV that are based on HR at a point in time. A time domain variable essentially reflects the parasympathetic component of HRV and is an index of vagally-mediated cardiac control that is a strong indicator of inhibition. While Chih included PWA with varying aphasia severities (4 mild to moderate severity; 3 profound severity), she did not investigate aphasia types (fluent vs nonfluent) that could have potentially yielded information on the individual differences in HRV and their linguistic capabilities.

Both the above studies successfully provide an avenue for use of HRV in PWA but the various issues discussed above limit their potential for any conclusive evidence. Therefore the current study is an attempt to provide a better picture of inhibitory control in PWA and its physiological correlates.

Purpose and Study Aims

One of the primary functions of the prefrontal cortex is inhibition (Knight, Staines, Swick, & Chao, 1999; Miyake et al., 2000; Prabhakaran, Narayanan, Zhao, & Gabrieli, 2000; Stuss & Alexander, 2000). Inhibitory processes are associated with many cognitive functions such as WM (Conway & Engle, 1994; Jonides, Smith, Marshuetz, Koeppe, & Reuter-Lorenz, 1998; McNab et al., 2008; Oberauer, 2005), set-shifting (Costa, 2010; Gade, Schuch, Druey, & Koch, 2014; Kiesel et al., 2010; Koch, Gade, Schuch, & Philipp, 2010; Rubinstein, Meyer, & Evans, 2001), and response inhibition (Bokura, Yamaguchi, & Kobayashi, 2001; Kramer, Humphrey, Larish, & Logan, 1994; Verbruggen & Logan, 2008, 2009). A common inhibitory network supports a range of cognitive and affective processes, and multiple pathways that connect the prefrontal cortex to the inhibitory action of the medullary cardio-acceleratory circuits. This has been explained by a neurovisceral integration model (NVIM; (Thayer & Lane, 2000), which describes that cognitive, affective, and physiologic regulation are connected in the service of a goal-directed behavior (Thayer et al., 2009; Thayer & Lane, 2000) and linked to vagally-mediated cardiac function (Jennings, 1992; Öhman, 2005) indexed by the heart rate (HR) and heart rate variability (HRV).

Given the role of HRV in inhibitory processing as hypothesized by the neurovisceral integration model, it is reasonable to posit that efficient inhibitory control is associated with increased HRV. This study focuses on establishing this relationship in PWA. Therefore, the primary aims of this study are as follows:

1. To assess if inhibition can be physiologically indexed by HRV in PWA

Inhibition involves the selection of optimal responses and suppression of less functional responses. It is an important cognitive process to consider in PWA due to their potentially diminished attentional systems. Assessment of inhibition in PWA has been challenging due to the requirement of linguistic processing during cognitive tasks and basing judgement of inhibitory ability solely on behavioral performance. Therefore, there is new push towards understanding the physiological determinants (such as, cardiovascular activity) of inhibitory performance in PWA.

The purpose of the first aim is to assess whether inhibition can be physiologically indexed by HRV in PWA. Heart rate variability was recorded during processing of inhibitory tasks. To demonstrate any increase or decrease in cardiovascular activity HRV recordings will be compared to HRV recordings collected during rest (no task condition), a high demand inhibition task and a low demand inhibition task. It is hypothesized that PWA would demonstrate significantly reduced HRV during the high demand inhibition task opposed to the low demand task, suggesting that there is a significant change (decrease) in cardiovascular activity during greater inhibitory processing than lesser inhibitory processing. Also, it is hypothesized that HRV would reduce during tasks compared to baseline condition.

2. To establish if WM ability is associated with inhibitory performance in PWA

Inhibition is often associated with the availability of attentional resources towards a task/activity. PWA manifest with difficulties in allocating attention resources required for processing of linguistic and cognitive functions. According to resource dependent

model of inhibition, individuals with high WM use attentional resources to assist in task performance such as inhibition of irrelevant and weaker information. In other words, participants "with greater attentional resources also have greater capacity for inhibiting information that is irrelevant to the task" (Conway & Engle, 1994; p. 368). Examining the relationship between WM ability and inhibitory performance is the second aim of this study.

The objective of the second aim is to find the association between inhibitory performance and WM ability. To do so, a continuous performance working memory updating task will be used to measure WM ability, which will be compared with behavioral performance on the inhibition task as well as the potential physiologic measure (cardiovascular activity; HRV) recorded during the inhibitory task. It is hypothesized that participants with lower WM ability will demonstrate decreased performance on the behavioral and/or physiological inhibitory measures. Such findings will determine whether WM performance is related to performance on inhibition tasks.

In summary, earlier research studies in neurologically intact adults have explored the *relationship between* autonomic regulation of cardiovascular activity and cognitive processing (as described in previous sections). However, there are no direct observations and evidence from healthy group research studies investigating the changes in HRV during inhibition tasks as designed for this study. Therefore, to be able to compare and contrast the results obtained from PWA, a neurologically intact age- and education-matched control group will also be recruited. Outcomes of these analyses would help in establishing whether the relationship between inhibition and HRV is similar across both PWA and neurologically intact healthy participant groups.

CHAPTER 3

METHOD

Participants

Two groups of participants were recruited for the study; one group composed of PWA (referred to as aphasia group) and a second group included neurologically intact age- and education-matched controls (referred to as healthy group).

Aphasia group. Thirteen PWA were recruited to participate in the study; one was excluded after he failed to comprehend the instructions for the cognitive tasks. Participants who met the following selection criteria were included in the study: (a) native or primary speakers of English language, (b) history of single left hemisphere cerebrovascular incident at least three-months prior to participation in the study, (c) free from self-reported history of mental illness or substance abuse, and (d) should not have implanted pacemakers or history of atrial fibrillation. Participants were also required to demonstrate an aphasia quotient of 93.7 and below on the Western Aphasia Battery-Revised (WAB-R; Kertesz, 2007). Participants' post-stroke cognitive impairments were also recorded on the Cognitive Assessment scale for Stroke Patients (CASP; Barnay et al., 2014; Barnay et al., 2012). All participants were recruited from the Speech and Hearing Clinic at University of Georgia (UGA) and referrals from speech-language pathologists from local hospitals in Athens and Atlanta, Georgia.

Healthy group. Twelve healthy neurologically intact age and education matched controls were recruited from the Osher Lifelong Learning Institute at UGA. All healthy control participants met the following criteria: (a) native or primary speakers of English language, (b) have no history of neurological trauma, cerebrovascular accident, neurodegenerative diseases, such as Parkinson's disease, Alzheimer's disease, or frontotemporal dementia, (c) free from self-reported history of mental illness or substance abuse, and (d) should not have implanted pacemakers or demonstrate transient or persistent non-sinus rhythm during the ECG recording, such as atrial fibrillation.

Due to the impact of psychological distress on cognitive processing, participants of both groups were screened for anxiety and depression. Only participants with no depression (a score between 0 and 4) on the short form of the Geriatric Depression Scale (GDS; Van Marwijk et al., 1995; Yesavage, 1988; Yesavage et al., 1983) and low anxiety scores (a score between 0-21) on the Beck Anxiety Inventory (BAI; Beck & Steer, 1990) at the time of experiment were included for further experimental testing. Both participant groups showed minimal signs of anxiety and no signs of depression on the BAI and GDS respectively. Participants who demonstrated aided or unaided visual acuity of at least 20/40 on a Snellen chart (mounted 3 feet away on a wall passed for the vision screening) participated in the study. Additionally, participants of the healthy group were administered the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) to screen for any potential mild cognitive deficits. Participants who achieved a total score of 26 and above (considered as a normal on the test) only proceeded to the further phases of the study. All participants scored within the range of 26.00 to 29.00 on the MoCA test (M = 27.25, SD = 129). Participant characteristics of both groups are presented in Table 1.

Experimental Tasks

Continuous Performance Test-X (CPT-X). Traditional CPTs were developed to measure sustained attention and vigilance (Borgaro et al., 2003; Rosvold, Mirsky, Sarason, Bransome Jr, & Beck, 1956), or the ability to represent and maintain context information necessary to guide appropriate task behavior. Different versions of the CPT have been developed over the years in which either perceptual, memory load, or acuity is manipulated. Some of these include the CPT-X (Rosvold et al., 1956), CPT-AX (Rosvold et al., 1956), CPT-identical pairs (CPT-IP; Rosvold et al., 1956), and degraded stimulus CPT-DS; Adler et al., 2001; Hsieh et al., 2005; Kasai et al., 2002; Nuechterlein, Parasuraman, & Jiang, 1983) . In its original and simplest form, known as the CPT-X (Rosvold et al., 1956), the participants are shown a random sequence of different letters with a rate of about one per second. The instruction is to push a button only when the target letter X is shown and not to respond to any other letter. The target letter usually has a low probability (around .20) of being presented. In sustained attention tasks, participants are instructed in advance of the task to attend to the same specific stimulus (targets) across all stimulus presentations in the task. The presentation of the stimuli in the CPT-X is at constant interstimulus interval (ISI). Varying ISIs could possibly elicit varying decrements in vigilance, therefore this task stands out more as a sustained attention task with less inhibitory demands. The task is programmed using the SuperLab Pro for Windows software and is 14 minutes in duration. Bold black letters on a white background were presented on a 15-inch Dell laptop screen at ISI of 1000ms. The ratio of target stimuli to non-target stimuli was 10: 90. Participants were instructed to press the space bar to all target letters, the ‘X’s’. Participants initially completed a 1 minute

practice test. The dependent variables that were collected from the CPT-X are: 1) D-prime and 2) Hit RT. The choice of these dependent variables is explained after this section.

Continuous Performance Test 3 (CPT-3; Conners & Staff, 2014). The Connor's Continuous Performance Test-3 is designed for the assessment of sustained attention, and inhibition. Specifically, it provides information on three dimensions: inattention, impulsivity and vigilance. The use of this test as a measure of attention has been determined by comparing CPT scores to performance on the Child and Adolescent Psychiatric Assessment (CAPA; Angold & Costello, 1995, 2000; Epstein et al., 2003). CPT-3 has been used as a measure of executive function in various clinical populations-ADHD (Miller, Nevado-Montenegro, & Hinshaw, 2012; Pasini, Paloscia, Alessandrelli, Porfirio, & Curatolo, 2007), traumatic brain injury (Lipton et al., 2009), posttraumatic stress disorder (Aupperle, Melrose, Stein, & Paulus, 2012), depression and panic disorder (Micco et al., 2009), obesity (Lokken, Boeka, Austin, Gunstad, & Harmon, 2009) and aphasia (Lee, 2014; Lee & Sohlberg, 2013; Marshall, Basilakos, Williams, & Love-Myers, 2014; Mohapatra, Marshall, & Laures-Gore, 2014).

Conners' CPT-3 is a computerized software that requires participants to respond to individual letters that appear on a laptop screen at different ISIs (1, 2, or 4 seconds). Participants were required to depress the space bar as quickly as possible for all the letters except the letter 'X" (i.e., participants are required to 'inhibit' their responses to the letter 'X.'). The CPT consists of six blocks and three sub-blocks, each containing 20 letter presentations. The presentation order of the different ISIs varies between blocks. All participants complete a practice test (70 seconds) prior to the long experimental task

that is 14 minutes long. The dependent variables that were collected from the CPT-3 are: 1) D-prime and 2) Hit RT.

N-Back task. There are many variants of the n-back task that require participants to engage in encoding, temporary maintenance and rehearsal, tracking of serial order, updating, and comparison of pictures presented in a sequence (Collette & Van der Linden, 2002). The n-back task requires continuous updating of a mental set while responding to previously seen stimuli. Thus the n-back task engages in multiple processes within the WM system and qualifies as an ideal task for measuring WM ability (Downey et al., 2004; Wright, Downey, Gravier, Love, & Shapiro, 2007).

In the current study, the n-back task presentation is modelled after Wright et al.'s (2007) study and the visual stimuli is modeled after Downey et al.'s (2004) "fruit-back" task. The presentation of fruits potentially reduces verbal demands and is appropriate for PWA (Wright et al., 2007). The task requires participants to continuously monitor and respond to pictures of fruits presented on a computer screen. The task is programmed using the SuperLab 5.0 for Windows software on a Dell laptop and varies in processing load: 1-back and 2-back. For the 1-back task, participants are required to respond by pressing the space bar as quickly as possible to the picture of any fruit or vegetable that is the same as the one presented before; on the 2-back task the participants are required to respond to fruits or vegetables that is same as the item presented two before the target. Each task (1-back and 2-back) consists of four blocks of which two are practice tests and the other two are experimental tests. A stimulus onset asynchrony of 4000 ms and stimulus duration of one and a half seconds is maintained throughout the presentation

(Wright et al., 2007). The dependent variables from this task were: (1) D-prime and (2) Hit RT.

Dependent variables. Participants' responses were recorded in the form of number of correct, omission errors, commission errors, and reaction time for target stimuli. Two dependent variables were calculated from these-

1) D-prime: The hit rate and false alarm rates were converted to D-prime values. The hit rate is the number of hits (corrects) divided by the total number of target stimuli. The false alarm (commission) rate is the number of false alarms divided by the total number of non-target items. D-prime is calculated as the difference between z-score of the probability of hit rate and probability of false alarm. D-prime is a bias-free statistic and is recommended in signal detection theory as a measure of sensitivity i.e. how efficiently a person can discriminate between presence and absence of signal trials.

2) Hit Reaction time: This measure is the response time for the correct target stimuli.

Physiological Recordings

ECG activity was continuously recorded using BIOPAC Student Labs (BSL) PRO MP35 with a recording unit with BSLPro software. The BIOPAC system was connected to a computer where the tachograms were recorded and stored. The different time pints of the study were demarcated using markers. The dependent variables recorded were heart rate (HR; measured in beats per minute) and heart rate variability (HRV). While HR is defined as the number of beats per minute, HRV is referred to the amount of fluctuations in the inter-beat-interval between normal heart beats. The Task Force of the European Society of Cardiology (Cardiology, 1996) and the North American Society of Pacing and

Electrophysiology have established several standards such as frequency and time domain methods for HRV measurement. The time domain variable (based on HR at a point in time) that was considered for this study is rMSSD. It is the root mean square of successive differences between inter-beat-intervals that essentially reflect on the parasympathetic component of HRV. The rMSSD is an index of vagally-mediated cardiac control (Vagus nerve) that correlates highly (~.90) with spectrally derived measures of vagally-mediated HRV (Friedman, Allen, Christie, & Santucci, 2002; Thayer & Lane, 2000). A recording time of five minutes is usually recommended for rMSSD in the Task Force guidelines.

The frequency domain variable of interest is the high frequency band (HF; .15-.40Hz range) of the HRV spectrum. Activity in the HF range (marker of parasympathetic activity) is associated with the respiratory sinus arrhythmia (RSA), a vagally-mediated modulation of heart rate that is habitually associated with respiration (RSA increases during inspiration and decreases during expiration). A minimum recording time of 1 minute is required to measure the HF band. The Kubios HRV is an analysis software that was used for studying the variability of heart beat intervals and for calculating the time and frequency domain measures for each time segment (Tarvainen, Niskanen, Lipponen, Ranta-Aho, & Karjalainen, 2014). Therefore the dependent physiological measures that were considered for further analyses are: (1) HR, (2) rMSSD, and (3) HF-HRV.

Procedure

All procedures were approved by the Institutional Review Board at the UGA. Depending on the participant's location, they were ether assessed in the Aphasia and Aging Research Laboratory at UGA, Athens or in a clinical setup in Atlanta. The aphasia group was assessed in two sessions (screening and experimental testing days) with no more than three days apart. During the first session (i.e., the screening day), experimenter briefed participants on the purpose and design of the study, and a written informed consent was obtained from the participant. A brief history questionnaire was completed with information pertaining to age, sex, date of birth, education, handedness, history of head injuries, lesion location, date of stroke, other chronic illnesses, time post onset, use of drugs or alcohol, history of cardiovascular, respiratory, neurological diseases, and medications that could influence cardiovascular control. Screening assessments were administered for vision, GDS, BAI, and WAB-R. Participants who qualified after the screening questionnaire and assessments were eligible to participate in the experimental assessments and physiological recordings. On the screening day, the n-back task was administered and performance was recorded for each participant. As part of the study protocol, participants were instructed to abstain from smoking, caffeine, alcohol, and strenuous exercising for approximately 12 hours prior to the experimental testing day, and also have adequate sleep for 7 to 8 hours the night before the testing day. In the second session, participants were initially asked to describe any change in their behavior that was requested as part of the study protocol.

During the second session (i.e., the experimental testing day), participants were asked to complete the computerized inhibition tasks, and physiological information was

simultaneously collected during the process. HRV information was recorded using three ECG surface electrodes placed on the participant's body in a Lead II configuration (positive electrode on the left rib, negative electrode on the right collar bone, and ground electrode on the left collar bone). To avoid any interference in physiological data, participants were required to remove any external metal objects including watches and jewelry from their body. HRV was recorded continuously in five conditions: 1) during a baseline 10 minute resting pre-task period (*baseline condition*), 2) during the experimental CPT-X task, 3) during a 10-minute in-between task rest period, 4) during the experimental CPT-3 task, and 5) during baseline 10 minute resting post-task period (*recovery condition*). The order of CPT-X and CPT-3 was counterbalanced across participants of both groups.

On the CPT-3, the participants were instructed to depress the spacebar using their non-dominant hand for every target (all letters but X) and inhibit their response to every non-target (all X's). On the CPT-X, the participants were required to respond to all target letters (X's) by depressing the space bar as quickly as they see the target on the computer screen. Also, aphasia participants were instructed to use their post-morbid non-dominant hand. If participants had restricted mobility on any part of their body due to hemiparesis or paralysis, then they used their preferred hand (details are presented in Table 1). During both the experimental tasks, the experimenter provided verbal instructions to the participant. Instructions were repeated multiple times to ensure that the participant understood the complete task. All PWA participants were also shown pictographic instructions. Before starting the actual experimental tasks, practice opportunities were given to the participants. For CPT-X, CPT-3, and n-back approximately 1 minute practice

tasks were provided. All procedures were video recorded for later behavioral and quantitative analyses. Physiological data was recorded throughout the five conditions (baseline, CPT-X, rest, CPT-3, and recovery). During all the rest conditions, participants were asked to stay awake, sit relaxed, and remain silent while breathing spontaneously. For short-term assessments of HRV, Task Force of the European Society of Cardiology & Task Force of the European Society of Cardiology (1996) has recommended a recording time of at least 5 minutes during the task and preceded by a 5 minute stabilization period (Esco & Flatt, 2014). Therefore, only 5 minutes of HRV recording during each condition was considered for statistical analyses and interpretation.

Participants in the healthy group were tested in a single day with adequate breaks offered within screening and experimental testing. During the screening phase, the healthy control group also performed on the cognitive screening MoCA test.

CHAPTER 4

RESULTS

Group Characteristics

Independent samples t-tests were conducted to compare the age and education of the two participant groups. There was no significant difference in age between the aphasia group (M = 66.50, SD = 11.09) and the healthy group (M = 68.42, SD = 10.05), $t(22) = -.444$, $p = .662$. Similarly, there was no significant difference in years of education between the aphasia group (M = 15.08, SD = 5.14) and the healthy group (M = 18.08, SD = 3.63), $t(22) = -1.651$, $p = .113$.

Data Analyses

All data were screened for presence of outliers. To identify the outliers, boxplots were inspected and values +/- 3SD from the mean were excluded from further analyses on the dependent variable of interest. Shapiro-Wilk's test, histograms and normal Q-Q plot results were reviewed to verify assumptions of normality. Data transformations were carried out on measures that violated the assumptions of normal distribution and homogeneity of variance. For positively skewed variables, log 10 transformations were performed on the data. For negatively skewed variables, initial data reflection was done to each individual score in the variable and then log 10 transformations were done. All assumptions for parametric analyses were established. To ensure the assumption of sphericity were upheld, Maulchy's test was conducted. If the sphericity assumption was

violated, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity. Alpha level of .05 was applied to all comparisons but in case of multivariate analyses Bonferroni alpha adjustments were made. Behavioral and physiological performance was compared through mixed and multivariate analysis of variances. Follow-up pairwise comparisons were performed to examine specific between and within group differences. To evaluate the associations between behavioral and physiological data, Pearson correlation coefficients were calculated. Regression analyses were performed to determine if physiological performance could predict behavioral performance. The magnitude of effect for each relationship was calculated using the partial eta- squared statistic.

Preliminary Analyses of Cognitive Behavior

To assess whether there were any differences on behavioral and physiological dependent variables on the two inhibition tests while taking the effects of test order into consideration, independent t-tests were conducted. The test orders were: (a) Test order 1: first CPT-X, second CPT-3; (b) Test order 2: first CPT-3, second CPT-X. No significant difference was observed in behavioral and physiological performance patterns with respect to test order. Due to non-significant differences in each of the comparisons, test order was not taken into consideration for any of the further analyses. Results of the analyses are summarized in Table 2 and 3.

1. **Behavioral performance on inhibition tests**

A mixed effect multivariate analysis of variance (MANOVA) was conducted to determine if there are differences between groups on the dependent variables in two tests.

Two measures of behavioral performance were assessed: D-prime and HitRT scores. Participants (between-group measure) completed two tests: CPT-X and CPT-3 (within-group measure). Descriptive statistics are provided in Table 4. The multivariate contrast was significant for group, Wilk's $\Lambda = .46$, $F(2,21) = 12.44$, $p < .001$, partial $\eta^2 = .54$ and test, Wilk's $\Lambda = .26$, $F(2,21) = 29.62$, $p < .001$, partial $\eta^2 = .74$. There was non-significant interaction between group x test, Wilk's $\Lambda = 0.99$, $F(2,21) = 0.07$, $p = .93$, partial $\eta^2 = .01$ and no further analyses were done on the interaction. Follow-up univariate ANOVAs for the between subject factor (i.e. group) indicated that the effect of group was significant on D-prime score, $F(1,22) = 17.15$, $p < .001$, partial $\eta^2 = .44$ and HitRT, $F(1,22) = 14.73$, $p = .001$, partial $\eta^2 = .40$ across the two groups. Follow-up univariate ANOVAs for the within subject factor (i.e. test) indicated that the effect of test was significant on D-prime score, $F(1,22) = 57.84$, $p < .001$, partial $\eta^2 = .72$ and HitRT score, $F(1,22) = 13.33$, $p = .001$, partial $\eta^2 = .38$. The data is represented in Figures 2 and 3.

2. Behavioral performance on WM tasks

One aphasia participant failed to comprehend the 2-back instruction and could not complete the task; another aphasia participant could not identify any targets on the 2-back test (proportion of omissions =0) and had a negative D-prime score. Therefore n-back information from both participants was excluded from further analyses. A mixed effect MANOVA was conducted to assess group differences in dependent variables (D-prime and HitRT) on the two levels of the n-back task (1-back, 2-back). The multivariate contrast was significant for group, Wilk's $\Lambda = .69$, $F(2,19) = 4.19$, $p = .031$, partial $\eta^2 = .31$ and n-back task levels, Wilk's $\Lambda = .09$, $F(2,19) = 101.75$, $p < .001$, partial $\eta^2 = .92$.

There was non-significant interaction between group and task levels, Wilk's $\Lambda = .80$, $F(2,19) = 2.32$, $p = .126$, partial $\eta^2 = .20$ and no further analyses were conducted on the interaction effect.

Follow-up univariate ANOVAs for the between subject factor (i.e. group) indicated that the effect of group was significant on D-prime, $F(1,20) = 7.94$, $p = .011$, partial $\eta^2 = .28$ and non-significant for HitRT, $F(1,20) = .65$, $p = .43$, partial $\eta^2 = .03$. Follow-up univariate ANOVAs for the within subject factor (i.e. task levels) indicated that the effect of task levels was significant on D-prime, $F(1,20) = 211.56$, $p < .001$, partial $\eta^2 = .91$, and HitRT, $F(1,20) = 49.22$, $p < .001$, partial $\eta^2 = .71$. Descriptive statistics are presented in Table 5 and expressed in Figures 4 and 5.

Correlational Analyses

1. Relationship among behavioral inhibitory performances

In PWA, significant moderate positive correlation was observed between the CPT-X Hit RT and CPT-3 Hit RT (r=.62; p=.031) suggesting that when participants' took longer time to respond on the low demand inhibition task (CPT-X), they also took longer time to respond on the greater demand inhibition task (CPT-3). In healthy participants, significant strong correlation was observed between CPT-X D-prime and CPT-3 D-prime (r=.73; p=.007) suggesting that with increase in participant's sensitivity to CPT-X , sensitivity on the CPT-3 also increased. Table 6 presents the product moment correlation coefficients between each of the above variables.

2. Relationship among physiological inhibitory performances

In both participant groups, significantly strong positive correlations ($p < .05$) were observed between HR, time domain HRV (rMSSD), and frequency domain (HF-HRV) variables on both the tests (CPT-X and CPT-3), signifying that with increase in physiological change on one inhibitory test, there was also increase on the second inhibitory test. Table 7 presents the product moment correlation coefficients between each of the above variables.

3. Relationship between age, education, WAB-R AQ, and behavioral inhibitory performances

Pearson correlations were calculated between the descriptive variables (age, education, and AQ) and the inhibition behavioral variables (D-prime and Hit RT on CPT-X and CPT-3) in the aphasia and healthy groups. Significant correlations was observed only between education and CPT-3 D-prime (r= -.69; *p*=.013*)*, suggesting that participants with higher education demonstrated better sensitivity on the greater demand inhibition task (CPT-3). In the healthy group, participants demonstrated moderate correlations between age and D-prime on both the CPT-X (r= .64, p= .025) and CPT-3 (r= .63, p=.029). Table 8 presents the product moment correlation coefficients between each of the above variables.

4. Relationship between age, education, WAB-R AQ, and physiological inhibitory performances

Pearson correlations were calculated between the descriptive variables (age, education, and AQ) and the inhibition physiological variables (HR, rMSSD, and HF-

HRV on CPT-X and CPT-3) in the aphasia and healthy groups. In aphasia group, participants demonstrated strong negative correlations between WAB-R-AQ and HR on both the CPT-X (r= -.78, p= .003) and CPT-3 (r= -.72, p=.008) suggesting that with increase in aphasia severity, the HR decreased. Similarly, strong negative correlations were observed between age and HF-HRV on both the CPT-X (r= -.80, p=.002) and CPT-3 (r= -.78, p=.003) suggesting that with increase in age, HRV decreased in PWA. In healthy groups no significant correlations were observed. Table 9 presents the product moment correlation coefficients between each of the above variables.

5. Speed-Accuracy trade off in inhibitory performances

To determine if there was trade off in performance between speed and accuracy on both the inhibition tests, Pearson correlations were conducted between sensitivity (D-prime) and response time (Hit RT) scores in participants of both groups. To demonstrate speed-accuracy trade-off, sensitivity scores and Hit RT scores were plotted in a graphical representation. A linear positive trend was observed between the variables which suggested that participants with greater accuracy scores on the task took lesser time to respond to the trials. Similar findings were observed in overall performance in participant of both groups on CPT-X and CPT-3 tests. The findings are represented in Figures 6 and 7.

Specific Aim 1: Relationship between behavioral and physiological inhibitory performances

1. **Physiological performance on inhibition tasks**

To determine whether physiological activity is different on two different inhibition tasks, and whether it is different across both the participants groups, a mixed MANOVA was conducted. The analyses provide information about whether there are any differences between groups (aphasia and healthy) on the dependent variables (HR, rMSSD, HF-HRV) in two tests (CPT-X, CPT-3). Descriptive statistics are presented in Table 10. The multivariate contrast was significant for main effect of group, Wilk's Λ = .16, $F(3,20) = 35.13$, $p < .001$, partial $\eta^2 = .84$ and test, Wilk's $\Lambda = .13$, $F(3,20) = 44.72$, $p < .001$, partial $\eta^2 = .87$. The multivariate statistic was non-significant for interaction between group and test, Wilk's $\Lambda = .85$, $F(3,20) = 1.21$, $p = .333$, partial $\eta^2 = .15$ and no further analyses were done on the interaction.

Follow-up univariate ANOVAs revealed that the between subject factor (i.e. group) was significant on HR [$F(1,22) = 7.99$, $p = .010$, partial $\eta^2 = .277$], rMSSD [$F(1,22) = .61.74$, $p < .001$, partial $\eta^2 = .74$], and HF-HRV [$F(1,22) = 38.59$, $p < .001$, partial $\eta^2 = .64$] measures. Follow-up univariate ANOVAs for the within subject factor (i.e. test) is significant on HR [$F(1,22) = 36.28$, $p < .001$, partial $\eta^2 = .62$] with aphasia participants demonstrating greater HR than healthy participants. Also on the rMSSD [$F(1,22) = 44.04$, $p < .001$, partial $\eta^2 = .67$], and HF-HRV [$F(1,22) = 43.92$, $p < .001$, partial $\eta^2 = .67$] measures, aphasia participants demonstrated decreased HRV than healthy participants.

2. Behavioral and physiological performance relationship

To explore the hypothesis of contribution of physiological (HR, rMSSD, and HF-HRV and descriptive variables (age, education, and WAB-R AQ) on inhibitory performance in aphasia, correlation and regression analyses were performed.

Dependent variable used in the regression analyses: In the aphasia group significant correlations were observed between rMSSD measure and D-prime score on both CPT-X and CPT-3 tests (Table 11). Therefore, D-prime measure was considered as the dependent variable of interest.

Predictors used in the regression analyses: Descriptive variables (age and WAB-R AQ) were significantly correlated with the physiological variables (see table 9). But education was not correlated with any of the physiological variables. Therefore, to avoid any multicollinearity (variance inflation factors or VIF >3.0) between the predictors in the regression model, the descriptive variables (age and WAB-R AQ) were not used in the regression model to predict the D-prime.

Regression models: The first regression model included education, HR, rMSSD, and HF-HRV as the predictors on the behavioral D-prime scores. However the model was statistically non-significant. In a second regression model only the physiological variables, HR, rMSSD, and HF-HRV were used as predictors of variance in D-prime scores of CPT-X and CPT-3. It was observed that rMSSD significantly predicted D-prime and HitRT scores of the CPT-X and CPT-3 in the aphasia group. Both models were also statistically significant ($p < .05$) and predicted approximately 60% (R^2) of the variance in the outcome variable (D-prime; see Table 12).

3. Physiological activity across time points

A mixed effect MANOVA was conducted to assess the group differences in physiological measures (HR, rMSSD, HF-HRV) across the time points (baseline, CPT-X, CPT-3, recovery). The descriptive statistics are provided in Table 10. The multivariate contrast was significant for the interaction between group x time points, Wilk's $\Lambda = 0.22$, $F(9,14) = 5.57$, $p = .002$, partial $\eta^2 = .78$, which means that the effect of the time points on the dependent variables is not the same for aphasia and healthy participants. Follow-up univariate tests for individual dependent variables revealed nonsignificant interaction on HR [$F(3,66) = 1.89$, $p = .141$, partial $\eta^2 = .08$], but significant interaction effect was obtained for rMSSD [$F(2.034,44.739) = 3.839$, $p = .028$, partial $\eta^2 = .149$] and HF-HRV [$F(2.275,50.043) = 6.68$, $p = .002$, partial $\eta^2 = .23$] measures.

In the absence of significant interaction effect on HR, follow up main effects on group revealed that aphasia group had greater values in comparison to the healthy group [$F(1,22) = 6.31$, $p = .020$, partial $\eta^2 = .22$]. Also main effect of time points [$F(3,66) = 49.61$, $p < .001$, partial $\eta^2 = .69$] was observed. Pairwise comparisons of time points were significant ($p < .05$; Table 13 and Figure 8). Heart rate increased from baseline to tests and reduced during recovery phase.

Follow-up simple effect analyses of time points in aphasia group revealed that there was suppression of rMSSD from baseline to inhibition tests and recovery phase (all $p < .05$). In the healthy group, there was also suppression of rMSSD from baseline to inhibition tests ($p < .05$) but between baseline and recovery phases, no significant difference was observed ($p > .05$; see Table 14 and Figure 9).

Follow-up simple effect analyses on HF-HRV was significantly greater in the healthy group than the aphasia group across all time points (p <.01). In the aphasia group, there was decrease in HF-HRV during CPT-X and CPT-3 compared to baseline and recovery (all four comparisons $p < .05$; see Table 15 and Figure 10). In healthy group, HF-HRV decreased significantly from baseline to CPT-X and also CPT-3 ($p < .05$), but HF-HRV increased during the recovery phase and got nearer to the baseline values ($p > .05$).

Specific Aim 2: Relationship between working memory and behavioral/physiological inhibitory performances

1. **Relationship between behavioral inhibition and WM performance**

Multiple correlations were conducted to estimate the relationship between the CPT-X and CPT-3 variables with working memory 1-back and 2-back performance variables. Of the different significant correlation, two results are of importance: 1)In aphasia and healthy groups, HitRT score on 1-back was correlated with HitRT score on CPT-X ($p < .05$). In healthy group, HitRT score on 2-back was correlated with HitRT score on the CPT-X. The significant correlations coefficients were mostly moderate to strong correlations. Table 16 presents the product moment correlation coefficients between each of these variables.

2. **Relationship between physiological inhibition and WM performance**

Multiple correlations were conducted to estimate the relationship between inhibitory physiological performances with WM performance variables. From Aim1

objective 3, only rMSSD measure was significantly correlated with D-prime. Therefore, in this comparison, only rMSSD was correlated with the different n-back measures.

Results reveal that, in aphasia group, rMSSD also correlated significantly with 1-back D-prime measure ($p < .05$) on both CPT-X and CPT-3 tests. In healthy groups no significant correlations were observed. The strength of the correlation coefficients were moderate. Table 17 presents the product moment correlation coefficients between each of these variables.

CHAPTER 5

DISCUSSION

The purposes of the current study were twofold. The first specific aim was to examine if inhibition can be physiologically indexed by HRV in PWA and healthy control participants. The second specific aim of the study was to examine whether working memory is associated with inhibitory physiological/behavioral performance in aphasia and healthy participants. Prior to addressing the aims of the study, behavioral performance was compared between both the groups on two inhibition tasks of varying demands (CPT-X and CPT-3). Findings indicated that the aphasia group had less sensitivity (measured by D-prime) and took more time to respond to targets (measured by HitRT) than the healthy groups, and a similar trend was evident across both the inhibition tests. This signifies reduced inhibitory processing in PWA compared to healthy controls. Inhibitory processing enables adults to filter out irrelevant content and pay attention to information that is required to perform a task. However, in PWA inhibitory deficits allow irrelevant information to be encoded into memory (Hasher & Zacks, 1988), which in turn leads to competition between resources during the retrieval process, and hence causes impaired inhibition (May, Zacks, Hasher, & Multhaup, 1999; Ryan, Leung, Turk-Browne, & Hasher, 2007). Also, the behavioral performance on the CPT-3 was reduced in comparison to the CPT-X, thereby emphasizing that the CPT-3 imposed greater inhibitory demands than the CPT-X in both participant groups. A significant interaction effect was expected between the groups and inhibition tests. However, the lack of

significant interaction signifies that the magnitude of the effect (difference between CPT-X and CPT-3) is not different in the heathy group with respect to the aphasia group.

The standard deviation in performances within the aphasia group was also greater than the healthy group signifying that there was more variability in performance within the aphasia participants. This was further demonstrated by the number of participants that fell within +/- 1 SD of the mean. Less than 50% of the aphasia participants were within the +/-1 SD, signifying that there were a relatively large number (more than 50%) of participants that showed variability in behavioral performance with respect to the mean of the group.

On WM tasks, PWA demonstrated significantly lower sensitivity scores than the healthy controls. Although aphasia participants had increased reaction times, a significant difference was not observed between the groups. One possible explanation for this finding is that majority of the aphasia participants were of mild aphasia severity demonstrating lesser cognitive difficulties, and this manifested in an increased performance on the WM task too. Additionally, participants' use of hand could have possibly affected response times; all healthy participants used the non-dominant hand, but not all PWA could use their non-dominant hand due to hemiparesis and some resorted to using their dominant hand to depress the space bar. This discrepancy in use of non-dominant/dominant and non-preferred/preferred hand may have contributed to the non-significant differences between groups on the reaction times. With respect to the tasks, participants demonstrated higher sensitivity and lower reaction time scores on the 1-back versus the 2-back, suggesting that the 1-back level poses lesser cognitive demands than the 2-back level.

An important factor to consider in interpreting the behavioral measures is the trade-off between accuracy and speed on the inhibition tasks. The speed–accuracy tradeoff is described as the 'phenomenon where, at a given level of stimulus discriminability, decision makers may produce faster responses but make more errors' (Liu & Watanbe, 2012, p.107). This response accuracy trade-off was observed in both participant groups in inhibition and WM tests. Participants were instructed to respond as quickly as possible to the targets while maintaining maximum accuracy and making fewer errors. As such participant's behavior demonstrated a speed-accuracy trade-off, demonstrating their ability to make more errors and still maintain faster response times.

The first aim of the study hypothesized that cardiac vagal control (as indexed by HRV) would be greater for the low demand inhibition task (CPT-X) compared to the high demand inhibition task (CPT-3) in both aphasia and healthy participant groups. Additionally, it was hypothesized that HRV would be lower across test conditions compared to baseline and recovery conditions. To address aim 1, three different comparisons were conducted. The first comparison was done to compare the group differences in physiological behaviors on the two tests. Results indicated that the vagal activity was characterized by reduced HRV and greater HR reactivity to the CPT-3 test than the CPT-X test, suggesting that autonomic activity of the participants reduced significantly while completing the cognitive task with greater level of inhibition. Therefore with an increase in cognitive demands, parasympathetic activity decreases to produce low HRV (Thayer et al., 2009). Also the aphasia group participants demonstrated significantly greater HR and reduced HRV compared to the healthy group participants. The implications are that inhibition influences heart rate variability in both

groups of participants, and decreases with increase in inhibition demands. Both rMSSD and HF-HRV was higher on the CPT-X than the CPT-3 test, reflecting upon parasympathetic activity arousal during inhibitory processing (Grossman, 1983). Additionally, parasympathetic activity mediates the fluctuations in HR in the high (.15 - .40 Hz) frequency ranges of the spectrum.

Through a second comparison, a highly significant association was observed between the HRV time domain measure (rMSSD) and behavioral performance outcome (d') on both the tests in PWA. This findings links reduced HRV to cognitive (specifically, inhibitory) deficits in PWA. Multiple regression analyses were conducted to predict the behavioral performance from the physiological performances on each inhibition test. Both the models were statistically significant suggesting that it sufficiently predicts the outcome. The model identified rMSSD as a significant predictor of inhibitory performance. Time domain rMMSD measure made the strongest contribution to explaining the outcome (sensitivity measure of both tests). The two tests were administered to observe difference in performances over ihibition demands, signifying that with increase in task complexity, there is pattern of increased frontal activation (Badre et al., 2010; Badre & Wagner, 2007). Therefore, the different tasks demanded increase in phasic vagal cardiac control, and as such, the likelihood of seeing relationships between the HRV measures, and task performance was evident (Capuana, 2014).

With respect to the regression model, it was hypothesized that age, education and WAB-R AQ along with the physiological variables would also predict behavioral performance. But it was observed that there is significant correlation between the

descriptive variables (age, education, and aphasia quotient) to physiological variables (HR, rMSSD, and HF-HRV). In case of strongly correlated predictor variables, there is a reduction in amount of information available to assess the effects of a predictor, and the estimates become unstable and difficult to interpret. As such the inclusion of these variables (age, education, and WAB-R AQ) to the regression model to predict behavioral performances was not significant and therefore these were removed from the regression model.

An important component to note is that rMSSD is related to the parasympathetic activity, which also reflects upon the magnitude of inhibitory control imposed on the cardiac activity (Janszky et al., 2004). The rMSSD measure is an index of vagally mediated cardiac control that is associated with RSA, and is an appropriate measure to demonstrate parasympathetic activity. RSA signifies the changes in HR due to respiration, such that HR increases during inspiration and decreases during exhalation (Berntson et al. 2005). It is a time domain measure and correlates very well with frequency domain HF-HRV measure. The importance of this measure has been relatively understudied in the few number of HRV studies that are present in the aphasia literature (Chih, 2011; Christensen & Wright, 2014). Thus, the results of this study indicate that rMSSD is a primary component that is sensitive to change with cognitive behavior and should be utilized in studies to understand HRV reactivity in aphasia. Also, rMSSD is reliable for short duration measurements and is appropriate for studying HRV changes during cognitive tasks similar to this study. While Chih (2011) utilized both low (0.04-0.15Hz) and high frequency (.15-.40 Hz) HRV, Christensen and Wright (2014) utilized the mid frequency band (.07-.14 Hz) to understand the HRV changes in their studies.

Low frequency band is the least reliable of all frequency bands and is not appropriate for use in experimental purposes (Jorna, 1992). Although mid-frequency band is a good indicator of variations in HRV, our primary interest was to understand parasympathetic activity related to inhibition. Therefore high frequency band (.15-.40 Hz) was utilized in this study to understand the changes. Additionally, Christensen (2012) did not see any significant relationship between frequency domain HRV and behavioral performance in PWA; however in this study there was significant correlation between time domain measure (rMSSD) and behavioral performance in PWA. This further highlights the importance of utilizing time domain measures of HRV in PWA.

A third comparison analyzed the group differences in physiological activity from baseline to task conditions to recovery. Results revealed that HR significantly increased when participants were engaged in inhibition tasks as opposed to baseline and recovery conditions. The differences were significant between the baseline and test condition for all the physiological measures (HR, rMSSD, and HF-HRV), where HR increased from baseline to test condition and deceased during recovery. However, rMSSD and HF-HRV decreased from baseline to test condition and increased during recovery conditions, which was similar to what was predicted. It has been suggested that physiological measures, such as the rMSSD and HF-HRV are very sensitive to rest-task differences (Jorna, 1992) and this phenomenon was very evident in this study. In comparing the differences across both the groups, participants in the aphasia group had significantly lower HRV than the healthy group. Analysis of HRV data confirmed evidence for an overall reduction in cardiac vagal activity in PWA (Boneva et al., 2007; Burton, Rahman, Kadota, Lloyd, & Vollmer-Conna, 2010). With the onset of a cognitive task, the HRV

response to the stressor for PWA was significant from the baseline condition with a subsequent continuous, gradual decline in HRV throughout the session (from baseline to second task and increase during the recovery period). Also, PWA demonstrated prolonged HRV recovery after the cognitive tasks, as compared to the healthy group. This was also supported from the non-significant correlations between baseline and recovery HRV data in healthy group that suggested that healthy participants' HRV during the recovery phase increased and returned to the baseline condition in less time than was observed for aphasia participants. Although reduced vagal activity during cognitive challenges has been described in many studies in healthy individuals (Duschek, Muckenthaler, Werner, & del Paso, 2009), this is the first study indicating a differential vagal response in PWA compared with healthy control participants in response to varying cognitive challenges imposed on them. Hansen, Johnson, and Thayer (2003) examined the association between baseline HRV related to performance on various cognitive tasks in young healthy participant groups. Participants completed an n-back working memory task and a continuous performance battery. The results indicated that participants with higher baseline RSA made fewer errors on the working memory task, and they also had lower reaction times to correct responses and made fewer false positive responses on components of the continuous performance battery that required executive control. Findings indicated that there was no evidence of relationship between HRV and performance on non-executive components but on the executive function components of the tests. The study findings provide support for the link between autonomic regulation and cognition, and also highlight the importance of this 'relationship for performance on tasks that specifically tap executive functions' (Capuana, 2014). Similar to this case, the

current study has also utilized cognitive tasks that tap into the domain of executive function, by specifically measuring the inhibition component of executive function.

For the second aim of the study, it was hypothesized that participants with lower WM ability would demonstrate decreased performance on the behavioral and/or physiological inhibitory measures. The first comparison was conducted to examine the associations between behavioral performance on the inhibition tests (CPT-X, CPT-3) and behavioral performance on the working memory tasks (1-back, 2-back). Moderate positive correlations were observed between reaction time scores on the 1- and 2-back with the reaction time scores of the CPT-X and CPT-3. This denotes that performance of PWA participants on the inhibition tasks corresponded to their performance on the working memory tasks (i.e., increase in response times on the WM test was also associated moderately with increase in response times on the inhibition test). This suggests that due to impaired attentional allocation in PWA, WM as well as inhibitory functioning may be affected (Hula & McNeil, 2008; McNeil et al., 1991; Murray, 2012). Sensitivity scores on n-back and inhibition tests were not correlated.

A second comparison was conducted to understand the association between behavioral working memory and physiological inhibitory performance. Strong associations were observed between the 1- and 2-back sensitivity scores and the CPT-X and CPT-3 time domain rMSSD measure. The potential implication of the results is that WM ability is also associated with inhibitory physiological performance in aphasia. It suggests that WM as measured with an updating n-back task places a higher load on the inhibitory processing in PWA, thereby potentially restricting attention to task-relevant information (Hasher & Zacks, 1988; Hasher, Zacks, & May, 1999). Attentional

dysregulation, therefore, results in disinhibition of irrelevant information and hence, leads to impaired performance. This is consistent to what Hasher and Zacks (1988) suggest, that attention-control processes are central to explaining individual differences in WM (Wright & Fergadiotis, 2012).

In summary, loss of inhibitory control in PWA due to aberrant neural structures and deficits in attention allocation might result in a disruption of autonomic outflow that is characterized by reduced vagal tone (reflected as low HRV) and heightened stress reactivity. The results additionally reveal a novel insight regarding autonomic activation at rest and during cognitively challenging tasks in PWA and also provide important information that implicates reduced vagal activity and its association with inhibitory impairment in aphasia.

Limitations. A lack of significant interaction effect was observed between groups and tests on most behavioral measures than it was expected. This could be attributed to the makeup of the participants in the aphasia group that were mostly of mild aphasia severity. The likelihood of seeing significant differences within the groups is obscured by the homogeneity of the performances and less variability within the participants. Therefore, expanding the study to include participants with moderate and severe WAB-R AQ would be beneficial in determining performance across aphasia severities. Furthermore, there was relatively small number of participants in both the groups. Therefore increasing the group size will result in decreased standard error or less variation (and more precision) in the results, and increased power in detecting an effect.

Another limitation of the study is that there was very limited information about the lesion location in people with aphasia. Information about the lesion location would

possibly enhance our understanding regarding the event in which behavioral and physiological responses tend to decrease with respect to frontal lobe deactivation. For example: information regarding frontal versus dorsal lesion may lead to interpretation of the role of frontal cortex in mediating the differences in behavioral and physiological patterns across tests. From the results it was also observed that behavioral performances on the WM 1- back task only significantly correlated with behavioral performances on the inhibition tasks. No significant correlations were observed with respect to the higher demand WM 2-back task. Correlations between 1-back, CPT-X, and CPT-3 probably suggest that these tests might be similar with respect to the underlying cognitive constructs (possibly, inhibition). Therefore, utilizing WM assessments with other taxed underlying cognitive constructs could possibly yield varied results.

In spite of the limitations enumerated above, the results of this study do signify the importance of HRV as predictive indicator of cognitive ability in PWA, and also as a biomarker of overall health and fitness in individuals with and without aphasia.

CHAPTER 6

CONCLUSION

Several researchers in the area of aphasia have suggested a link between cognitive symptoms and linguistic deficits in individuals with aphasia (Erickson et al., 1996; McNeil et al., 1991; Murray et al., 1997a, 1997b). Most cognitive deficits in PWA are in the areas of attention, executive function, working memory, speed of processing, and visuospatial skills (Caspari et al., 1998; Erickson et al., 1996; Murray, 2004; Tseng et al., 1993; Wright & Shisler, 2005). The basis of most of these higher –level cognitive functions is inhibition. Inhibitory control might account for and influence attention allocation in PWA, and impaired attention control is considered a primary cognitive deficit in aphasia. Often, assessment of cognitive functions in PWA is hindered by the fact that cognitive tasks require some degree of linguistic processing to perform effectively and efficiently on them (Friedmann & Gvion, 2003; Murray et al., 1997a, 1997b; Sung et al., 2009). Given that aphasia is also associated with impaired language capacities, it is particularly difficult to assess PWA on these cognitive tasks that require linguistic processing. Therefore, it is important to expand our research to alternative procedures that could effectively assess cognitive behavior in PWA. However, there is relatively little data available concerning the physiological underpinnings of cognitive behavior in PWA and specifically how physiological behavior could determine cognitive control in aphasia.

This study takes an innovative approach towards understanding inhibitory deficits in aphasia. The overall goal of this study is to identify an alternative determinant of inhibitory behavior in aphasia, specifically, heart rate variability (HRV). Changes in HRV may reflect an increase or decrease in cardiac autonomic control through the sympathetic and parasympathetic nervous activity on the sinoatrial node of the heart as a reaction to confounding factors such as stress and anxiety (Gillie, Vasey, & Thayer, 2014). The neurovisceral integration model (Thayer & Lane, 2000) posits that cardiac vagal tone, indexed by HRV, 'can indicate the functional integrity of the [cortical and sub-cortical] neural networks implicated in emotion–cognition interactions' (Park & Thayer, 2014; p. 1). The model of neurovisceral integration signifies that autonomic, attentional, and emotional systems share some dependent underlying cortical and subcortical structures in the service of a goal-directed behavior that also support self-regulation and successful adaptation (Anderson, 2004). The capacity of an individual to perform effectively with changing environmental demands would also indicate that the individual also has good higher-order cognitive control (Gillie et al., 2014; Thayer et al., 2012; Thayer & Lane, 2007, 2009). Although research studies demonstrating this model have been undertaken in different clinical and non-clinical populations, it has yet to be addressed in aphasia. To our knowledge, this is the first study to demonstrate the neurovisceral effect in the context of an inhibitory processing. The findings of the study demonstrate that HRV is a sensitive indicator of central autonomic control, thereby also reflecting inhibitory control. The current study supports these findings and suggests a role of neurovisceral integration in cognitive processing of inhibitory behavior.

To summarize the main findings of the study- a) There is significant reduction in inhibitory and working memory performance in PWA compared with healthy participants, b) PWA demonstrate increased HR and decreased HRV reactivity to high demand task than low demand cognitive task, c) PWA demonstrate suppression of HRV during cognitive tasks in comparison to rest conditions, d) PWA demonstrate prolonged HRV recovery after cognitive challenge compared to healthy controls, e) in PWA significant reduction in cognitive performance is associated with their physiological activity, and f) WM may be related to both behavioral and physiological inhibitory performance in PWA. The overall results reveal that there is association between reduced cardiac activity and cognitive impairment in PWA, due to diminished parasympathetic (vagal) activation. This also adds to the argument for the ability of HRV to differentiate between different cognitive demands tasks, and therefore is a suitable index of cognitive behavior in PWA. Additionally, both time domain and frequency domain components are sensitive measures of HRV reactivity in PWA, and may be utilized in future studies. Further, future studies may utilize HRV as a dependent variable to understand how cortical functions might influence and predict HRV in PWA. Future research may also employ tasks that employ both executive and nonexecutive components. Also, inclusion of more participants and with diverse participants with damage to frontal, parietal, or temporal lobes would further provide information on the importance of localization of deficits and its impact on neurovisceral integration in aphasia. Since HRV is related to behavioral performance in PWA, an important future implication is to determine if it is possible to manipulate HRV in order to produce changes in cognitive performance in PWA (Thayer et al., 2009).

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Table 1

Demographic information of participants in the participant groups (aphasia and heathy)

Aphasia	Age	Gender	Years of Education	Months post onset	WAB-R AQ	WAB-R Profile	Paresis/Paralysis of upper limb	Use of hand for task
1	66	M	17	9	76.3	Mild	no	right
2	67	M	14	62	75.8	Moderate	right	left
3	84	M	25	48	76.3	Mild	no	left
4	74	M	11	140	15.5	Severe	right	left
5	75	M	15	52	86.6	Mild	right	left
6	66	M	14	139	77.6	Mild	no	left
7	48	F	16	151	55.2	Moderate	right	left
8	64	M	12	45	17.2	Severe	right	left
9	74	M	25	48	89.6	Mild	no	left
10	76	M	12	90	78.8	Mild	left	right
11	51	M	10	37	89.6	Mild	right	left
12	53	F	10	29	86.1	Mild	left	right
M (SD)	66.5 (11.09)	M=10 F=2	15.08 (5.14)	70.83 (47.75)				
Control (*n*=12)	68.42 (10.05)	F=9 M=3	18.08 (3.63)	N/A	N/A	N/A	No paresis of limbs	Use of non-dominant hand

N/A- not applicable; WAB-R- Western Aphasia Battery- Revised

Table 2

Independent t-tests comparing test order effects on behavioral inhibitory performance in in the participant groups (aphasia and heathy)

Test		Order	Mean	SD	*t*	*df*	*p*
Aphasia (*n*=12)							
CPT-X	D-prime	1	4.24	0.76	-.98	10	.353
		2	4.62	0.54			
	Hit RT	1	585.83	84.88	.57	10	.579
		2	547.48	139.92			
CPT-3	D-prime	1	1.86	0.72	-1.43	10	.183
		2	2.52	0.86			
	Hit RT	1	504.69	71.5	.63	10	.543
		2	479.89	64.55			
Healthy (*n*=12)							
CPT-X	D-prime	1	5.3	0.36	.61	10	.554
		2	5.18	0.35			
	Hit RT	1	442	53.57	-.76	10	.464
		2	462.61	39.08			
CPT-3	D-prime	1	3.47	0.92	.54	10	.603
		2	3.24	0.54			
	Hit RT	1	415.03	49.79	.44	10	.669
		2	400.65	62.52			

Order- indicates test presentation orders; Order 1- first CPT-X, second CPT-3; Order 2- first CPT-3, second CPT-X

Table 3

Independent t-tests comparing test order effects on physiological inhibitory performance in both participant groups

Test		Order	Mean	SD	*t*	*df*	*P*
Aphasia (*n*=12)							
CPT-X	HR	1	341.47	207.45	-.33	10	.746
		2	383.84	232.03			
	rMMSD	1	70.82	9.28	-.90	10	.388
		2	74.85	5.82			
	HF-HRV	1	48.13	19.05	.64	10	.538
		2	42.27	11.93			
CPT-3	HR	1	228.15	173.05	-.25	10	.811
		2	252.67	172.26			
	rMSSD	1	78.07	4.11	.88	10	.402
		2	75.48	5.97			
	HF-HRV	1	33.62	15.53	.11	10	.915
		2	32.71	13.346			
Healthy (*n*=12)							
CPT-X	HR	1	902.92	209.16	-.96	10	.358
		2	1036.56	268.17			
	rMMSD	1	70.35	3.7	.13	10	.900
		2	70.13	1.93			
	HF-HRV	1	95.25	13.48	.09	10	.931
		2	94.15	27.39			
CPT-3	HR	1	709.02	237.72	-.63	10	.543
		2	794.8	234.27			
	rMSSD	1	71.91	3.93	.05	10	.961
		2	71.83	1.68			
	HF-HRV	1	86.47	14.073	.24	10	.242
		2	84.33	16.43			

Order- indicates test presentation orders; Order 1- first CPT-X , second CPT-3; Order 2- first CPT-3, second CPT-X

Table 4

Descriptive statistics of behavioral performance on two inhibition tests (CPT-X, CPT-3) in the participant groups (aphasia, healthy)

Aphasia (*n*=12)				
	CPT-X		CPT-3	
	D-prime	Hit RT	D-prime	Hit RT
n	12	12	12	12
Mean	4.43	566.66	2.19	492.29
Minimum	3.42	360.33	0.88	361.14
Maximum	5.26	718.47	3.87	607.19
Range	1.85	358.14	2.99	246.05
Median	4.56	563.70	2.40	495.48
Mode	3.42	360.33	.88	361.14
SD	0.66	112.14	0.83	66.22
SE	0.19	32.37	0.24	19.12
Skewness	-0.28	-0.23	0.3	-0.51
Kurtosis	-1.45	-0.81	0.28	0.65
Healthy (*n*=12)				
n	12	12	12	12
Mean	5.24	452.30	3.35	407.84
Minimum	4.59	371.50	1.85	343.62
Maximum	5.67	540.82	4.51	516.38
Range	1.08	169.32	2.67	172.76
Median	0.00	447.65	3.46	386.96
Mode	5.49	371.50	1.85	343.62
SD	0.34	45.98	0.73	54.41
SE	0.10	1.23	0.21	15.71
Skewness	-1.05	0.26	-0.69	1.26
Kurtosis	0.13	0.41	0.73	0.70

SD- Standard Deviation; SE- Standard Error of mean

Table 5

Descriptive statistics of behavioral performance on two working memory tasks (1-back, 2-back) in the participant groups (aphasia, healthy)

	1-back		2-back	
Aphasia (*n*=12)				
	D-prime	Hit RT	D-prime	Hit RT
n	12	12	12	12
Mean	3.08	587.50	0.88	684.47
Minimum	0.06	369.10	0.19	424.00
Maximum	4.38	860.00	1.97	862.58
Range	4.32	490.90	1.78	438.58
Median	3.15	544.47	1.01	688.88
Mode	4.38	369.10	0.19	424.00
SD	1.32	147.97	0.54	144.89
SE	0.40	42.71	0.17	45.82
Skewness	-1.24	0.78	0.58	-0.46
Kurtosis	1.56	-0.18	0.28	-0.70
Healthy (*n*=12)				
n	12	12	12	12
Mean	3.83	517.59	1.98	640.00
Minimum	2.27	413.17	1.06	511.24
Maximum	4.38	684.95	3.32	778.46
Range	2.12	271.78	2.26	267.23
Median	4.11	485.96	2.01	597.67
Mode	4.38	413.17	1.06	511.24
SD	0.73	78.16	0.70	107.79
SE	0.21	22.56	0.20	31.12
Skewness	-1.30	0.98	0.41	0.23
Kurtosis	0.51	0.49	-0.68	-2.02

SD- Standard Deviation; SE- Standard Error of mean

Table 6

Correlations among behavioral inhibitory performance in the participant groups (aphasia, healthy)

		Aphasia (*n*=12)		
		CPT-X D-prime	CPT X Hit RT	CPT-3 D-prime
CPT-X HitRT	*r*	.364		
	p	.244		
CPT-3 D-prime	*r*	.560	.308	
	p	.058[a]	.330	
CPT-3 HitRT	*r*	.405	.622	.184
	p	.192	.031*	.567
		Healthy (*n*=12)		
CPT-X HitRT	*r*	-.051		
	p	.874		
CPT-3 D-prime	*r*	.732	.009	
	p	.007**	.977	
CPT-3 HitRT	*r*	.108	.101	-.182
	p	.739	.755	.572

** Correlation is significant at $p < .01$; * $p<.05$; 2-tailed
[a] Correlation is nearly significant at 0.05 level (2-tailed)
r - correlation coefficient

Table 7

Correlations among physiological inhibitory performance in the participant groups (aphasia, healthy)

Aphasia (*n*=12)						
		CPT-X HR	CPT-X rMSSD	CPT-X HF-HRV	CPT-3 HR	CPT-3 rMSSD
CPT-X rMSSD	*r*	.30				
	p	.349				
CPT-X HF-HRV	*r*	.33	.13			
	p	.292	.69			
CPT-3 HR	*r*	.91**	.25	.25		
	p	.000	.44	.44		
CPT-3 rMSSD	*r*	.24	.90**	-.14	.2	
	p	.453	.000	.66	.533	
CPT-3 HF-HRV	*r*	.31	.31	.97**	.27	.04
	p	.327	.34	.00	.405	.91
Healthy (*n*=12)						
CPT-X rMSSD	*r*	.13				
	p	.685				
CPT-X HF-HRV	*r*	-.21	.07			
	p	.519	.837			
CPT-3 HR	*r*	.96**	.24	-.10		
	p	.000	.445	.747		
CPT-3 rMSSD	*r*	.07	.93**	-.01	.16	
	p	.837	.000	.967	.609	
CPT-3 HF-HRV	*r*	-.13	.21	.94**	-.06	.12
	p	.677	.508	.000	.86	.717

** Correlation is significant at $p < .01$; 2-tailed; *r* - correlation coefficient

Table 8

Correlations among descriptive variables and behavioral inhibitory performance in the participant groups (aphasia, healthy)

		Aphasia (*n*=12)			
		CPT-X		CPT-3	
		D-prime	Hit RT	D-prime	Hit RT
age	*r*	.20	-.02	-.03	.08
	p	.525	.957	.923	.794
education	*r*	-.47	-.46	-.69*	-.20
	p	.119	.133	.013	.531
WAB-R AQ	*r*	-.19	-.25	-.47	-.52
	p	.546	.439	.122	.084
		Healthy (*n*=12)			
age	*r*	.64*	.45	.63*	.38
	p	.025	.138	.029	.218
education	*r*	-.01	-.25	.32	.33
	p	.991	.439	.312	.295

* Correlation is significant at $p < .05$; 2-tailed; *r* - correlation coefficient
WAB-R AQ- Western Aphasia Battery- Revised Aphasia Quotient

Table 9

Correlations among descriptive variables and physiological inhibitory performances in the participant groups (aphasia, healthy)

		Aphasia (*n*=12)					
		CPT-X			CPT-3		
		HR	rMSSD	HF-HRV	HR	rMSSD	HF-HRV
age	*r*	-.07	.10	-.80**	-.19	.29	-.78**
	p	.829	.762	.002	.559	.353	.003
education	*r*	-.07	-.45	-.18	-.34	-.35	-.31
	p	.819	.147	.575	.274	.258	.322
WAB-R AQ	*r*	-.78**	-.30	-.09	-.72**	-.34	-.06
	p	.003	.338	.784	.008	.274	.848
		Healthy (*n*=12)					
age	*r*	.31	-.14	-.01	.18	-.06	.10
	p	.321	.674	.983	.569	.854	.755
education	*r*	-.30	-.40	-.07	-.45	-.34	-.10
	p	.342	.203	.825	.142	.277	.760

** Correlation is significant at $p < .01$; 2-tailed; *r* - correlation coefficient
WAB-R AQ- Western Aphasia Battery-Revised Aphasia Quotient

Table 10

Mean and Standard deviation scores of physiological inhibitory performance across different time points in the participant groups (aphasia, healthy)

Time points		HR	rMSSD	HF-HRV
Aphasia (*n*=12)				
Baseline	Mean	71.04	56.83	362.66
	SD	5.47	11.68	211
CPT-X	Mean	74.5	45.2	240.41
	SD	4.87	15.46	165.12
CPT-3	Mean	76.78	33.17	175.85
	SD	5.07	13.81	137.34
Recovery	Mean	73.38	48.16	281.3
	SD	5.34	16.72	194.66
Healthy (*n*=12)				
Baseline	Mean	67.9	120.3	969.74
	SD	3.52	31.66	239.68
CPT-X	Mean	70.24	94.7	751.91
	SD	2.81	20.59	229.44
CPT-3	Mean	71.87	85.4	640.85
	SD	2.88	14.63	231.78
Recovery	Mean	68.61	108.34	896.13
	SD	3.83	23.39	258.18

HR- heart rate; rMSSD- root mean square of successive differences (time domain HRV); HF-HRV- high frequency heart rate variability (frequency domain HRV); SD- standard deviation

Table 11

Correlations between behavioral inhibitory and physiological inhibitory performance in the participant groups (aphasia, healthy)

		Aphasia (*n*=12)			
		CPT-X		CPT-3	
		D-prime	Hit RT	D-prime	Hit RT
HR	*r*	-.17	.25	.42	.50
	p	.604	.437	.171	.101
rMSSD	*r*	.73**	.47	.79**	.26
	p	.007	.127	.002	.418
HFHRV	*r*	-.20	.01	.184	.20
	p	.532	.973	.568	.529
		Healthy (*n*=12)			
HR	*r*	.05	.12	.42	.03
	p	.890	.711	.172	.928
rMSSD	*r*	.06	-.17	-.02	.01
	p	.858	.606	.944	.986
HFHRV	*r*	-.24	.02	-.24	-.05
	p	.453	.943	.455	.869

**Correlation is significant at $p < .01$(2-tailed); *r*- correlation coefficient

HR- heart rate; rMSSD- root mean square of successive differences (time domain); HF-HRV- high frequency heart rate variability (frequency domain)

Log transformed values of behavioral dependent variables (D-prime, Hit RT) were used in the correlation analyses.

Table 12

Multiple regression analyses for predicting behavioral performance on two inhibition tests (CPT-X, CPT-3) from physiological variables

	CPT-X D-prime			**CPT-3 D-prime**		
	B	SE_B	*β*	*B*	SE_B	*β*
Aphasia (*n*=12)						
Model	$F(3,8) = 6.98$, $p = .013$*, adj. $R^2 = .62$			$F(3,8) = .69$, $p < .582$, adj. $R^2 = -.09$		
Intercept	0.76	0.39		-0.76	0.82	0.38
HR	-0.01	0.01	-0.39	0.01	0.01	0.40
rMSSD	.007*	0.00	0.86	0.00	0.00	-0.07
HF-HRV	0.00	0.00	-0.19	0.00	0.00	-0.15
Healthy (*n*=12)						
Model	$F(3,8) = 6.26$, $p = .017$*, adj. $R^2 = .59$			$F(3,8) = .19$, $p = .903$, adj. $R^2 = -.29$		
Intercept	-0.18	0.36		0.28	1.30	
HR	0.01	0.01	0.25	.001*	0.02	0.02
rMSSD	.006*	0.00	0.73	0.00	0.00	0.08
HF-HRV	0.00	0.00	0.09	0.00	0.00	-0.25

*$p < .05$ (2-tailed); *B*= unstandardized regression coefficient; $SE_{B=}$ Standard error of the coefficient; *β*=standardized coefficient; Adj. R^2 = coefficient of determination; measure of the proportion of variance in the dependent variable that is explained by the predictor variables

Table 13

Pairwise comparisons between time points on heart rate measure in all participants

Pairs	Mean difference	Standard Error difference	95% Confidence Interval for Difference		*p*
			Lower	Upper	
HR					
Baseline-CPTX	-2.90*	.44	-4.18	-1.63	.000*
Baseline-CPT3	-4.85*	.48	-6.26	-3.45	.000*
Baseline-Recovery	-1.53*	.45	-2.83	-.22	.016*

*$p < .05$ (2-tailed); HR- heart rate
All participants were grouped together due to lack of interaction effect between groups and time points

Table 14

Pairwise comparisons between time points on rMSSD (time domain HRV measure) in the participant groups (aphasia, healthy)

Pairs	Mean difference	Standard Error	95% Confidence Interval for Difference		*p*
			Lower	Upper	
Aphasia					
rMSSD					
Baseline-CPTX	11.62	2.673	3.05	20.20	.007*
Baseline-CPT3	23.67	1.791	17.92	29.41	.000*
Baseline-Recovery	8.67	2.261	1.41	15.92	.017*
Healthy					
rMSSD					
Baseline-CPTX	25.60	4.79	10.23	40.98	.001*
Baseline-CPT3	34.90	6.03	15.56	54.24	.001*
Baseline-Recovery	11.96	4.14	-1.31	25.23	.088

*$p < .05$; rMSSD- root mean square of successive differences

Table 15

Pairwise comparisons between time points on HF-HRV (frequency domain HRV measure) in the participant groups (aphasia, healthy)

Pairs	Mean difference	Standard Error	95% Confidence Interval for Difference		*p*
			Lower	Upper	
Aphasia					
HF-HRV					
Baseline-CPTX	122.25	24.24	44.49	200	.002*
Baseline-CPT3	186.81	31.94	84.33	289.28	.001*
Baseline-Recovery	81.35	20.97	14.07	148.64	.015*
Healthy					
HF-HRV					
Baseline-CPTX	217.83	20.70	151.42	284.24	.000*
Baseline-CPT3	328.89	33.90	220.13	437.65	.000*
Baseline-Recovery	73.60	39.14	-51.96	199.17	.521

*$p < .05$ (2-tailed); HF-HRV – High frequency heart rate variability

Table 16

Correlation between behavioral inhibitory and working memory performance in the participant groups (aphasia, healthy)

			Aphasia			
			CPT-X		CPT-3	
			D-prime	HitRT	D-prime	HitRT
1-back	D-prime	*r*	-.53	-.56	-.61*	-.64*
		p	.094	.074	.048	.035
		n	11	11	11	11
	HitRT	*r*	.19	.65*	.40	.61*
		p	.561	.023	.196	.035
		n	12	12	12	12
2-back	D-prime	*r*	-.11	-.63	-.16	-.37
		p	.771	.051	.663	.298
		n	10	10	10	10
	HitRT	*r*	-.40	.37	-.15	.46
		p	.256	.293	.686	.181
		n	10	10	10	10
			Healthy			
1-back	D-prime	*r*	-.38	-.25	-.36	-.12
		p	.224	.432	.245	.722
		n	12	12	12	12
	HitRT	*r*	-.23	.76*	-.08	.36
		p	.468	.004	.795	.255
		n	12	12	12	12
2-back	D-prime	*r*	-.26	-.71*	.03	-.43
		p	.412	.009	.929	.164
		n	12	12	12	12
	HitRT	*r*	.17	.66*	.01	.49
		p	.589	.019	.964	.104
		n	12	12	12	12

*Correlation is significant at $p < .05$ (2-tailed); Log transformed values of CPT- X and CPT-3 behavioral dependent variables (D-prime, Hit RT) were used in the correlation analyses; '*n*' (sample size) is reported in the table because some of the participant performances were outliers and were removed from the analyses.

Table 17

Correlation between physiological inhibitory and working memory performance in the participant groups (aphasia, healthy)

			CPT-X rMSSD	CPT-3 rMSSD
Aphasia				
1-back	D-prime	*r*	-.64*	-.61*
		p	.035	.048
		n	11	11
	HitRT	*r*	.26	.15
		p	.407	.646
		n	12	12
2-back	D-prime	*r*	-.15	.12
		p	.675	.740
		n	10	10
	HitRT	*r*	-.28	-.49
		p	.436	.150
		n	10	10
Healthy				
1-back	D-prime	*r*	.04	-.10
		p	.914	.763
		n	12	12
	HitRT	*r*	.06	.16
		p	.857	.615
		n	12	12
2-back	D-prime	*r*	-.33	-.32
		p	.291	.306
		n	12	12
	HitRT	*r*	-.08	-.02
		p	.813	.946
		n	12	12

* Correlation is significant at $p < .05$ (2-tailed)
'*n*' (sample size) is reported in the table because some of the participant performances were outliers and were removed from the analyses.

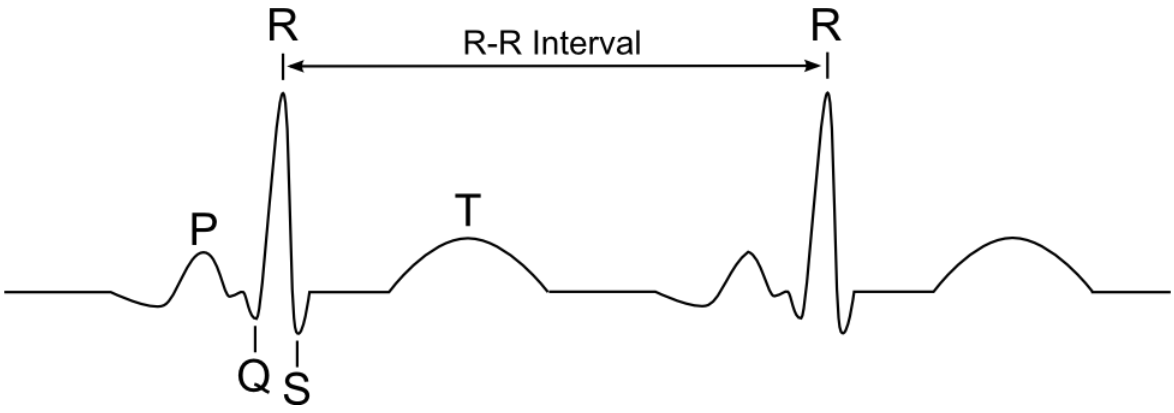


Figure 1. ECG wave showing the R-R interval. HRV is calculated by measuring the difference in the distance between two R waves

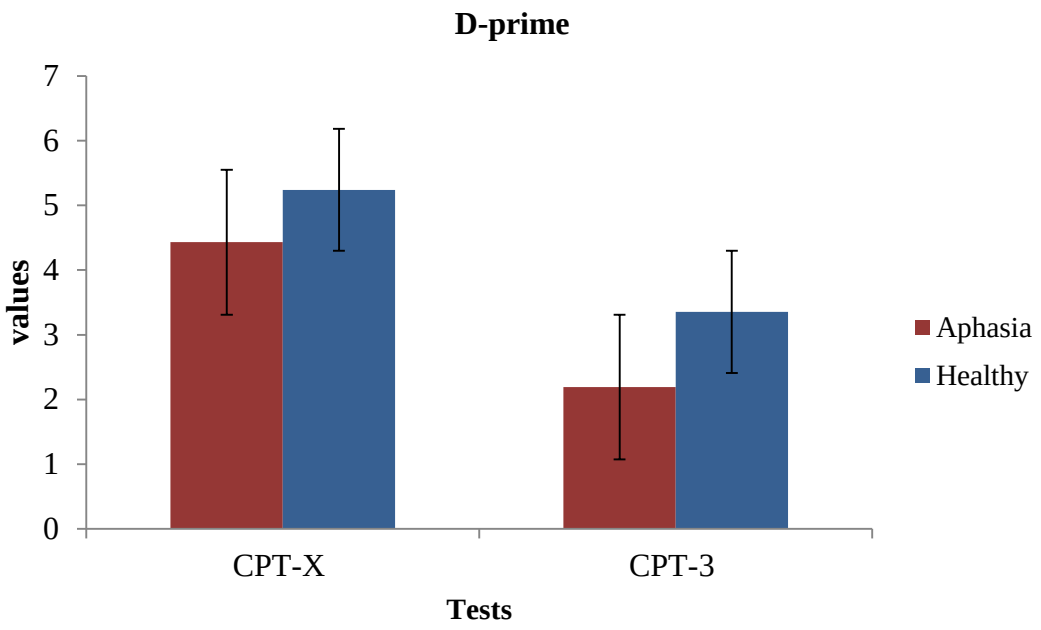


Figure 2. D-prime scores on the CPT-X and CPT-3 tests in aphasia and healthy control participants. Error bars represent standard error of the mean.

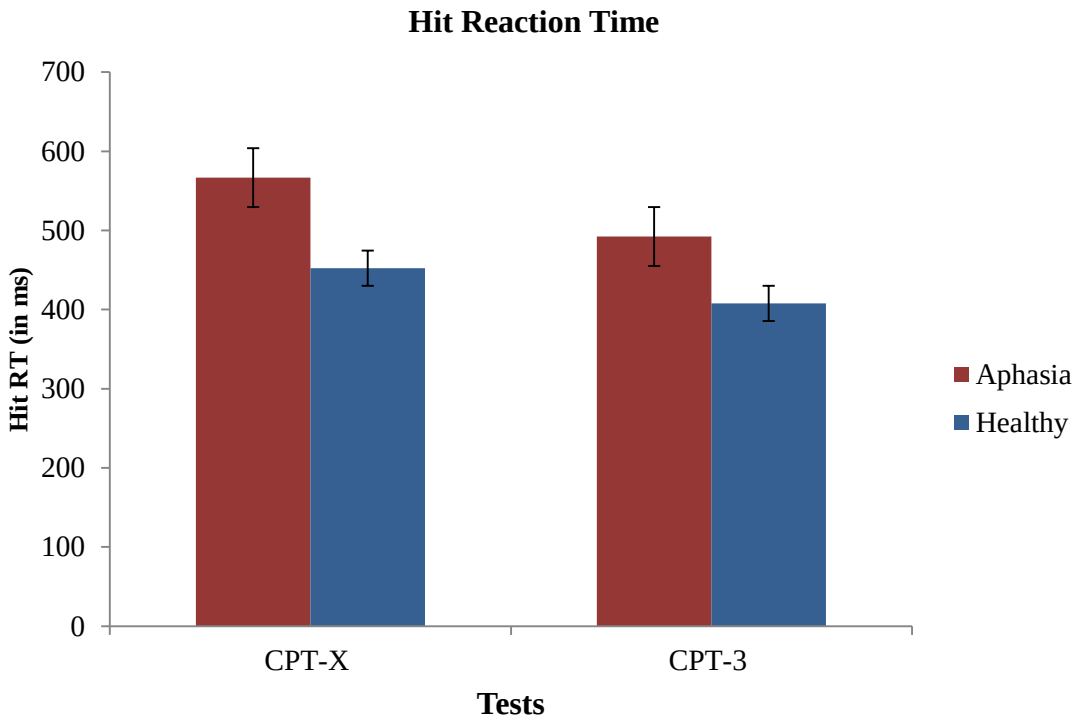


Figure 3. HitRT scores on the CPT-X and CPT-3 tests in aphasia and healthy control participants. Error bars represent standard error of the mean.

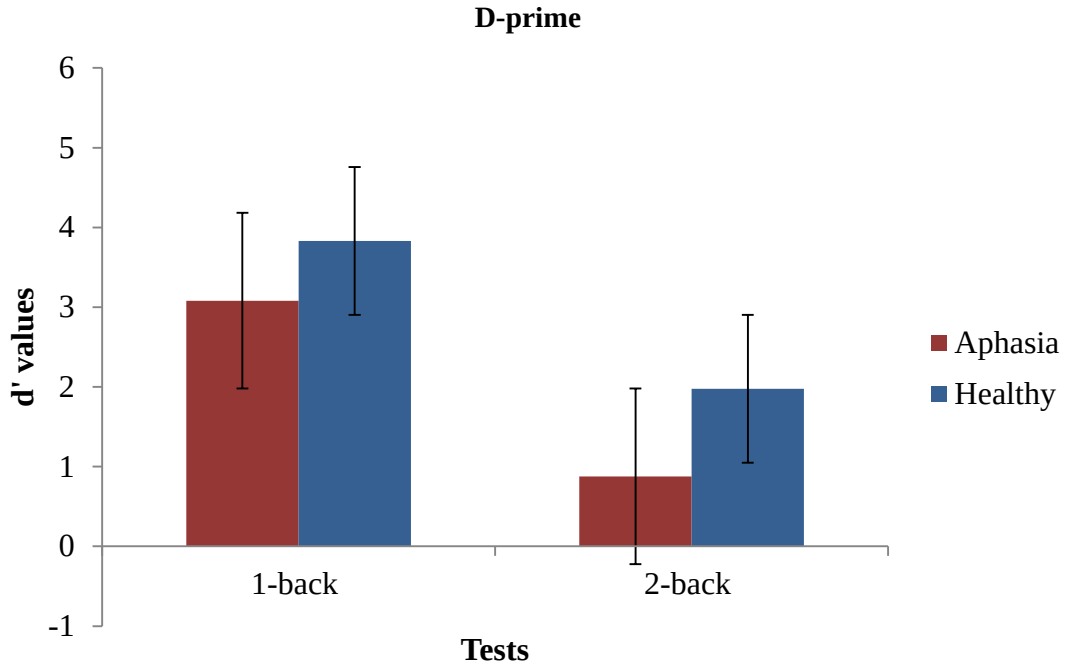


Figure 4. D-prime scores on the 1-back and 2-back tasks in aphasia and healthy control participants. Error bars represent standard error of the mean.

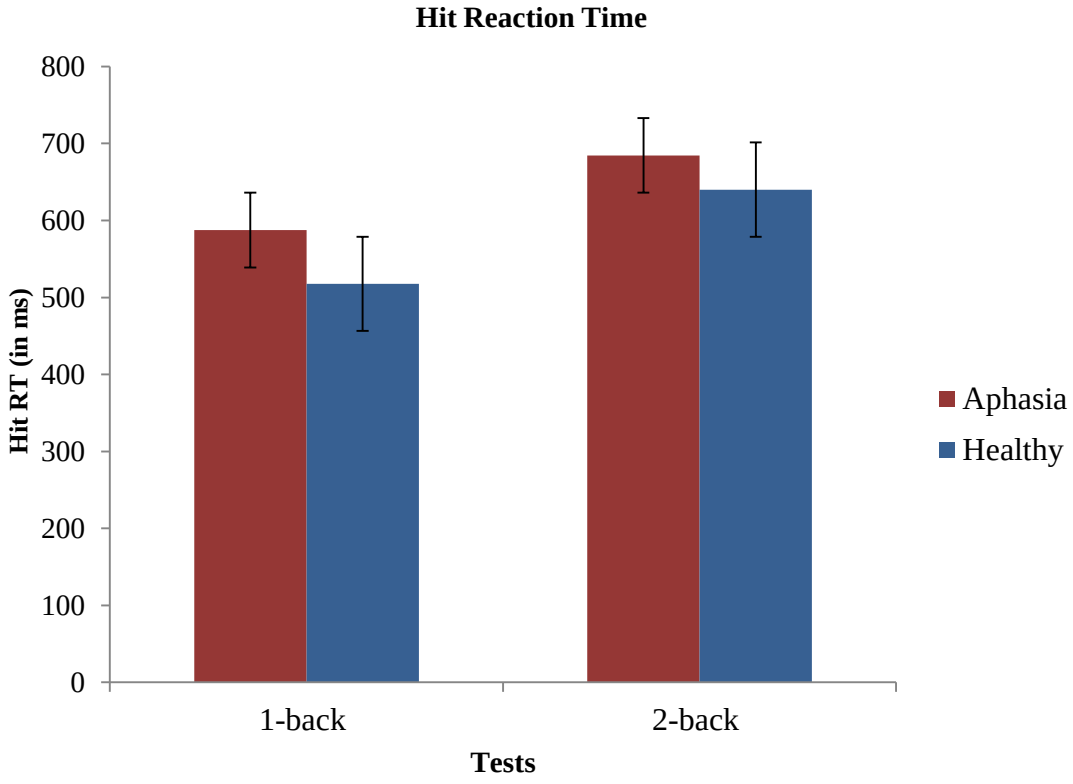


Figure 5. HitRT scores on the 1-back and 2-back tasks in aphasia and healthy control participants. Error bars represent standard error of the mean.

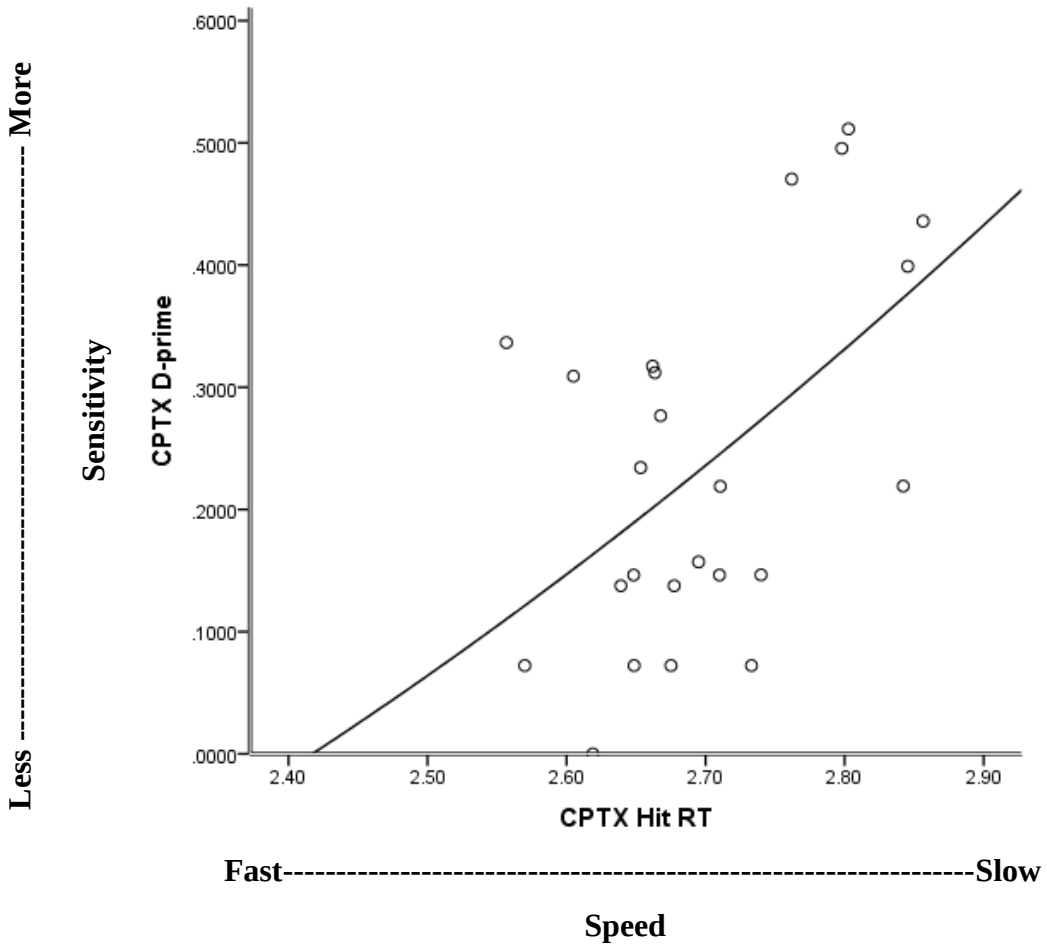


Figure 6. Speed-accuracy trade-off functions in CPT-X in participants from both groups. Log transformed values of behavioral dependent variables (D-prime, Hit RT) are presented in the graph.

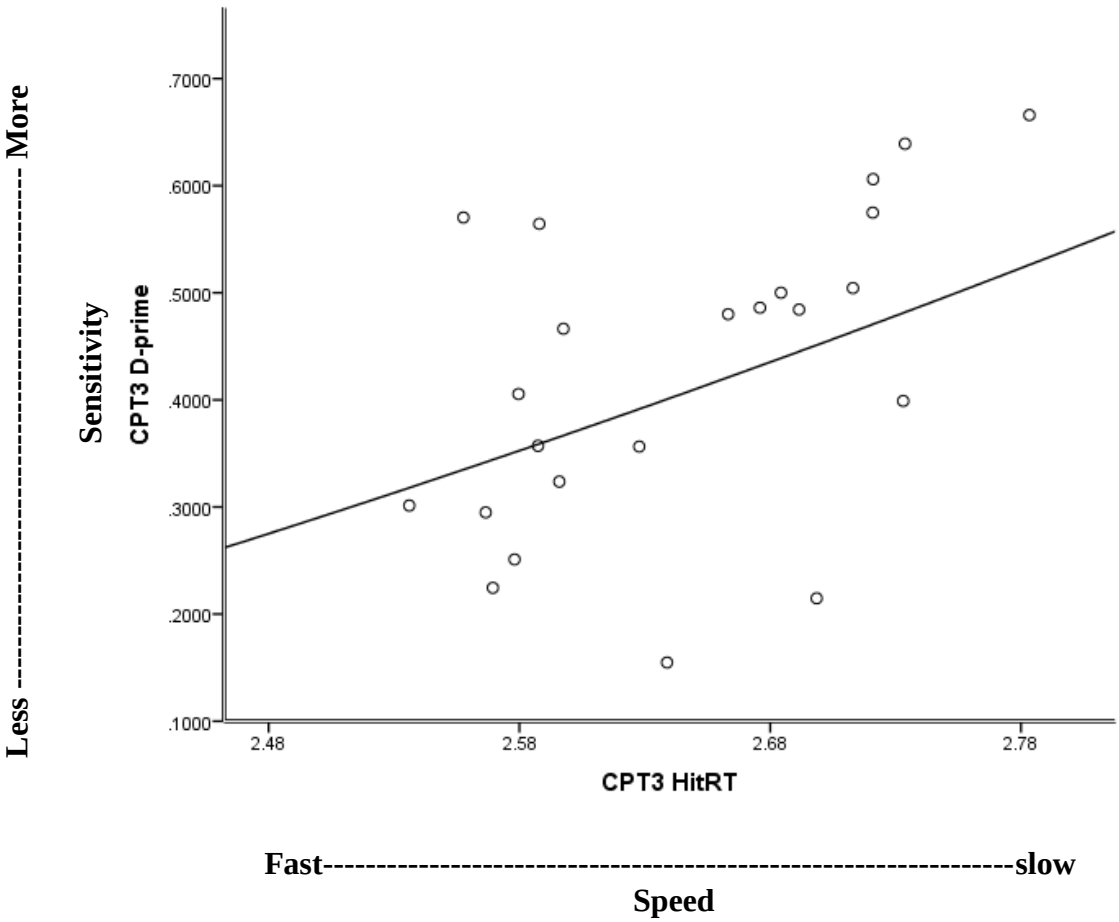


Figure 7. Speed-accuracy trade-off functions in CPT-3 in participants from both groups. Log transformed values of behavioral dependent variables (D-prime, Hit RT) are presented in the graph.

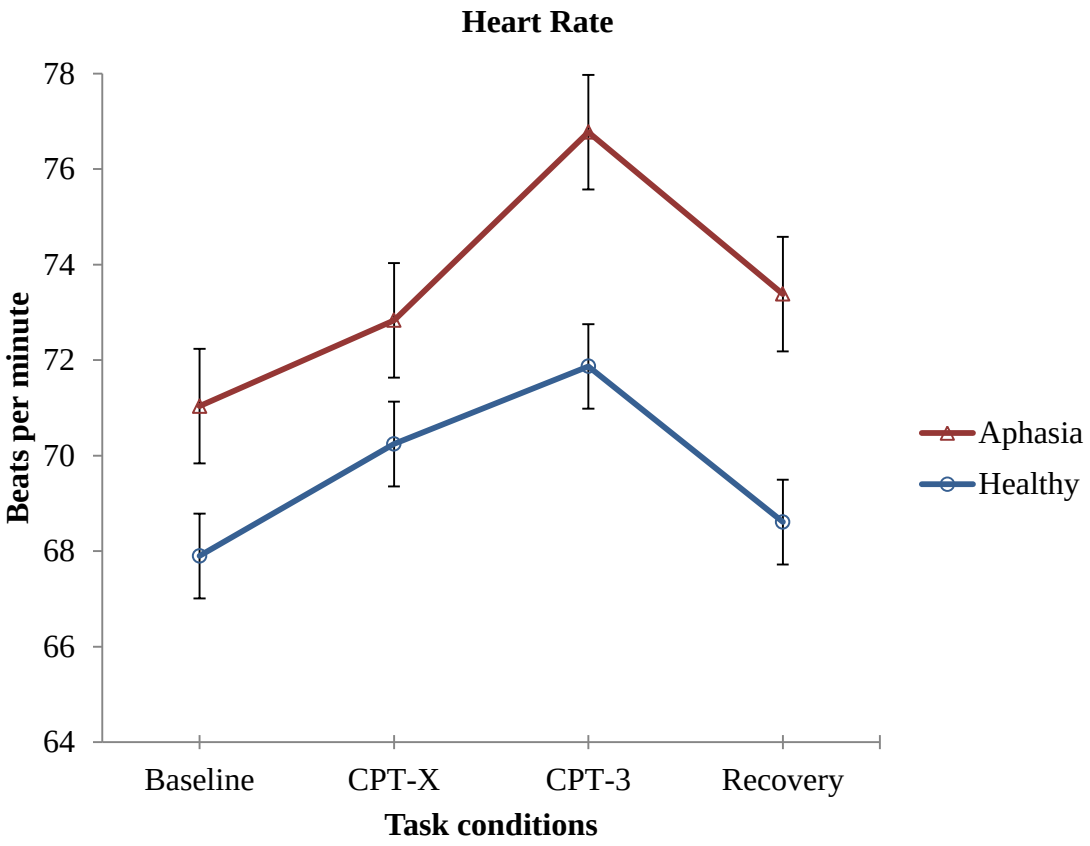


Figure 8. Average changes in HR during baseline, CPT-X, CPT-3, and recovery in aphasia and healthy control participants. Error bars represent standard error of the mean. (HR= Heart Rate in beats per minute; CPT-X is the low demand task, CPT-3 is the high demand task)

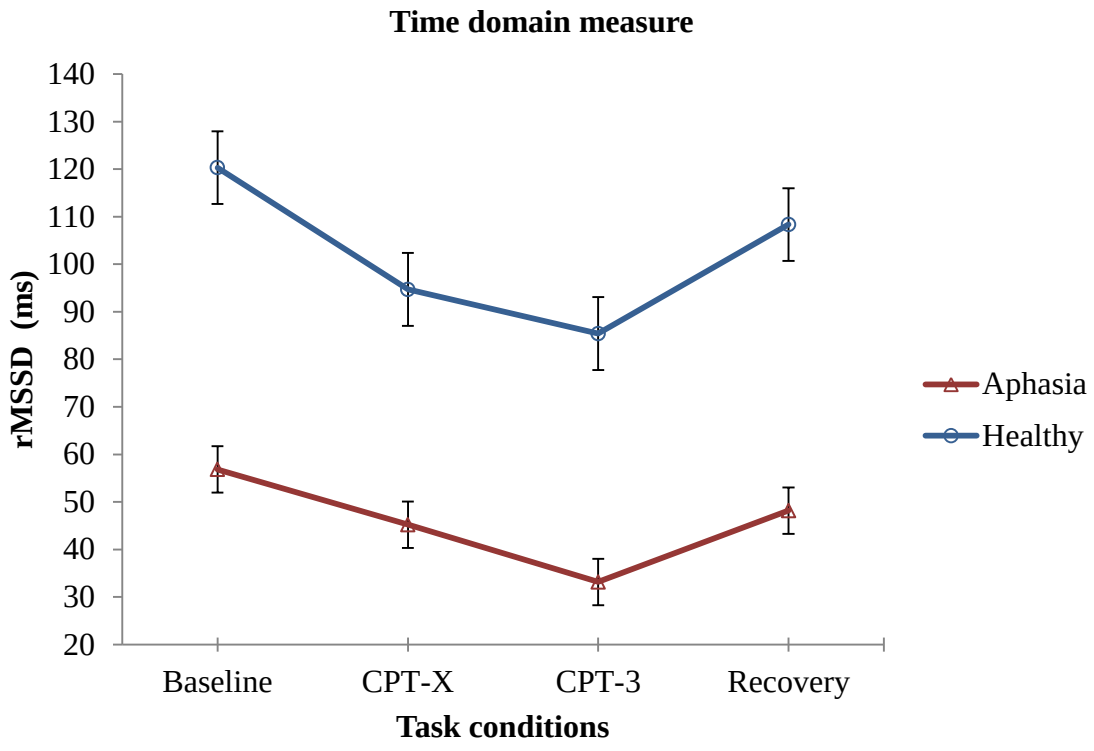


Figure 9. Average changes in rMSSD during baseline, CPT-X, CPT-3, and recovery in aphasia and healthy control participants. Error bars represent standard error of the mean. (rMSSD= root mean square of successive differences; it is a time domain measure of HRV; HRV= Heart rate variability)

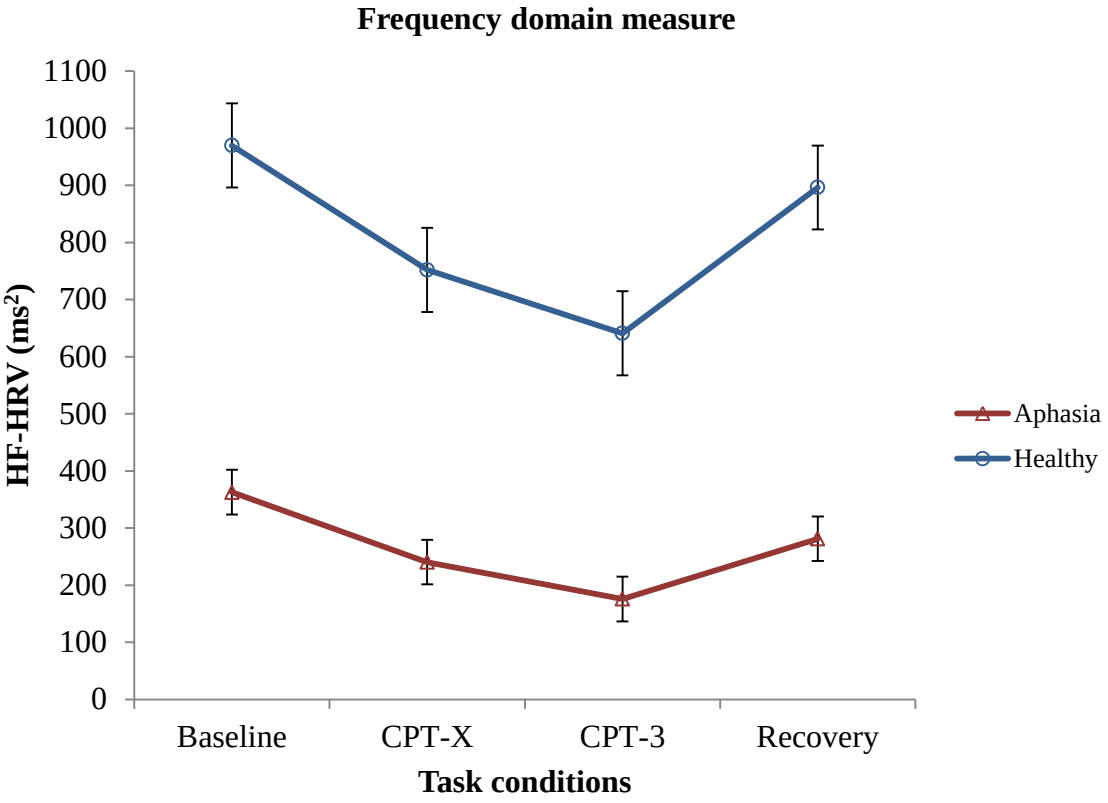


Figure 10. Average changes in HF-HRV during baseline, CPT-X, CPT-3, and recovery in aphasia and healthy control participants. Error bars represent standard error of the mean. (HF-HRV= High frequency heart rate variability; it is a frequency domain measure of HRV; range from .15-.40Hz)

APPENDIX A

APHASIA PARTICIPANTS' BEHAVIORAL PERFORMANCE ON INHIBITION TESTS

	CPT-X		CPT-3	
Participants	**D-prime**	**HitRT**	**D-prime**	**HitRT**
1	4.50	360.33	1.80	361.14
2	4.78	465.20	2.45	474.13
3	5.23	495.41	2.49	460.46
4	3.71	578.02	0.88	607.19
5	3.94	718.47	2.46	491.46
6	5.01	695.29	2.35	483.38
7	5.26	549.38	3.01	540.77
8	4.16	700.47	1.48	526.04
9	4.62	460.82	3.87	499.49
10	3.42	634.96	1.76	525.87
11	5.01	513.49	2.59	395.85
12	3.54	628.02	1.16	541.70

APPENDIX B

APHASIA PARTICIPANTS' BEHAVIORAL PERFORMANCE ON WORKING MEMORY TASKS

	1-back		2-back	
Participants	**D-prime**	**HitRT**	**D-prime**	**HitRT**
1	4.38	369.10	1.97	424.00
2	4.38	489.20	0.94	800.00
3	2.95	508.43	1.10	650.75
4	0.06	860.00	--	--
5	3.15	502.17	1.18	524.20
6	2.39	822.50	0.29	862.58
7	4.07	560.00	1.16	849.38
8	0.11	742.50	--	--
9	4.12	484.65	1.08	624.36
10	1.76	622.53	0.43	782.00
11	3.80	553.79	0.19	727.00
12	2.81	535.15	0.44	600.40

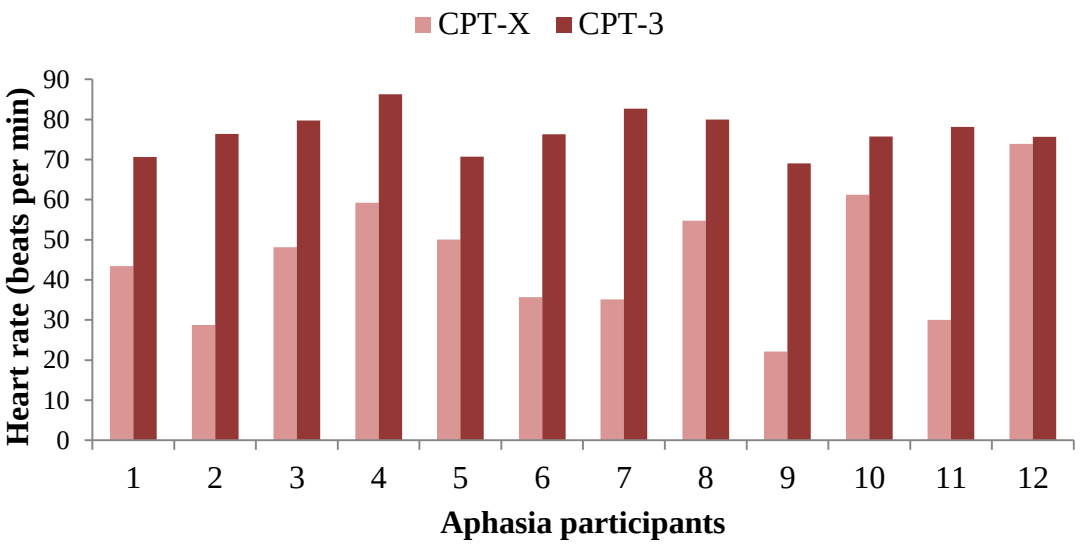
APPENDIX C

APHASIA PARTICIPANTS' PHYSIOLOGICAL PERFORMANCE ON INHIBITION TESTS

Descriptive Statistics

	CPT-X			CPT-3		
	HR	rMSSD	HF-HRV	HR	rMSSD	HF-HRV
Mean	72.84	45.20	240.41	76.78	33.17	175.85
SE of Mean	2.22	4.46	47.67	1.46	3.99	39.65
Median	71.95	45.81	228.15	76.33	38.92	157.93
Mode	53.96	22.10	257.98	69.04	11.10	45.98
Std. Deviation	7.68	15.46	165.12	5.07	13.81	137.34
Skewness	-1.14	0.28	1.08	0.18	-0.34	1.49
Kurtosis	2.53	-0.67	0.61	-0.25	-1.68	1.49
Range	28.57	51.80	509.99	17.23	38.60	432.91
Minimum	53.96	22.10	57.99	69.04	11.10	45.98
Maximum	82.53	73.90	567.98	86.27	49.70	478.89

Example of physiological data (heart rate) from individual aphasia participants



APPENDIX D

EXAMPLE OF INSTRUCTIONS

Inhibition tests

CPT-X

You will see some letters that will flash very quickly on the computer screen, one at a time. You have to press the space bar each time you see the letter X. Do not press the space bar for any other letter. If you make a mistake don' t worry about it and just keep going. Respond as fast and as accurately as you can. Now place your finger on the space bar.

CPT-3

You will see some letters that will flash very quickly on the computer screen, one at a time. You have to press the space bar each time you see a letter, except when it's the letter X. Do not press the space bar for the letter X. if you make a mistake don' t worry about it and just keep going. Respond as fast and as accurately as you can. Now place your finger on the space bar.

Working Memory tasks

1-back

I am going to show you some different fruits and vegetables. Here are some examples. (*Point to each shape and name*). You are going to look for the same fruit or vegetable in a row. So every time the item you see is the same as the one before, press the space bar. For example, if you see this shape first, and then you see this shape, that is a match. (*Use*

example pictures). *(Press the SPACE bar when you see an item that matches the one before it.)* Respond as fast and as accurately as you can.

2-back

I want you to watch for every other shape to match. So, whenever the shape you see is the same as the fruit/vegetable you saw two before, press the space bar. *(Indicate an example of a 2-back with stimuli).* I will also show you an example using these cards. Remember, I want you to look for all of the times when the shape that you see is the same as the shape you saw 2 before. Respond as fast and as accurately as you can.