AWARENESS OF MEMORY AND BRAIN FUNCTION ON A CONTINUUM OF INSIGHT: ASSESSING THE PRESENCE OF A DYSNOSOGNOSIA

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A Thesis Presented to the Faculty of the Graduate School at Middle Tennessee State University in Partial Fulfillment of the Requirements for the Degree of Master of Arts in Clinical Psychology

Middle Tennessee State University

May 2014

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ACKNOWLEDGEMENTS

I would like to especially thank my major professor and advisor, Dr. Paul S. Foster, for his guidance and training throughout my time in this program. His counsel and support have made a lasting impression and have been invaluable in my experiences and direction for the future. I would like to thank the other two members of my thesis committee, Dr. Chris Tate and Dr. Kim Ujcich Ward, for their time and effort on this project. Additionally I would like to thank the other members of the Clinical Psychology program faculty, Dr. Mary Ellen Fromuth and Dr. David Kelly for their excellent teaching and guidance throughout my time in this program. Lastly I wish to thank my classmates and colleagues whose support and collaboration were essential to both my success and my survival throughout our graduate school experience.

ABSTRACT

The purpose of this study was to determine whether healthy individuals displayed deficits in their ability to estimate their memory function as it relates to the concept of human self-awareness. An extensive literature review indicated that patients diagnosed with Alzheimer's disease (AD) have a tendency to overestimate their memory abilities in similar paradigms. Additionally, neuroimaging and neuropsychological studies have found significant involvement of the right frontal lobe in memory prediction/performance paradigms. As such it was hypothesized that the healthy participants who were inaccurate in their memory estimations would show relative deficits on tests of right frontal lobe function. Results did not support the initial hypothesis. Subsequent analyses were conducted to determine whether those participants who overestimated their memory would perform differently compared to those who were accurate and those who underestimated. Results did indeed show that those participants who overestimated their performance evidenced a relative deficit on a test of right frontal lobe function. Additionally it was found that those participants who underestimated performed better on a test of right frontal lobe function than those who were accurate.

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CHAPTER I

Introduction

Anosognosia

Anosognosia is one of a conglomerate of syndromes belonging to the family of agnosias (general lack of knowledge) known as asomatagnosias (the loss of knowledge of a person's sense of bodily condition) and refers specifically to a lack of awareness of deficit or a denial of illness (Kolb & Whishaw, 2008). The syndrome can be both a temporary and permanent condition. The severity of the condition may differ in degree, with the milder forms being transient and resolving with the patient being made aware of the deficit, and the severe forms being more persistent and including symptoms of extreme denial in the form of delusions (Sandifer, 1946). Confabulations can often accompany delusional denial (Sandifer, 1946). Anosognosia is a deficit in the ability to "recognize being ill and to assign a correct meaning to deficits, symptoms, and their functional implications" (Orfei, Robinson, Bria, Caltagirone, & Spalletta, 2008, p. 203). Terminology in the research regarding insight, awareness, and the clinical phenomena that affect these constructs has been defined in varying ways depending upon both the construct being studied and the opinions of the researchers. For the purposes of the current investigation, *insight* and *awareness* will remain synonymous and used interchangeably. The clinical manifestation of deficits of insight and awareness is *anosognosia*.

The French neurologist Joseph Babinski (1914) and colleagues (Langer, 2009) described two cases of patients who displayed an astonishing lack of awareness of their

deficits despite having a left side hemiplegia following right hemisphere lesions due to stroke. These patients both were unaware of their hemiplegia, and persisted in their lack of awareness despite efforts made to convince them otherwise. Following Babinski's initial discovery report (Babinski, 1914) in which he coined the term *anosognosie* or *anosognosia*, the term was applied to patient denial of any deficit or disease (Gerstmann, 1942). Subsequent reporting, upon discovery that the syndrome accompanied many different types of deficits caused by brain insult, has applied the term to describe unawareness of nearly any type of neuropsychological or neurological dysfunction (Adair & Barrett, 2012; Fisher, 1989). The syndrome has been described in so many clinical cases Fisher (1989) posited that anosognosia may be considered to be a "principle of cerebral dysfunction in humans" (p. 127). Some authors have noted in reviews of the literature that anosognosia has been associated with hemispatial neglect, hemianesthesia, hemianopia and cortical blindness (Anton-Babinski Syndrome), amnesias, prosopagnosia, the dementias (Dementia of the Alzheimer's Type (DAT) or Alzheimer's Disease (AD) and Frontotemporal Dementia in particular), aphasias, cortical deafness, apraxia, dysfunction in activities of daily living (ADL), traumatic brain injury, and the disorganized thought associated with schizophrenia (Adair & Barrett, 2012; Kashiwa et al., 2005; McGlynn & Schacter, 1989). Others have noted the presence of anosognosia in psychiatric disorders and behavioral problems (Migliorelli et al., 1995), hemiballismus, alexia, other agnosias (Fisher, 1989), cerebrovascular infarction (Anderson & Tranel, 1989), and general loss of memory and mild cognitive impairment (MCI; Vogel et al., 2004). Additionally, the syndrome has been described as rather domain specific within

differing conditions (hemiplegia, AD, etc.) afflicting the individual patient (e.g. anosognosia for memory impairment vs. anosognosia for behavioral problems in AD).

Regarding the dementias, anosognosia has been extensively studied and most frequently described in patients with Alzheimer's disease (AD), constituting the majority of awareness research done in the dementias (Ecklund-Johnson & Torres, 2005). Feher, Mahurin, Inbody, Crook, and Pirozzolo (1991) noted that anosognosia may be more common in AD than in the other dementias. Much of the dementia research has been devoted to studying the syndrome in its relation to the standard memory impairment occurring as part of the symptom presentation of the disease, with prevalence rates reported from 20% (Migliorelli et al., 1995; Starkstein, Sabe, Chemerinski, Jason, & Leiguarda, 1996) to 80% (Sevush & Leve, 1993). Anosognosia also has been found to correlate with other features of dementia such as behavior problems, emotional problems, activities of daily living, and self-care (Migliorelli et al., 1995; Vasterling, Seltzer, Foss, & Vanderbrook, 1995). Indeed, research suggests that within AD, anosognosia is a domain specific syndrome and is not a global construct, differing according to deficit (Vasterling et al., 1995). For example, a patient may have anosognosia for memory impairment but not for behavioral problems. A deficit in awareness of memory impairment is the most frequently observed domain-specific anosognosia in Alzheimer's disease (Mimura, 2008). Although research has been devoted to many domains of awareness in AD, it is memory impairment that has yielded the most data and provided the most information concerning anosognosia and awareness of cognitive state. Memory itself is a historically heavily researched area, and the ability of both healthy and clinical

populations to judge their own memory abilities has been a useful tool for elucidating the larger construct of self-awareness and its relationship to insight and deficits thereof (i.e. anosognosia).

Discussions of the concept of insight have involved a variety of issues with regard to nomenclature and concept and, for the purpose of clarity, this must be addressed. As stated earlier, for the purpose of this study, *insight* and *awareness* shall remain synonymous. As such, the term *unawareness* should be synonymous with anosognosia in regards to cognitive functioning in the dementias (Anderson & Tranel, 1989). Larger theoretical issues dealing with the ideas of *self-awareness* and *theory of mind* are concerned with the ways in which individuals are able to infer their own mental state and the mental states of others, respectively. Within the broader construct of self-awareness lies the construct of insight. David (1990) defines insight as a patient's ability to understand that an illness is present and the subsequent ability to assign meaning to symptomology that would otherwise be considered nonpathological. Though he wrote specifically to address psychotic disorders, his definition is in line with previous and subsequent attempts to define clearly the construct as it applies to all different types of neuropsychiatric syndromes. Given the inherent, complex, and varied ways in which individuals may differ both neurologically and psychologically, it must be conceived that insight will vary just as other attributes among differing individuals. Thus, insight should fall along a continuum ranging from full awareness to a complete lack of awareness of deficit (i.e. anosognosia).

Clinical Populations

Anosognosia has increasingly been shown to accompany the syndrome of mild cognitive impairment. Mild cognitive impairment (MCI) may be defined as the transitional period between cognitive decline due to normal aging and the onset of probable Alzheimer's disease (Peterson et al., 2001). Additionally anosognosia accompanying MCI has been found to be a predictor of a transition from MCI to later AD (Tabert et al., 2002**)**. However, diagnostic criteria for MCI are at issue and different studies have shown varied results due to the inclusion of participants based upon subjective memory complaints. Indeed, subjective memory complaints are considered a requirement for the diagnosis of MCI (Peterson et al., 2001).

Research findings have been variable regarding deficits of awareness in MCI. Ries et al. (2002) examined MCI patients and found participants to possess varying levels of insight into their cognitive deficits and described this insight along a continuum of awareness ranging in degree from "mildly limited" to "severely impaired" (Ries et al., 2007). Tabert et al. (2002), in their study of varying functional deficits in MCI, concluded that within the MCI populations a certain proportion exhibit a deficit of awareness in their assessment of functional abilities and that this deficit in awareness may be a predictor of the future onset of Alzheimer's disease.

Vogel et al. (2004) excluded the criterion of subjective memory complaint in participant selection and found that not only do MCI patients possess deficits in awareness to the extent seen in anosognosia, but that they did not differ significantly from that of the mild Alzheimer's disease (mAD) patients examined. Another study

found similar results in that anosognosia was a feature of MCI when subjective memory complaints were not included as a necessary criterion for diagnosis (Galeone, Pappalardo, Chieffi, Iavarone, & Carlomagno, 2011). These findings suggest that not only is anosognosia present in MCI populations but, due to the potential that it is a predictor of transition to a dementing disorder, it is important that subjective cognitive or functional complaints not be a requirement of assessment or diagnosis of mild cognitive impairment.

Some research suggests that patients with mild Alzheimer's disease (mAD) have significantly greater deficits of awareness than those with MCI. Specifically, those patients with MCI did have insight deficits but that it was not to an extent that met the full clinical picture of anosognosia, as with the mAD patients (Orfei et al., 2010). This finding could lend further support to the idea of the continuum of insight. However, the authors note that they used the traditional method for diagnosing MCI in including subjective memory complaints. Again, this is a potential confound because it substitutes an ex-ante condition for what would otherwise be an ex-post result. In other words, by including subjective memory complaints as a diagnostic criterion, the probability of finding deficits of awareness has been virtually eliminated as a variable. The effect would be to essentially nullify any comparison between AD and MCI in regards to levels of insight into various aspects of deteriorating cognitive function. Unfortunately, this potential confound is difficult to control as the diagnostic criteria for MCI remain an issue. Yet another study, using similar clinical diagnostic criteria, found that participants

with mAD presented with anosognosia as a symptom but those participants with MCI did not (Kalbe et al., 2005).

Individuals with MCI should theoretically fall on the continuum of awareness. In fact, research does suggest that onset of deficits of awareness in patients with MCI is an indicator of a likely progression to AD and subsequently a greater deficit of awareness comparable to anosognosia. Among the neurodegenerative diseases, the presence of anosognosia has been greatest in Alzheimer's disease. The methodologies used to assess insight in AD have been as variable as the prevalence. However, and in sharp contrast to the variable findings seen in MCI, different methodologies have yielded similar results that anosognosia is a major feature of Alzheimer's disease.

The research on anosognosia in Alzheimer's disease suggests that AD patients overestimate their ability in memory performance paradigms (Ansell & Bucks, 2006; Antoine, Nandrino, & Billiet, 2013; Clare, Whitaker, & Nelis, 2010; Correa, Graves, & Costa, 1996; Cosentino, Metcalfe, Butterfield, & Stern, 2007; Duke, Seltzer, Seltzer, & Vasterling, 2002; McGlynn & Kaszniak, 1991; Ries et al., 2012; Stewart, McGeown, Shanks, & Venneri, 2010). Additional research has found that patients deny or underestimate the severity of their deficits (Duke et al., 2002; McGlynn & Kaszniak, 1991; Ott et al., 1996; Sevush & Leve, 1993) or possess a general deficit of awareness of impairment in regards to cognitive functioning (Anderson & Tranel, 1989; Ansell & Bucks, 2006; Barrett, Eslinger, Ballentine, & Heilman, 2005; Correa et al., 1996; Kotler-Cope & Camp, 1995; Wagner, Spangenberg, Bachman, & O'Connell, 1997). These findings clearly show that deficits of awareness are a prominent feature of AD.

Moreover, the presence of anosognosia in both MCI and AD suggests that severity of illness is not necessarily correlated with severity of awareness deficit. The presence of anosognosia in both AD and MCI lends further credence to the idea of the syndrome existing on a continuum, such that anosognosia exists as a product of its neuropathology independent of the overarching disease state that causes such pathology. In this sense, deficits of awareness would increase or decrease according to the degree of neuropathological changes in brain regions associated with self-awareness. These changes would inherently be caused by the neuropathological characteristics of AD or MCI, but the clinical manifestation would remain independent of the disease. Otherwise stated, deficits of awareness such as anosognosia may be a feature of AD or MCI or may be caused by AD or MCI rather than being a characteristic symptom of either disease itself. Although the syndrome may be domain-specific, this does not negate the possibility that it is inherently a clinical manifestation of damage to a larger self-awareness system. Considering the syndrome independently, it possible to view it as the extreme clinical presentation of a deficit in self-awareness rather than simply a deficit of explicit knowledge about one's own memory functioning or any other domain-specific lack of awareness. It is thus possible to view anosognosia as part of the larger continuum of awareness in order to determine precisely where, and the reasons why, both clinical and healthy populations fall somewhere on the spectrum. This continuum would be irrespective of group differences between those who would be considered "healthy" and those considered "diseased", due to its inherent existence as a normal brain function.

Nonclinical Populations

As mentioned previously, research devoted to memory awareness in healthy populations provides information as to the varying degrees of awareness seen in normal individuals. This information may allow us to understand more clearly how insight differs in degree on the continuum. A significant amount of research has been devoted to the concepts of *metamemory* (i.e., awareness of memory functioning) or *metacognition* (Lovelace & Marsh, 1985). Metacognition has been defined as the knowledge an individual possesses regarding their own cognitive abilities and other aspects of function (Souchay & Isingrini, 2004). Many research investigations have been conducted to examine the abilities of normal individuals to judge their own memory capabilities and then to assess the true nature of the discrepancy between their beliefs about their memory ability and their actual memory ability as measured by objective memory assessments. Individual belief about memory ability is a construct known as *memory self-efficacy* (Pearman & Trujillo, 2013). The research, to date, has been variable concerning the relative ability of individuals to judge their own prospective memory performance or memory ability. Specifically, much of the literature has been devoted to examining the differences in predictive ability between different age groups and, in particular, between younger and older adult populations. Additionally, the methodologies used have contributed to this variability in results.

Murphy, Sanders, Gabriesheski, and Schmitt (1981) found that younger adults generally underestimated their memory ability while older adults generally overestimated their ability. Other research findings suggest that younger adults are more accurate in

their ability to judge their memory functions, whereas older adults have been found to overestimate memory ability (Bruce, Coyne, & Botwinick, 1982; Lovelace & Marsh, 1985). Variability in memory estimations even has been found within a single study. Specifically, Devolder, Brigham, and Pressley (1990) found that neither younger nor older adults were accurate in their predictive abilities, with neither evidencing a greater underestimation or overestimation than the other. Rather, the participants were generally inaccurate in their predictions, with variability existing in awareness of performance ability among the different tasks used in the study such that younger adults occasionally underestimated and older adults occasionally overestimated and vice versa (Devolder et al., 1990). Another more recent study found that both young and older adults underestimated their memory abilities, with greater underestimation exhibited by the older adults (Pearman & Trujillo, 2013). Yet another study examined young adults and found that they underestimated their performance before a memory task (Meeks, Hicks, & Marsh, 2007). One study using a prediction/performance paradigm for AD patients and healthy controls found that both the healthy controls and the AD patients were likely to overestimate their abilities to perform cognitive tasks (Antoine et al., 2013). Younger adults in the preceding studies were generally classed as those below 40 years of age, whereas older adults were generally classed as those over 55 years of age.

As indicated above, results of these studies are highly variable and equivocal. Despite similar objectives in attempting to assess prediction/performance discrepancies and metamemory, the methodologies used in these studies are as variable as their individual results. Indeed, methodology is an inherent factor in attempting to assess the

degree to which individuals are self-aware. As such, it is necessary to describe the most valid means of assessing subjective memory beliefs and objectively evaluating such beliefs. As a domain-specific continuum of insight, memory state awareness may differ in degree as does the awareness seen in other domains of cortical function. As in other cases, individuals within nonclinical populations should exhibit a varying degree of insight into their own metamemory ability. As will be presented later, objective memory assessment will provide the most definitive discrimination between those individuals who are accurate in their ability to predict their memory, and therefore show normal insight, and those who are less so, therefore showing different degrees of insight along the continuum.

Realistically, healthy populations are not likely to fall in proximity to clinical states such as anosognosia on the continuum. Rather, they should fall along this continuum in order from normal state awareness and intact memory functions to just shy of a cognitive impairment or a clinical manifestation of awareness deficit. Otherwise stated, individuals that remain on the continuum within normal limits, should not display a remarkable or notable defect of awareness, but will still differ in degree of awareness that may only be detected through testing.

Anosognosia on a Continuum of Insight

As the aforementioned research would suggest, unawareness of deficit may differ in degree and severity (Correa et al., 1996; Sandifer, 1946). Indeed theoretical accounts also suggest the idea that the syndrome exists on a continuum of insight ranging from a complete lack of insight, or the deficit of awareness known as anosognosia, to full insight

or awareness. It has even been posited that the syndrome of anosognosia itself differs in degree from a mild condition to nearly delusional denial (Hannesdottir & Morris, 2007). Regardless, most individuals, whether healthy or suffering from a neurological illness, would likely fall somewhere on this continuum of insight. Those without neurological impairment should remain well within the bounds of normal awareness with some being "more aware" of their state than others.

Though it is possible to delineate the idea of a continuum of insight ranging from intact awareness to a clinical state of anosognosia, the existing research concerning concepts of insight and anosognosia existing on a continuum within a dimensional spectrum is extremely limited. Indeed, there is little existing research to support such an idea and that which does focuses almost entirely on the presence of awareness deficits in dementias, specifically Alzheimer's disease. Studies of the awareness and predictive abilities of healthy subjects in memory performance paradigms rarely present a discussion of an insight continuum or of anosognosia as a clinical manifestation of a deficit of awareness of memory ability. Those studies that do address the issue mention only a need for a more dimensional model of anosognosia or awareness and a need to find ways to more clearly and validly assess the syndrome in clinical populations.

The research concerning anosognosia in AD has shown a somewhat paradoxical inverse relationship in which some patients with mild Alzheimer's disease (mAD) show a marked impairment of insight and awareness and, conversely, those within a more developed stage of the disease showing a relatively intact awareness (Feher et al., 1991). Explanations of this variability in insight may be explained by the degree to which

patients exhibit frontal pathology (Feher et al., 1991). In other words the degree to which the frontal lobes are adversely affected by the disease process is of greater relevance than the severity of the disease itself. Research has implicated a dimensional rather than categorical model of anosognosia due to the large variability found in unawareness of cognitive deficits among patients, and suggests that unawareness must be considered as a continuum rather than being an "all or nothing" syndrome (Correa et al., 1996; Derouesne et al., 1999).

From a practical standpoint, it would be rational to conclude that such a continuum existed and that any individual, whether healthy or impaired, should fall on the spectrum. This conclusion follows from the basic assumption that all individuals differ and, as such, all individual brains differ. Meeting this basic assumption allows us to take one step further and conclude that the functional neuroanatomy of every individual will vary substantially enough to manifest as explicit differences in multiple domains of cognitive, emotional, and ultimately, behavioral functioning. As all of these domains contribute to an individual's awareness of his own state of being, the degree to which they are differentially developed will, in turn, result in differences in the degree to which that individual possesses insight. The question remains, however, as to the true neurological substrates of this variable insight.

Neuropathology and Neuropsychological Correlates

Anosognosia may result from either focal or diffuse brain damage (Sandifer, 1946). As previously mentioned, the syndrome exists independent of whatever overarching disease state may have caused its etiological neuropathology. Indeed, the

symptomology of Alzheimer's disease, to include anosognosia, may vary depending on neuropathological involvement of different brain structures (Reed, Jagust, & Coulter, 1993). Theoretical accounts of anosognosia have posited that it is either a domain-specific disturbance, such that a patient may have anosognosia for memory impairment but not for another deficit such as hemiplegia or cortical blindness, or that it is the product of a disruption of some higher order cognitive process (Weinstein, Friedland, & Wagner, 1994). Schacter (1990) distinguishes between first and second order accounts of anosognosia in memory impairment. Specifically, he emphasizes both a need to consider the syndrome within the sphere of a second order account, or dysfunction of a domain specific cognitive process, and to consider it within the sphere of first order accounts, or dysfunction of a particular awareness system operating across multiple domains. However, he also notes that any second order account does not negate the possibility that a higher order cognitive awareness system exists, but that the anosognosic state may be present as a result of a dysfunction in access to information associated with a particular domain (e.g., memory or inability to access information about the state of memory ability). An integrated model containing both accounts would best serve as a causative explanation for the syndrome. It would only be when the central awareness system is disrupted, either focally or in its connections to a particular domain specific ability (somatosensory, memory, motor, etc.), that an individual would slip into the extreme end of the spectrum into which the anosognosic state exists. Additionally evidence suggests that the syndrome is even domain specific with regard to the dementias (i.e. memory

impairment, ADL, behavioral problems, etc.) and within AD it may manifest in one or many domains (Agnew & Morris, 1998).

Various models have been put forth to describe the phenomenon from a cognitive neuropsychological perspective. McGlynn and Schacter (1989) posit a system, derived from a model by Schacter (1990), consisting of an awareness system located in the inferior parietal lobes that receives input from various cognitive, sensory, and motor systems. This posterior system is linked to a frontal lobe executive system that monitors more complex cognitions and behaviors. They propose that anosognosia may result from damage to either the parietal awareness system itself or its connections to the outlying modules from which it receives information. Additionally the syndrome may result from damage specifically to the frontal executive system or its connections to the posterior parietal awareness system. Thus, they explain that anosognosia for perceptual and motor disturbances occurs due to damage or disconnect to the posterior "awareness" system and anosognosia for behavioral, mnemonic, and more complex cognitive behaviors occurs as a result of damage to the anterior "executive" system. This model has limitations in regard to explaining every domain of anosognosia as it cannot entirely do so and fails with respect to adequately addressing the neural substrates of awareness.

Expounding on the work of McGlynn and Schacter (1989), Agnew and Morris (1998) proposed a more detailed model by incorporating it into a larger framework that describes three different types of the syndrome and explains them in terms of their cognitive heterogeneity and presentation. Their model incorporates a "mnemonic comparator" mechanism within the executive system that compares incoming sensory

information with a “personal knowledge base” of memory functions. In “mnemonic anosognosia” there is a detected problem at the level of the comparator mechanism but that problem fails to be processed into the semantic memory store. In “executive anosognosia” there is an error in the comparator mechanism itself in which the individual is aware of a memory error but fails to update their personal knowledge database. In “primary anosognosia” the individual is completely unaware of any errors in memory function and the only processing of error occurs within the realm of implicit knowledge. This model of Agnew and Morris (1998) incorporates a more thorough examination of the various presentations of anosognosia in dementia by allowing these presentations to be viewed within the framework of their impact on the mechanisms within the system.

Hannesdottir and Morris (2007) expounded upon the previous model by Agnew and Morris (1998) in their Cognitive Awareness Model (CAM). They posit systems similar to those elucidated by Schacter (1990) and Agnew and Morris (1998), but add a series of comparator mechanisms designed specifically for various cognitive abilities. Additionally they propose a “metacognitive awareness system” (MAS) designed to compile information from other parts of the system. Disruptions occurring at either the level of the MAS or the comparator mechanisms are termed either primary or secondary anosognosias, respectively (Hannesdottir & Morris, 2007).

From a cognitive neuropsychological framework, these theorists attempt to provide a systemic explanation for anosognosia as a deficit of awareness and incorporate neuropathology as much as is possible. However, they fail with regard to explaining the neurological substrates of insight in a way that they may be localized to particular areas

of the right hemisphere. Indeed, the researchers neglect isolating these prescribed systems to the right hemisphere at all and rather speak of anterior/posterior or frontal/parietal areas. Weinstein et al. (1994) suggested that the neuropathology of anosognosia tends to affect more than one lobe or hemisphere and their results suggest that deficits in awareness are more likely in patients with frontal lobe involvement than those with damage limited to the parietal, temporal, or limbic areas. Indeed, the previously mentioned cognitive neuropsychological models suggest that anosognosia for memory impairment, and less severe deficits of awareness of memory functioning, must involve specific areas within the frontal lobes, specifically those serving executive functions. As of the present time, more definitive data concerning the localization of anosognosia has come from neuroradiological studies.

Anosognosia can be viewed as resulting directly from dysfunction of specific neuroanatomic areas that are negatively affected by Alzheimer's disease. A variety of neuroimaging studies have sought to map the neuropathology of the disorder, with varying results. Several neuroradiological studies of anosognosia in Alzheimer's disease have implicated the frontal lobes (Derouesne et al., 1999; Salmon et al., 2006; Shibata, Narumoto, Kitabayashi, Ushijima, & Fukui, 2008; Starkstein et al., 1995; Vogel, Hasselbalch, Gade, Ziebell, & Waldemar, 2005), and more specifically the right frontal lobe (Harwood et al., 2005) and dorsolateral prefrontal cortex (Starkstein et al., 1995; Reed, Jagust, & Coulter, 1993). Additionally, several studies of anosognosia in Alzheimer's disease have implicated right hemisphere dysfunction (Auchus, Goldstein, Green, & Green, 1994), frontal lobe dysfunction (Correa et al., 1996; Mangone et al.,

1991; Michon, Deweer, Pillon, Agid, & Dubois, 1994; Starkstein et al., 1995) or found anosognosia to be correlated with deficits on tests of frontal lobe and executive function (Antoine et al., 2013; Armanzio et al., 2012; Michon et al., 1994; Ott et al., 1996; Starkstein, Fedoroff, Price, Leiguarda, & Robinson, 1993).

Using positron emission tomography (PET), Salmon et al., 2006 found that deficits in the ability to evaluate cognitive function were correlated with metabolic activity in the right parahippocampal region and the orbitofrontal cortex. Additionally, they relate the involvement of the hippocampal formation to the role of the aforementioned comparator mechanism of Agnew and Morris (1998) and posit that medial temporal lobe dysfunction may damage a comparator mechanism that exists to relate self-knowledge with current sensory processes. Using functional magnetic resonance imaging (fMRI), Ries et al. (2012) found that deficits in self-appraisal accuracy were associated with altered functional connectivity in the medial prefrontal cortex (MPFC), and specifically with MPFC connections to the dorsolateral prefrontal cortex (DLPFC) bilaterally. Salmon et al. (2005) found that anosognosia may be a result of reduced metabolism in networks located in the superior frontal sulcus that are associated with self-referential processing. Using fMRI in a similar study, Johnson et al. (2002) found activation in the anterior medial prefrontal cortex during a self-reflection paradigm. Similarly, Rosen et al. (2010) found that self-appraisal accuracy was associated with grey matter volume in the right ventromedial prefrontal cortex, specifically overestimation of cognitive performance.

These results suggest not only a frontal lobe contribution to disordered awareness, but more specifically, the involvement of the right hemisphere in some way that relates to executive functioning and awareness. Taken together it can be posited that awareness of deficit is a product of disruption of some mechanisms within, or connected to, a system of the right frontal lobe. As such it is important to continue to address the role of this area in its contribution to awareness and anosognosia. Tests of executive and frontal lobe functions may yield more specific data to clarify whether there is a correlation between awareness and performance on these measures. If behavior is more sensitive than neuroimaging, then neuropsychological test performance may provide a more accurate appraisal of the link between awareness of memory functioning and the right frontal lobe.

Methods of Assessment

Research examining the presence of anosognosia among AD populations has yielded varied results, due in large part to the inconsistent methodologies used to assess the syndrome as seen across studies. There have traditionally been three methods by which anosognosia is assessed in participant populations. The first one involves the clinician inquiry as to the patient's beliefs about their abilities and judges this subjective belief against the clinician's perceived state of the patient (Anderson & Tranel, 1989; Auchus et al., 1994; Cosentino et al., 2007; Ott et al., 1996; Reed et al., 1993; Sevush & Leve, 1993). The second method consists of some form of discrepancy comparison being made between the patient and the caregiver acting as an informant, whether with the use of questionnaires or direct interviewing (Clare et al., 2010; Correa et al., 1996; Kotler-Cope & Camp, 1995; Mangone et al., 1991; Michon et al., 1994; Ott et al., 1996; Ries et

al., 2012; Salmon et al., 2006; Shibata et al., 2008; Starkstein et al., 1995; Stewart et al., 2010; Vogel et al., 2005). The third method is one in which patients are asked to predict their level of performance on objective tests of memory function or other neuropsychological assessments, and this is then compared with their actual performance (Ansell & Bucks, 2006; Antoine et al., 2013; Barrett et al., 2005; Clare et al., 2010; Cosentino et al., 2007; Duke et al., 2002; Harwood et al., 2005; Kashiwa et al., 2005; McGlynn & Kaszniak, 1991; Mimura, 2008; Wagner et al., 1997). Though these three techniques are notable for their prevalence in studies of insight and awareness, they are simply the most commonly used rather than being the only methods that exist. Comparing the patient's subjective assessment with that of a caregiver tends to be the most commonly used method (Ecklund-Johnson & Torres, 2005). Many methodological problems have been encountered in attempts to assess the presence of anosognosia in dementia patients and in attempts to directly measure awareness of memory in healthy populations. Indeed the method used to assess the syndrome has in some cases affected the presence or degree of the syndrome itself, calling for a need for more precise and empirical approaches (Derouesne et al., 1999).

A comprehensive review of the methods of assessment used in insight evaluations by Clare, Markova, Verhey, and Kenny (2005) goes further and distinguishes between five different methods traditionally used to assess awareness in dementias. Their first method, "the clinician rating method" requires clinicians to make ratings of awareness following structured interviewing, questioning, or simply a review of case records. The authors note the limitations of this method as being its inherent inability to detect domain

specific awareness (e.g., memory, behavior, etc.) and the heavy reliance on subjective reports by the patient that do not consider actual behavior. The second method indicated is the "questionnaire-based method" and includes the subjective rating made by the patient, the rather informal discrepancy comparison between informant rating and patient rating of ability, and the more detailed discrepancy comparisons made between informants and patients on parallel forms of questionnaires. The greatest limitations of these particular types of assessment are their reliance on informant accuracy in their rating of the patient's functioning, something subject to external influence. The third method of assessment is termed "performance based methods" (or the prediction/performance method) and involves the use of discrepancy comparisons between subjective self report and objective standardized assessment. In this case standardized assessments of the particular domain of interest are used to measure the patient's performance objectively and the results are compared with the patient's subjective report of function. The major limitation of this method is noted as being the problem that the self report measures used may not be correlated with the objective measures. Clare et al. (2005) also noted that the problem of asking participants to evaluate their predictive performance on objective neuropsychological tests is that the results may not be ecologically valid as indicators of how they would actually perform if given tasks relevant to normal activities of daily functioning. The fourth and fifth methods are the "phenomenological method" and "multidimensional method", consisting of experiential approaches or a conglomeration of other methods, respectively.

The review noted above described two additional classes of assessment of insight and awareness and described the limitations of each approach to assessment. Though many studies have assessed anosognosia for memory impairment using all of these approaches, the clinician rating method, the questionnaire based method, and the performance based method seem to be the most commonly used. The phenomenological approach lacks significant research and the multidimensional approach is simply a conglomeration of the first three approaches. Of the original three, the prediction/performance approach remains the method with the fewest limitations based upon subjective validity: having a participant subjectively rate their own ability would appear to be the most face valid method of obtaining an indication of the individual's insight. Taking this subjective judgment in the form of asking them to predict how they will perform on an objective neuropsychological test provides the closest indication of the discrepancy between what the participant truly believes and what their actual performance outcomes are on the specific tests used. Insight is thus assessed as the discrepancy between a purely subjective assessment and a purely objective assessment. Despite the aforementioned limitations with regards to ecological validity, as noted by Clare et al. (2005), there does not appear to be any method more precise in its evaluation than to simply ask the patient what they believe about their own ability (subjective self report) and subsequently have them complete an objective measure of that ability, calculating the discrepancy between the two at the conclusion. It remains unclear at this time what methods might better address the issue of ecological validity.

Considering the possibility that the prediction/performance method may be the most face valid approach, assessing deficit of insight of memory functioning in nonclinical populations would require a very precise measurement. Asking participants to predict the number of units of information they will recall and then objectively assessing that specific variable has more face validity than other measures. Most other measures consist of a process in which objectively evaluating memory is methodologically different than how the participants subjectively evaluate their predicted memory performance. As such this method should enhance both the validity and precision of the overall assessment of insight. Tests of supra-span list learning, such as the Hopkins Verbal Learning Test-Revised (HVLT-R) and the California Verbal Learning Test-II (CVLT-II), provide a precise assessment of number of words remembered in immediate and delayed recall trials. Asking participants to estimate the number of words they believe they can remember, and subsequently administering the tests to see how many words they actually remember over the immediate and delayed trials, provides that immediate discrepancy index in order to determine where each individual falls on the continuum.

Summary and Purpose of the Current Study

As it is believed that anosognosia as a clinical syndrome exists on a continuum of insight and self-awareness, and as such that all individuals fall somewhere on this continuum ranging from full insight to the complete deficit of awareness known as anosognosia, participants will fall on this spectrum into one of three groups: those who overestimate their performance, those who accurately estimate their performance, and

those who underestimate their performance. The hypothesis is that those individuals who are found to be inaccurate (overestimate or underestimate) should display relative deficits on tests of right frontal functioning and no relative deficits on tests of left frontal functioning or left and right posterior functioning. Our group consisting of those participants who accurately estimate their memory should not show significant deficits on neuropsychological tests and would thus fall on the spectrum within the range of full insight.

CHAPTER II

Method

Participants

The participants consisted of 60 individuals with an age range of 18-38 years (*M* = 20.66, *SD* = 3.32). They were recruited from an undergraduate population at a major university. Exclusion criteria included a history of traumatic brain injury, stroke or other cerebrovascular insult, a history of neurological illness, a history of psychological disorders, current use of psychotropic medications, and any other psychiatric or neurological ailment. These data were procured via a subject history and demographics form participants filled out prior to beginning the study. Participants were provided with written informed consent to participate and our study was approved by the Institutional Review Board of Middle Tennessee State University.

Apparatus

Animal Naming (AN). The AN (Strauss, Sherman, & Spreen, 2006) test is a measure of semantic fluency requiring the participant to name as many different animals as possible within 60 seconds. The dependent variable is the number of accurate words produced within the specified time limit.

Beck Depression Inventory-II (BDI-II). The BDI-II (Beck, Steer, & Brown, 1996) is designed to assess the presence and degree of self-reported depression in a 21 item self report format. The items are related to different symptoms commonly associated with clinical depression. Each item is endorsed by the patient on a scale of 0 to 3 with a range of possible scores from 0 to 63. The dependent variable is the patient's raw score.

Boston Naming Test (BNT-2). The BNT-2 (Kaplan, Goodglass, & Weintraub, 1983) is a measure of visual naming to confrontation in which participants are shown a black and white line drawing of a common object and asked to name the object. The objects are presented with increasing difficulty involving a range from common objects to more rare objects. The dependent variable is the number of items correctly identified out of 60 total line drawings.

California Verbal Learning Test-II (CVLT-II). The CVLT-II is a test of verbal learning and memory using a supra-span list learning format. The test measures both recall and recognition of word lists. Initially, sixteen words are presented over five immediate recall trials, after which one interference trial of sixteen novel words are presented in an immediate recall format followed by a short delay free recall and a short delay cued recall of the words from the initial list. After 20-25 minutes, during which nonverbal testing is administered, the long delay free recall trial is administered followed by the long delay cued recall trial, both consisting of words from the first list (Delis, Kramer, Kaplan, & Ober, 2000). The dependent variable is the discrepancy between the participant self estimation of word recall and actual participant performance.

Cognitive Estimation Test (CET). The CET (Axelrod & Millis, 1994) is a measure of the ability to generate a problem solving plan in response to questions requiring participants to give approximate answers. Participants are presented a series of questions regarding topics for which they may have relevant knowledge and are asked to make an estimate of the answer. The dependent variable is the deviation score dependent

upon how much each answer given varies from the range of accurate responses such that the higher deviations mean more impaired performance.

Controlled Oral Word Association Test (COWAT). The COWAT (Strauss, Sherman, & Spreen, 2006) is a measure of lexical fluency requiring the participant to generate as many words as possible within 60 seconds using a specified letter (F, A, and S). The words may not be proper nouns, numbers, or stem words with different endings. The dependent variable is the number of accurate words produced within the specified time limit.

Coren, Porac, and Duncan Laterality Questionnaire (CPD). The CPD (Coren, Porac, & Duncan, 1979) is a self-report questionnaire consisting of 13 items designed to assess the patient's lateral preferences for the foot, hand, eye, and ear. Items are scored as +1, -1, or 0 for "right", "left", or "both" respectively with a range of scores from -13 to +13.

Grip Strength (Hand Dynamometer). The grip strength test (Strauss et al., 2006) measures the strength of grip of each hand using the Lafayette Hand Dynamometer (Lafayette Instrument Company). This test assesses the integrity of motor function and requires participants to hold the handle in one hand and squeeze the control with the fingers as hard as possible. Additionally, participants are required to estimate their ability to squeeze the control with half the strength of the first trial for each hand by then squeezing it with half as much force. The dependent variable is the kilograms of grip strength and perseverative measurement for each hand.

Line Bisection Task (LB). The LB is a measure of visual perception and spatial neglect. Participants are presented with a horizontal line drawn across a page and asked to bisect the line by placing a mark in the exact center of the line. The measure is scored by the distance the participant's mark deviates from the true center in millimeters. The dependent variable is the average deviations across all five trials. Specifically, deviations to the left of true center are negative and deviations to the right of true center are positive.

Ruff Figural Fluency Test (RFFT). The RFFT (Ruff, 1996) is a measure of nonverbal figural fluency. The test consists of five parts, each consisting of a different stimulus pattern composed of dots. Participants are instructed to draw as many figures as possible by connecting at least two dots within a five dot matrix. Additionally, they must use straight lines and are instructed to make as many unique patterns as possible within the specified time limit. The dependent variable is the overall total number of unique designs produced across the five trials.

Stroop Color-Word Test (SCWT). The SCWT (Strauss et al., 2006) is an executive functioning measure that assesses selective attention and cognitive flexibility. The Golden version consists of three pages of 100 items per page. The first page are color words printed in black ink, the second page are Xs printed in red, green, or blue ink. The third page consists of color words printed in colors that do not match the words. Patients are instructed to read the items on each page as quickly as possible and given 45 seconds per page to do so. The dependent variable is the number of words read from the Color-Word trial.

Trail Making Test (TMT). The TMT (Tombaugh, 2004) is an executive functioning measure that assesses visual scanning, processing speed, cognitive flexibility, and general executive function. It consists of two parts, A and B, with a practice trial preceding each part. Part A requires participants to connect 25 circled numbers in numerical order using straight lines as quickly as possible without removing their pencil from the paper. Part B requires participants to connect 25 circled letters and numbers in numerical-alphabetical order, however in this part they must alternate between numbers and letters and do so using straight lines as quickly as possible without removing their pencil from the paper. The dependent variable on each part is the time required to complete the task.

Procedure

Initially, written informed consent was obtained from all participants. Additionally, relevant demographic information was obtained, such as age, sex, years of education as well as any history of psychological disorder or neurological illness. All participants filled out a form indicating whether they were using psychotropic medications at the time of the study. Participants were then seated at a table in the laboratory and administered the BDI and CPD prior to testing. Following these questionnaires, they were told, “I am going to read a list of 16 words. How many of those 16 words do you think you can remember?”, their response recorded, and then administered the standardized instructions for the CVLT-II followed by all five trials. Following the immediate recall trials of the CVLT-II, the participants were administered the TMT, SCWT, LB, CET, RFFT, and the Hand Dynamometer (grip strength and

estimated half grip strength). At the end of 20-25 minutes the participants were asked, "Do you remember those 16 words I read before? How many of those 16 words do you think you can remember?", their response recorded, and then administered the long delay free recall trial of the CVLT-II. Following completion of the CVLT-II the participants were administered the COWAT (FAS), AN, and BNT-2. Testing was concluded with a debriefing. The order of administration for all tests was randomized to control for sequence effects.

CHAPTER III

Results

We first grouped our participants according to whether they were accurate (ACC) or inaccurate (IACC) in their estimation of their memory functions. Research has shown individual working memory to be capable of handling 7 +/- 2 units of information (Miller, 1956). As such, participants whose estimation deviated by two or more words from their actual performance comprised the IACC group. Those whose estimations were within one word of their actual performance comprised the ACC group. All analyses were conducted using an experimentwise alpha of .05. Additionally, all multiple comparisons were done using Tukey's HSD.

Initial analyses were conducted to determine if group differences existed in regard to age, lateral preference, and depression. A series of one-way between-subjects ANOVA's were conducted on each of these dependent variables. The results indicated no significant differences, $F(1, 58) = .161$, $p = .690$, in age between the ACC ($M = 20.42$, $SD = 3.13$) and the IACC ($M = 20.79$, $SD = 3.49$) groups. No significant difference in laterality was found, $F(1, 58) = 1.392$, $p = .243$, between the ACC ($M = 6.23$, $SD = 5.71$) and IACC ($M = 8.0$, $SD = 5.40$) groups. Additionally no significant difference in depression, $F(1, 58) = .203$, $p = .654$, was found between the ACC ($M = 8.28$, $SD = 7.10$) and IACC ($M = 7.56$, $SD = 5.17$) groups. Hence, these variables were not confounds given their lack of significance (see Table 1 for Descriptive Statistics).

Accurate vs. Inaccurate

Primary analyses were then conducted using the same groups to determine if differences existed in regard to neuropsychological functioning. A series of one-way between subjects ANOVA's indicated no significant differences in tests of left frontal lobe functioning (FAS (F(1, 58) = 1.493, p = .227), SCWT (F(1, 58) = .481, p = .491), HDR (F(1, 58) = .669, p = .417), TMT (F(1, 58) = .80, p = .779), CET (F(1, 58) = .379, p = .540)) between the ACC and IACC groups. There were also no significant differences in tests of right frontal lobe function (RFFT (F(1, 58) = .004, p = .953), HDL (F(1, 58) = .047, p = .829)) between the ACC and IACC groups. There were no significant differences in tests of left parietal lobe function (BNT (F(1, 58) = 1.523, p = .222), AN (F(1, 58) = .002, p = .961)) between the ACC and IACC groups. Lastly there were no significant differences in a test of right parietal lobe function (LB (F(1, 58) = .033, p = .856)) between the ACC and IACC groups (see Table 1 for Descriptive Statistics).

Overestimate vs. Underestimate

The lack of significance in our primary analysis may have been due to the fact that the inaccurate group was comprised of both those individuals who overestimated their performance and those individuals who underestimated their performance. This may have added extraneous variance to the extent that there is any systematic difference between those who overestimate and those who underestimate. Hence, subsequent analyses were conducted by dividing participants into more specific groups, allowing us to determine whether there was a significant difference between those who underestimated (U) their performance, classified according to a deviation of minus one

word or more from accuracy, and those who overestimated (O) their performance, classified according to a deviation of plus one word or more from accuracy. Those who were accurate in their estimation (i.e. a deviation score of 0) were not included in this analysis.

A series of one-way between groups ANOVA's were conducted to determine whether there were significant differences between the two groups in terms of neuropsychological function. Analyses indicated no significant differences in either tests of left parietal (BNT ($F(1, 51) = .100$, $p = .753$), AN ($F(1, 51) = .277$, $p = .601$)) or right parietal (LB ($F(1, 51) = .040$, $p = .842$)) lobe function. Results indicated no significant differences in four tests of left frontal lobe function (FAS ($F(1, 51) = .411$, $p = .525$), HDR ($F(1, 51) = .052$, $p = .820$), CET ($F(1, 51) = .092$, $p = .763$) SCWT ($F(1, 51) = .071$, $p = .791$)) and a test of right frontal lobe function (HDL ($F(1, 51) = .1.405$, $p = .241$)). Results did indicate a significant difference between the two groups on a test of left frontal lobe function (TMT ($F(1, 51) = 6.683$, $p = .013$)) and a test of right frontal lobe function (RFFT ($F(1, 51) = 5.792$, $p = .020$)). Specifically, we found that those participants who overestimated their memory function showed a relative deficit on both a test of left frontal and a test of right frontal lobe function (see Table 2 for Descriptive Statistics).

Overestimate, Underestimate, Accurate

Final analyses were conducted to determine whether a more specific difference, in terms of neuropsychological function, existed depending on whether an individual overestimated or underestimated their memory functions while including those

individuals who were relatively accurate. We included both those participants who were accurate (left out of the previous analysis), and returned our original criterion of a plus or minus two word deviation from dead accuracy. We divided participants into three groups: those who overestimated their performance (O), those who underestimated their performance (U), and those who were fairly accurate in their estimation (A). Those who overestimated their performance were classified according to a deviation of plus two or more words from dead accuracy. Those who underestimated their performance were classified according to a deviation of minus two or more words from dead accuracy. Those who were accurate were classified according to a deviation of plus or minus one word from dead accuracy. A series of one-way between subjects ANOVA's were conducted to determine whether group differences existed in terms of neuropsychological function.

The results of these analyses indicated no significant differences in tests of left frontal lobe functioning (SCWT (F(2, 57) = .270, p = .765), FAS (F(2, 57) = .758, p = .473), HDR (F(2, 57) = .329, p = .721), TMT (F(2, 57) = 2.632, p = .081), CET (F(2, 57) = .202, p = .818)) between the three groups. There were no significant differences in tests of left parietal lobe function (BNT (F(2, 57) = .779, p = .464), AN (F(2, 57) = .382, p = .684)) between the three groups. There were no significant differences in a test of right parietal lobe function (LB (F(2, 57) = .044, p = .957)) between the three groups. There were no significant differences on one test of right frontal lobe function (HDL (F(2, 57) = .098, p = .907)) between the three groups. However, we did find significant differences in one test of right frontal lobe function (RFFT (F(2, 57) = 3.803, p = .028))

between those who overestimated and those who underestimated. Specifically, we found that those individuals who overestimated their memory function showed a relative deficit on a test of right frontal lobe functioning. An additional finding was that those individuals who underestimated their memory function actually performed significantly better on a test of right frontal lobe functioning than those overestimated (see Table 3 for Descriptive Statistics).

CHAPTER IV

Discussion

The findings of the primary analyses did not support the hypothesis that accuracy in memory estimation would be related to right frontal lobe functioning. Those participants who were inaccurate in their estimation of memory function did not significantly differ in performance to those who were accurate and did not show any relative deficits on tests of right frontal lobe function. Indeed, no significant results were found when analyzing participants according to whether they fell into the accurate or the inaccurate groupings.

Subsequent analyses were conducted to explore the lack of support for our primary hypothesis. The majority of the relevant literature positing a right frontal lobe contribution to disordered awareness in memory functioning was conducted using clinical populations, primarily consisting of dementia patients (Antoine et al., 2013; Armanzio et al., 2012; Harwood et al., 2005; Michon et al., 1994; Ott et al., 1996; Starkstein et al., 1993). Our review of the relevant literature was unable to find research concerning nonclinical populations that addresses the neuropsychological correlates of insight in memory functions. As such, our hypothesis emanated from a need to examine the continuum of a clinical phenomenon (anosognosia) with a nonclinical population. The majority of the existing clinical literature supports the theory that individuals with AD tend to overestimate their memory and cognitive functions or underestimate the severity of their deficits (Ansell & Bucks, 2006; Antoine et al., 2013; Clare et al., 2010; Correa et al., 1996; Cosentino et al., 2007; Duke et al., 2002; McGlynn & Kaszniak, 1991; Ott et

al., 1996; Ries et al., 2012; Sevush & Leve, 1993; Stewart et al., 2010). Given this data, it was necessary to further examine whether our participants would differ according to whether they overestimated or underestimated their memory functions.

Subsequent analysis was done after dividing participants into those who underestimated their memory functions and those who overestimated their memory functions. This analysis yielded significant results. Specifically, it was found that those individuals who overestimated their memory functions showed a relative deficit on a test of attention and cognitive flexibility (TMT) and a test of nonverbal fluency (RFFT). Research has indicated that performance on the TMT is related to left frontal lobe functioning. Specifically, patients with damage to the left dorsolateral prefrontal cortex perform worse than those with damage to the homologous right dorsolateral prefrontal cortex (Stuss et al., 2001). Further, the RFFT being a measure of nonverbal fluency has been shown to correlate significantly with right frontal lobe functions (Foster, Williamson, Harrison, 2005; Ruff, Allen, Farrow, Niemann, & Wiley, 1994). Hence, participants who overestimated their performance exhibited bilateral frontal lobe deficits relative to those who underestimated their performance.

The subsequent analysis described above did not take into consideration those who were accurate in their performance. Hence, the data were reanalyzed to include these individuals. Three groups were created: those who overestimated (plus two or more words), those who underestimated (minus two or more words), and those who were accurate (plus or minus one word). Hence, this final analysis was done after grouping participants in terms of those who overestimated, those who underestimated, and those

who were accurate in their estimation. Results again indicated that participants who overestimated their memory functions showed a greater relative deficit on a neuropsychological test than those who underestimated their memory and those who were accurate in their estimations. Specifically, those who overestimated evidenced a relative deficit on a test of nonverbal fluency (RFFT). More remarkable was the fact that those individuals who underestimated their memory functions actually performed the best on a test of nonverbal fluency (RFFT). As mentioned previously, the RFFT being a measure of nonverbal fluency has been shown to correlate significantly with right frontal lobe functions (Foster, Williamson, Harrison, 2005).

Research is not consistent concerning the definition of what constitutes awareness of cognitive functions. The presence of anosognosia in clinical populations, particularly in Alzheimer's disease, consists of those patients who overestimate their cognitive abilities. Specifically, patients tend to either overestimate their cognitive abilities or underestimate the severity of their deficits (e.g., "Doctor my memory is perfectly fine" or "Doctor I do not have trouble with that"). It does not stand to reason that patients who underestimate their abilities, and subsequently perform well on tests of cognitive function, possess a deficit of awareness consistent with anosognosia. Rather, it may be that they have increased insight to the point of being overly modest in regards to their personal self-reflection as they are analyzing their personal knowledge base concerning their own abilities and determining that they may be deficient. As such, it is possible that the reason we did not observe frontal lobe deficits in those participants who underestimated their cognitive functioning is due to the fact that the particular lack of

insight is not anosognosia but rather the precise opposite: awareness. This finding that participants who underestimated performed better on a test of right frontal lobe function than those who were accurate, lends credence to the idea that modesty is perhaps a function of insight.

Individuals with anosognosia deny deficiencies and claim proper functioning. Indeed this trend is in the same direction with regards to our current study. Otherwise stated, if those AD patients who overestimate their cognitive functions, and therefore possess anosognosia for memory deficits, then those healthy participants in our study who overestimated their cognitive functions may possess a deficit akin to that seen in the clinical populations, albeit not clinically significant. Thus, the key to understanding anosognosia as a deficit in awareness of particular cognitive functions is to relate it to healthy participants in paradigms in which they overestimate their cognitive functions. As such, it follows that our findings concerning individuals who overestimated their cognitive functions are clinically relevant to the syndrome of anosognosia. We found that healthy adult participants who overestimated their memory functions evidenced a deficit on a neuropsychological test of right frontal lobe functioning relative to those participants who underestimated their abilities. This is consistent with the relevant clinical research regarding the neuroanatomical substrates of anosognosia and general deficits of awareness in patients with Alzheimer's disease.

As noted earlier, the literature regarding the performance of healthy adult participants in memory prediction/performance paradigms is variable at best. This study was unable to find literature regarding the neuropsychological functions of healthy

participants completing memory prediction/performance paradigms in terms of its relation to the clinical phenomenon of anosognosia. Our findings indicate that individuals who tend to overestimate their cognitive functioning, in this case memory, also have a tendency to perform worse, relative to those who underestimate or whom are accurate, on a test of right frontal lobe function. The finding that individuals who underestimated their memory functions performed better on a right frontal test than those who were accurate has significant implications in itself. Future research into the neural substrates of awareness may elucidate the role that concepts such as "modesty" have to play in the way an individual self reflects and whether this is a function of self-awareness. Regarding our current findings, there remains significant clinical relevance to understanding the neuropsychological phenomenon of anosognosia and its presentation in patients with neurodegenerative diseases.

The clinical implications of results of memory prediction/performance paradigms are significant. Attempts to understand and localize the areas of the brain that govern awareness of cognitive function are paramount to understanding the syndromes accompanying both the areas and the functions themselves. The vast majority of the relevant literature indicates that awareness deficits and systems controlling insight may be localized to the right hemisphere in particular and to the right frontal lobe (Auchus et al., 1994; Derouesne et al., 1999; Harwood et al., 2005; Salmon et al., 2006; Shibata et al., 2008; Starkstein et al., 1995; Vogel et al., 2005). It has been noted that the presence of deficits on tests of awareness may contribute diagnostically to determining whether pathological changes seen in neuroradiology are indicative of Alzheimer's disease or

another dementia, due in part to the fact that deficits in awareness are more attributable to AD than the other cortical dementias (Wagner et al., 1997).

Although unawareness of progressive brain deterioration may be welcomed by family members of AD patients, these patients are particularly prone to high risk behaviors and unawareness may be related to deficits in different areas of cognitive function (Anderson & Tranel, 1989; Starkstein, Jorge, Mizrahi, Adrian, & Robinson, 2007; Wagner et al., 1997). Others have found that deficits in awareness occur in behavioral domains concurrently with their deficits in cognitive functions (Vasterling et al., 1995). Understanding the process by which anosognosia operates within Alzheimer's disease will allow for a better understanding of the risk to patients depending upon the neuropathological changes present in their brains. Additionally it will provide for more targeted interventions and methods by which clinicians may assist patient relatives in determining when care is needed (Mullen, Howard, David, Levy, 1996). Auchus et al. (1994) notes that AD patients with significant right hemisphere involvement in the early stages of the disease process may also experience deficits in awareness thereby preventing them from seeking medical treatment.

There are legal and ethical considerations regarding patient treatment in cases of anosognosia in Alzheimer's disease. Medical processes such as standard informed consent, power of attorney and legal custody, and protection of patients from exploitation are all considerations (Mullen et al., 1996; Vasterling et al., 1995). Additionally, patient compliance with treatment regimens becomes an issue with anosognosia (Mullen et al., 1996). Patients may have significantly unrealistic expectations for treatment outcomes

and significantly overestimate their own ability to care for themselves (Anderson & Tranel, 1989; Vasterling et al., 1995).

Perhaps the most direct implications are with regards to the daily functioning of normal individuals. The findings that healthy participants who did not accurately estimate their memory function also showed a relative deficit on a test of right frontal lobe function may imply potential deficits with regards to awareness of behavior patterns among young adults. Given the pattern of risk taking behavior among college age students, it may be imperative to examine the ways in which these individuals self-reflect and evaluate their proposed actions. Additionally there are summary implications regarding the general attitude of young adults with reference to their expectations about the world. If deficits in self-awareness do exist among this particular population, there may be unrealistic expectations about everything from the level of risk involved in typical youth behavior to their ability to withstand the normal difficulties and hardships fundamental to the reality of life. Understanding the construct of self-awareness, its neurological substrates, and how it functions in the healthy adult brain, are crucial to examining the role it plays in normal behavior.

Finally there are general considerations regarding the construct of human self-awareness. Any paradigm examining insight in cognitive functions or any other form of personal insight must take into consideration whether the results can be generalized to a discussion of how self-awareness functions in the human brain. Given the vast amount of clinical literature regarding anosognosia in AD and the literature regarding awareness of cognitive functions in normal populations, it stands to reason that there is a need to unify

the construct of self-awareness. This would best be done using the clinical aspects of self-awareness (anosognosia) and the data regarding healthy individuals with otherwise no deficits in insight. The aforementioned continuum of awareness can be further developed using these operational paths. Further research into the construct of self-awareness can lend valuable information as to the means by which it is present as a result of brain function and how it can be altered and destroyed by disease processes and neuropsychiatric conditions such as schizophrenia or bipolar I disorder.

Methodological considerations and limitations must be taken into account. There is a problem with generalizability of research concerning anosognosia in cognitive domains, as the majority of studies use awareness of memory function as the primary paradigm (Antoine et al., 2013). It is unclear how relevant to the overall construct of awareness any data may be that is gathered from memory awareness paradigms. Antoine et al. (2013) notes that the major methodological consideration in assessing anosognosia and examining awareness is identification of all of the possible cognitive domains affected by Alzheimer's disease and their relationships to awareness. Additionally it is important to determine which awareness paradigms are best applied to particular cognitive domains rather than simply using the same construct for each domain (Antoine et al., 2013). Assessing multiple cognitive domains would better advance the understanding of anosognosia (Vasterling et al., 1995).

Aside from inherent limitations regarding test validity and administration, testing environment, and participant conditions, our method of prediction/performance discrepancies has a major inherent limitation of ecological validity. In this respect it is

unclear how ecologically valid it is to have an individual estimate their memory function and subsequently objectively measure that memory. It has been noted that it may be difficult for research participants to estimate their performance on standardized tests administered in a laboratory setting that are not encountered in everyday living (Clare et al., 2005). Additionally it may be better for individual awareness of cognitive functions or an individual's awareness in general to be assessed using measures that can be attributed to everyday common situations (Clare et al., 2005). As such, we must direct future research in this area toward developing measures of self-awareness that correlate with activities with which normal individuals will be familiar.

Further research may seek to develop new and more ecologically valid methods of assessment into self-awareness. Additionally, given our finding that participants who underestimated their own cognitive abilities outperformed those who were accurate in their personal estimates, a very interesting area of further research may be to examine whether this finding can elucidate the limits of personal insight in the form of human modesty. This may also be explained in some other, as yet undefined, reason why individuals may have a tendency to assume they possess substandard ability in whatever domain is being assessed. In either case this should be examined in addition to further exploration of the finding that our participants who overestimated their cognitive functions evidenced a relative deficit on a test of right frontal lobe function. Ultimately, the research into the functions of particular areas of the right frontal lobe subsuming the human ability of self-awareness, may lead us to discovering the reasons why our species is unique in this particular ability.

References

Adair J. C., & Barrett A. M. (2012). Anosognosia. In K. M. Heilman & E. Valenstein (Eds.), *Clinical Neuropsychology* (198-213). New York: Oxford University Press.

Agnew, S. K. & Morris, R. G. (1998). The heterogeneity of anosognosia for memory impairment in Alzheimer's disease: A review of the literature and a proposed model. *Aging and Mental Health, 2*(1), 7-19.

Anderson S. W. & Tranel, D. (1989). Awareness of disease states following cerebral infarction, dementia, and head trauma: Standardized assessment. *The Clinical Neuropsychologist, 3*, 327-339. doi: 10.1080/13854048908401482

Ansell, E. L. & Bucks, R. S. (2006). Mnemonic anosognosia in Alzheimer's disease: A test of Agnew and Morris (1998). *Neuropsychologia, 44*, 1095-1102. doi: 10.1016/j.neuropsychologia.2005.10.019

Antoine, P., Nandrino, J.-L., & Billiet, C. (2013). Awareness of deficits in Alzheimer's disease patients: Analysis of performance prediction discrepancies. *Psychiatry and Clinical Neurosciences, 67*, 237-244. doi: 10.1111/pcn.12050

Armanzio, M., Vase, L., Leotta, D., Miceli, R., Palermo, S., & Geminiani, G. (2012). Impaired awareness of deficits in Alzheimer's disease: The role of everyday executive dysfunction. *Journal of the International Neuropsychological Society, 19*, 63-72. doi: 10.1017/S1355617712000896

Auchus, A. P., Goldstein, F. C., Green, J., & Green, R. C. (1994). Unawareness of cognitive impairments in Alzheimer's disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, *7*(1), 25-29.

Axelrod, B. N. & Millis, S. R. (1994). Preliminary standardization of the cognitive estimation test. *Assessment*, *1*, 269-274.

Babinski J. M. (1914). Contribution a l'etude des troubles mentaux dans l'hemiplegie organique cerebrale (anosognosie). *Review Neurologique (Paris)*, *22*, 845-848.

Barrett, A. M., Eslinger, P. J., Ballentine, N. H., & Heilman, K. M. (2005). Unawareness of cognitive deficit (cognitive anosognosia) in probable AD and control subjects. *Neurology*, *64*.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for Beck Depression Inventory-II (BDI-II)*. San Antonio, TX: Psychological Corporation.

Bruce, P. R., Coyne, A. C., & Botwinick, J. (1982). Adult age differences in metamemory. *Journal of Gerontology*, *37*, 354-357.

Clare, L., Markova, I., Verhey, F., & Kenny, G. (2005). Awareness in dementia: A review of assessment methods and measures. *Aging and Mental Health*, *9*, 394-413. doi: 10.1080/13607860500142903

Clare, L., Whitaker, C. J., & Nelis, S. M. (2010). Appraisal of memory functioning and memory performance in healthy ageing and early-stage Alzheimer's disease. *Aging, Neuropsychology, and Cognition*, *17*, 462-491. doi: 10.1080/13825580903581558

Coren, S., Porac, C., & Duncan, P. (1979). A behaviorally validated self-report inventory to assess four types of lateral preferences. *Journal of Clinical Neuropsychology*, *1*, 55-64.

Correa, D. D., Graves, R. E., & Costa, L. (1996). Awareness of memory deficit in Alzheimer's disease patients and memory-impaired older adults. *Aging, Neuropsychology, and Cognition, 3*, 215-228.

Cosentino, S., Metcalfe, J., Butterfield, B., & Stern Y. (2007). Objective metamemory testing captures awareness of deficit in Alzheimer's disease. *Cortex, 43*, 1004-1019.

David, A. (1990). Insight and psychosis. *British Journal of Psychiatry, 156*, 798-808.

Delis, D. C., Kramer, J. H., Kaplan, E., Ober, B. A. (2000). *California Verbal Learning Test-II* (2nd ed.). The Psychological Corporation.

Derouesne, C., Thibault, S., Lagha-Pierucci, S., Baudouin-Madec, V., Ancri, D., & Lacomblez, L. (1999). Decreased awareness of cognitive deficits in patients with mild dementia of the Alzheimer type. *International Journal of Geriatric Psychiatry, 14*, 1019-1030.

Devolder, P. A., Brigham, M. C., & Pressley, M. (1990). Memory performance awareness in younger and older adults. *Psychology and Aging, 5*, 291-303.

Duke, L. M., Seltzer, B., Seltzer, J. E., & Vasterling, J. J. (2002). Cognitive components of deficit awareness in Alzheimer's disease. *Neuropsychology, 16*, 359-369. doi: 10.1037/0894-4105.16.3.359

Ecklund-Johnson, E. & Torres, I. (2005). Unawareness of deficits in Alzheimer's disease and other dementias: Operational definitions and empirical findings. *Neuropsychology Review, 15*(3). doi: 10.1007/s11065-005-9026-7

Feher, E. P., Mahurin, R. K., Inbody, S. B., Crook, T. H., & Pirozzolo, F. J. (1991). Anosognosia in Alzheimer's disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, *4*(2), 136-146.

Fisher C. M. (1989). Neurologic Fragments. II. Remarks on anosognosia, confabulation, memory, and other topics; And an appendiz on self observation. *Neurology*, *39*, 127-132.

Foster, P. S., Williamson, J. B., Harrison, D. W. (2005). The Ruff figural fluency test: Heightened right frontal lobe delta activity as a function of performance. *Archives of Clinical Neuropsychology*, *20*, 427-434.

Galeone, F., Pappalardo, S., Chieffi, S., Iavarone, A., & Carlomagno, S. (2011). Anosognosia for memory deficit in amnestic mild cognitive impairment and Alzheimer's disease. *International Journal of Geriatric Psychiatry*, *26*, 695-701. doi: 10.1002/gps.2583

Gerstmann, J. (1942). Problem of imperception of disease and of impaired body territories with organic lesions. *Archives of Neurology and Psychiatry*, *48*, 890-893.

Hannesdottir, K. & Morris, R. G. (2007). Primary and secondary anosognosia for memory impairment in patients with Alzheimer's disease. *Cortex*, *43*, 1020-1030.

Harwood, D. G., Sultzer, D. L., Feil, D., Monserratt, L., Freedman, E., & Mandelkern, M. A. (2005). Frontal lobe hypometabolism and impaired insight in Alzheimer's disease. *American Journal of Geriatric Psychiatry*, *13*, 934-941.

Johnson, S. C., Baxter, L. C., Wilder, L. S., Pipe, J. G., Heiserman J. E., & Prigatano, G. P. (2002). Neural correlates of self-reflection. *Brain*, *125*, 1808-1814.

Kalbe, E., Salmon, E., Perani, D., Holthoff, V., Sorbi, S., Elsner, A.,…Herholz, K. (2005). Anosognosia in very mild Alzheimer's disease but not in mild cognitive impairment. *Dementia and Geriatric Cognitive Disorders, 19,* 349-356. doi: 10.1159/000084704

Kaplan, E. F., Goodglass, H., & Weintraub, S. (1983). *Boston Naming Test-2nd Edition (BNT-2).* Media, PA: Lippincott Wilkins & Williams.

Kashiwa, Y., Kitabayashi, Y., Narumoto, J., Nakamura, K., Ueda H., & Fukui K. (2005). Anosognosia in Alzheimer's disease: Association with patient characteristics, psychiatric symptoms and cognitive deficits. *Psychiatry and Clinical Neurosciences*, *59*, 697-704.

Kolb B. & Whishaw I. Q. (2008). *Fundamentals of human neuropsychology* (6th ed.). New York: Worth Publishers.

Kotler-Cope, S. & Camp, C. J. (1995). Anosognosia and Alzheimer's disease. *Alzheimer's disease and Associated Disorders*, *9*(1), 52-56.

Langer, K. G. (2009) Babinski's anosogonosia for hemiplegia in early twentieth-century French neurology. *Journal of the History of the Neurosciences, 18*, 387-405. doi: 10.1080/09647040802537064

Lovelace, E. A. & Marsh, G. R. (1985). Prediction and evaluation of memory performance by young and old adults. *Journal of Gerontology*, *40*(2), 192-197.

Mangone, C. A., Hier, D. B., Gorelick, P. B., Ganellen, R. J., Langenberg, P., Boarman, R., & Dollear, W. C. (1991). Impaired insight in Alzheimer's disease. *Journal of Geriatric Psychiatry and Neurology*, *4*, 189-193.

McGlynn S. M. & Schacter D. L. (1989). Unawareness of deficits in neuropsychological syndromes. *Journal of Clinical and Experimental Neuropsychology, 11*(2), 143-205.

McGlynn, S. M. & Kaszniak, A. W. (1991). When metacognition fails: Impaired awareness of deficit in Alzheimer's disease. *Journal of Cognitive Neuroscience, 3*(2).

Meeks, J. T., Hicks, J. L., & Marsh, R. L. (2007). Metacognitive awareness of event-based prospective memory. *Consciousness and Cognition*, *16*, 997-1004. doi: 10.1016/j.concog.2006.09.005

Michon, A., Deweer, B., Pillon, B., Agid, Y., & Dubois, B. (1994). Relation of anosognosia to frontal lobe dysfunction in Alzheimer's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, *57*, 805-809. doi: 10.1136/jnnp.57.7.805

Migliorelli, R., Teson, A., Sabe, L., Petracca, G., Petracchi, M., Leiguarda, R., & Starkstein, S. E. (1995). Anosognosia in Alzheimer's disease: A study of associated factors. *Journal of Neuropsychiatry*, *7*, 338-344.

Miller, G. A. (1956). The magical number seven, plus or minus two: Some limits on our capacity for processing information. *The Psychological Review*, *63*(2).

Mimura, M. (2008). Memory impairment and awareness of memory deficits in early stage Alzheimer's disease. *Tohoku Journal of Experimental Medicine, 215*, 133-140.

Mullen, R., Howard, R., David, A., Levy, R. (1996). Insight in Alzheimer's disease. *International Journal of Geriatric Psychiatry, 11*, 645-651.

Murphy, M. D., Sanders, R. E., Gabriesheski, A. S., & Schmitt, F. A. (1981). Metamemory in the aged. *Journal of Gerontology*, *36*(2), 185-193.

Orfei, M. D., Robinson, R. G., Bria, P., Caltagirone, C., & Spalletta, G. (2008). Unawareness of illness in neuropsychiatric disorders: Phenomenological certainty versus etiopathogenic vagueness. *Progress in Clinical Neuroscience*, *14*, 203-222. doi: 10.1177/1073858407309995

Orfei, M. D., Varsi, A. E., Blundo, C., Celia, E., Casini, A. R., Caltagirone, C., & Spalletta, G. (2010). Anosognosia in mild cognitive impairment and mild Alzheimer's disease: Frequency and neuropsychological correlates. *American Journal of Geriatric Psychiatry*, *18*, 1133-1140. doi: 10.1097/JGP.0b013e3181dd1c50

Ott, B. R., Lafleche, G., Whelihan, W. M., Buongiorno, G. W., Albert, M. S., & Fogel, B. S. (1996). Impaired awareness of deficits in Alzheimer's disease. *Alzhiemer's Disease and Associated Disorders*, *10*(2), 68-76.

Pearman, A. & Trujillo, A. (2013). Changes in memory prediction accuracy: Age and performance effects. *Educational Gerontology, 39*, 467-475. doi: 10.1080/03601277.2012.701132

Peterson, R. C., Doody, R. Kurz, A., Mohs, R., Morris, J. C., Rabins, P. V,.…Winblad, B. (2001). Current concepts in mild cognitive impairment. *Archives of Neurology, 58*.

Reed, B. R., Jagust, W. J., & Coulter, L. (1993). Anosognosia in Alzheimer's disease: Relationships to depression, cognitive function, and cerebral perfusion. *Journal of Clinical and Experimental Neuropsychology*, *15*, 231-244. doi: 10.1080/01688639308402560

Ries, M. L., Jabbar, B. M., Schmitz, T. W., Trivedi, M. A., Gleason, C. E., Carlsson, C. M.,…Johnson, S. C. (2007). Anosognosia in mild cognitive impairment: Relationship to activation of cortical midline structures involved in self-appraisal. *Journal of the International Neuropsychological Society*, *13*, 450-461. doi: 10.1017/S1355617707070488

Ries, M. L., McLaren, D. G., Bendlin, B. B., GuofanXu, Rowley, H. A., Birn, R.,…Johnson, S. C. (2012). Medial prefrontal functional connectivity: Relation to memory self-appraisal accuracy in older adults with and without memory disorders. *Neuropsychologia*, *50*, 603-611.

Rosen, H. J., Alcantar, O., Rothlind, J., Sturm, V., Kramer, J. H., Weiner, M., & Miller, B. L. (2010). Neuroanatomical correlates of cognitive self-appraisal in neurodegenerative disease. *NeuroImage*, *49*, 3358-3364. doi: 10.1016/j.neuroimage.2009.11.041

Ruff, R. M., Allen, C. C., Farrow, C. E., Niemann, H., &Wylie, T. (1994). Figural fluency: Differential impairment in patients with left versus right frontal lobe lesions. *Archives of Clinical Neuropsychology*, *9*, 41–55.

Ruff, R. M. (1996). *Ruff Figural Fluency Test*. Odessa, FL: Psychological Assessment Resources, Inc.

Salmon, E., Ruby, P., Perani, D., Kalbe, E., Laureys, S., Adam, S. & Collette, F. (2005). Two aspects of impaired consciousness in Alzheimer's disease. *Progress in Brain Research*, *150*. doi: 10.1016/S0079-6123(05)50021-9

Salmon, E., Perani, D., Herholz, K., Marique, P., Kalbe, E., Holthoff, V.,…Garraux, G. (2006). Neural correlates of anosognosia for cognitive impairment in Alzheimer's disease. *Human Brain Mapping*, *27*, 588-597. doi: 10.1002/hbm.20203

Sandifer, P. H. (1946). Anosognosia and disorders of body scheme. *Brain*, *69*(2), 122-137.

Schacter, D. L. (1990). Toward a cognitive neuropsychology of awareness: Implicit knowledge and anosognosia. *Journal of Clinical and Experimental Neuropsychology*, *12*(1), 155-178.

Sevush, S. & Leve, N. (1993). Denial of memory deficit in Alzheimer's disease. *American Journal of Psychiatry*, *150*(5).

Shibata, K., Narumoto, J., Kitabayashi, Y., Ushijima, Y., & Fukui, K. (2008). Correlation between anosognosia and regional cerebral blood flow in Alzheimer's disease. *Neuroscience Letters*, *435*, 7-10. doi: 10.1016/j.neulet.2008.01.065

Souchay, C. & Isingrini, M. (2004). Age related differences in metacognitive control: Role of executive functioning. *Brain and Cognition, 56*, 89-99. doi: 10.1016/j.bandc.2004.06.002

Starkstein, S. E., Fedoroff, J. P., Price, T. R., Leiguarda, R., & Robinson, R. G. (1993). Neuropsychological deficits in patients with anosognosia. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, *6*(1), 43-48.

Starkstein, S. E., Vazquez, S., Migliorelli, R., Teson, A., Sabe, L., & Leiguarda, R. (1995). A single photon emission computed tomography study of anosognosia in Alzheimer's disease. *Archives of Neurology, 52*, 415-420.

Starkstein S. E., Sabe, L., Chemerinksi, E., Jason, L., & Leiguarda, R. (1996). Two domains of anosognosia in Alzheimer's disease. *Journal of Neurology, Neurosurgery, and Psychiatry, 61*, 485-490.

Starkstein S. E., Jorge, R., Mizrahi, R., Adrian, J., & Robinson, R. G. (2007). Insight and danger in Alzheimer's disease. *European Journal of Neurology, 14*, 455-460. doi: 10.1111/j.1468-1331.2007.01745.x

Stewart, G., McGeown, W. J., Shanks, M. F., & Venneri, A. (2010). Anosognosia for memory impairment in Alzheimer's disease. *Acta Neuropsychiatrica, 22*, 180-187. doi: 10.1111/j.1601-5215.2010.00463

Strauss, E., Sherman, E. M. S., Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms, and commentary* (3rd ed.). New York: Oxford University Press.

Tabert, M. H., Albert, S. M., Borukhova-Milov, L., Camacho, Y., Pelton, G., Liu, X.,…Devanand, D. P. (2002). Functional deficits in patients with mild cognitive impairment: Prediction of AD. *Neurology*, *58*, 758-764.

Tombaugh, T. N. (2004). Trail making test A and B: Normative data stratified by age and education. *Archives of Clinical Neuropsychology*, *19*, 203-214.

Vasterling, J. J., Seltzer, B., Foss, J. W., & Vanderbrook, V. (1995). Unawareness of deficit in Alzheimer's disease: Domain-specific differences and disease correlates. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, *8*(1), 26-32.

Vogel, A., Stokholm, J., Gade, A., Anderson, B., Hejl, A., & Waldemar, G. (2004). Awareness of deficits in mild cognitive impairment and Alzheimer's disease: Do MCI patients have impaired insight?. *Dementia and Geriatric Cognitive Disorders*, *17*, 181-187. doi: 10.1159/000076354

Vogel, A., Hasselbalch, S. G., Gade, A., Ziebell, M., & Waldemar, G. (2005). Cognitive and functional neuroimaging correlates for anosognosia in mild cognitive impairment and Alzheimer's disease. *International Journal of Geriatric Psychiatry*, *20*, 238-246. doi: 10.1002/gps.1272

Wagner, M. T., Spangenberg, K. B., Bachman, D. L., & O'Connell, P. (1997). Unawareness of cognitive deficit in Alzheimer's disease and related dementias. *Alzheimer's Disease and Associated Disorders*, *3*, 125-131.

Weinstein, E. A., Friedland, R. P., & Wagner, E. E. (1994). Denial/unawareness of impairment and symbolic behavior in Alzheimer's disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, *7*(3), 176-184.

APPENDICES

APPENDIX A

Tables and Figures

Table 1
Descriptive Statistics for Primary Analysis

	1 (IACC)		2 (ACC)	
	M	SD	M	SD
AGE	20.79	3.49	20.42	3.13
CPD	8.00	5.40	6.23	5.71
BDI	7.56	5.17	8.28	7.10
TMT	66.69	30.60	64.47	25.77
HDL	26.10	8.30	25.57	10.26
HDR	30.05	8.99	28.04	9.15
HDLP	37.25	25.05	32.95	20.98
HDRP	48.94	21.53	46.66	16.80
CET	6.41	2.12	6.04	2.26
SCWT	45.02	11.06	47.00	9.38
RFFTUD	85.43	26.06	85.04	19.91
LB	-3.34	3.76	-3.16	3.07
FAS	36.20	9.05	39.61	12.37
AN	20.92	5.08	20.85	4.61
BNT	50.05	6.08	51.80	3.17

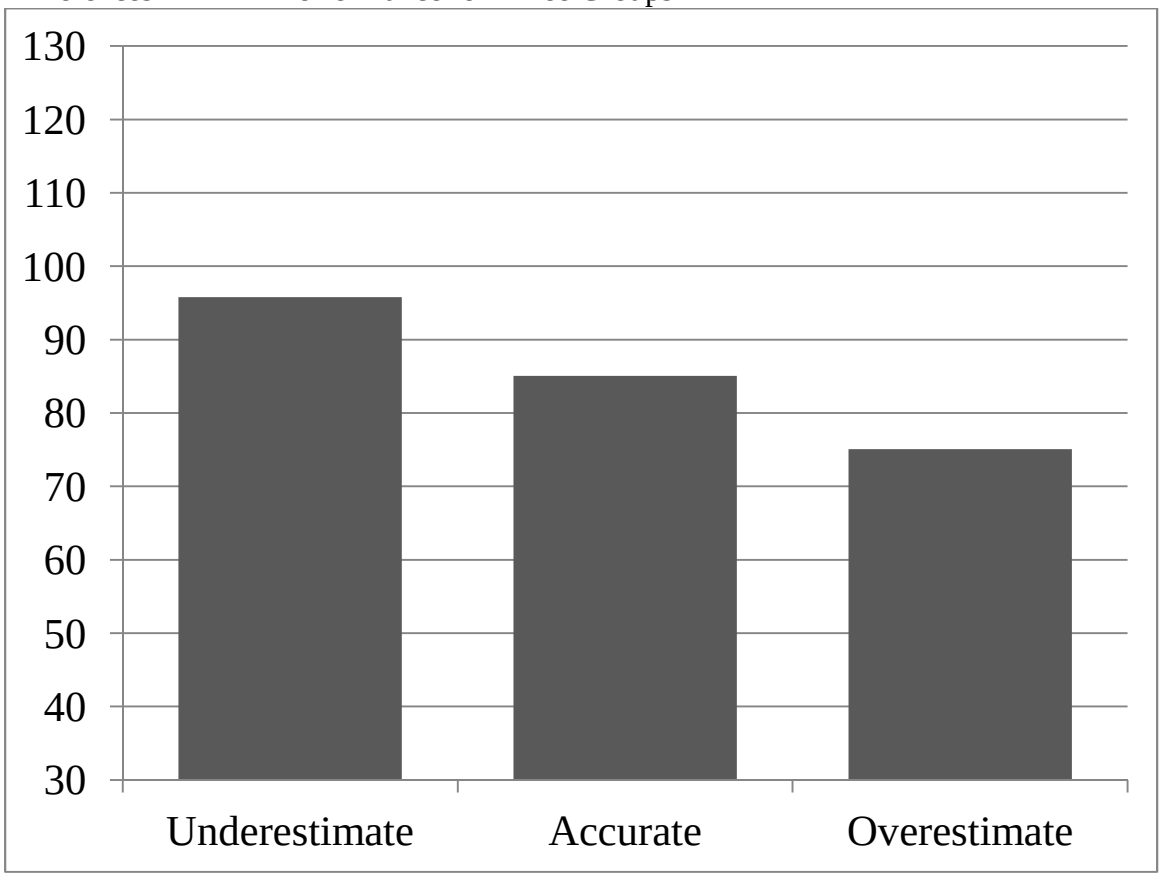
Table 2
Descriptive Statistics for Secondary Analysis

	1 (U)		2 (O)	
	M	SD	M	SD
AGE	20.33	1.80	20.89	4.25
CPD	8.37	4.62	7.24	5.52
BDI	8.45	5.29	7.27	6.85
TMT	55.75	16.96	75.82	34.73
HDL	23.95	7.11	26.89	10.26
HDR	28.83	8.12	29.41	10.00
HDLP	32.79	24.65	36.24	22.21
HDRP	47.00	21.22	47.86	20.47
CET	6.20	2.08	6.37	2.00
SCWT	45.83	9.82	46.62	11.39
RFFTUD	92.70	24.03	76.96	23.42
LB	-3.22	3.00	-3.03	4.01
FAS	36.66	10.74	38.48	9.86
AN	21.66	5.39	20.96	4.30
BNT	50.58	3.82	51.06	6.66

Table 3
Descriptive Statistics for Tertiary Analysis

	1 (U)		2 (A)		3(O)	
	M	SD	M	SD	M	SD
AGE	20.52	1.67	20.42	3.13	21.05	4.65
CPD	8.42	5.18	6.23	5.71	7.60	5.71
BDI	8.57	5.37	8.28	7.10	6.60	4.92
TMT	56.21	17.23	64.47	25.77	76.65	37.11
HDL	25.52	6.96	25.57	10.26	26.65	9.55
HDR	30.05	8.72	28.04	9.15	30.05	9.47
HDLP	34.63	26.89	32.95	20.98	39.75	23.60
HDRP	47.47	22.59	46.66	16.80	50.35	20.97
CET	6.47	2.09	6.04	2.26	6.35	2.20
SCWT	44.57	9.72	47.00	9.38	45.45	12.44
RFFTUD	95.78	24.51	85.04	19.91	75.60	24.09
LB	-3.47	2.86	-3.16	3.07	-3.21	4.53
FAS	36.57	9.20	39.61	12.37	35.85	9.12
AN	21.63	5.84	20.85	4.61	20.25	4.29
BNT	50.26	4.02	51.80	3.17	49.85	7.65

Histogram 1
Differences in RFFT Performance for Three Groups



Appendix B

MTSU Institutional Review Board Approval Form

October 29, 2013
Ransom W. Campbell
Psychology Department
rwc2y@mtmail.mtsu.edu

Protocol Title: "**Awareness of Memory and Brain Function on a Continuum of Insight: Assessing the Presence of a Dysnosognosia**"
Protocol Number: **14-111**

Dear Investigator(s),

The MTSU Institutional Review Board, or a representative of the IRB, has reviewed the research proposal identified above. The MTSU IRB or its representative has determined that the study poses minimal risk to participants and qualifies for an expedited review under 45 CFR 46.110 Category 7. Approval is granted for one (1) year from the date of this letter.

According to MTSU Policy, a researcher is defined as anyone who works with data or has contact with participants. Anyone meeting this definition needs to be listed on the protocol and needs to provide a certificate of training to the Office of Compliance. **If you add researchers to an approved project, please forward an updated list of researchers and their certificates of training to the Office of Compliance (Box 134) before they begin to work on the project.**

Any change to the protocol must be submitted to the IRB before implementing this change. Please note that any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615) 494-8918. You will need to submit an end-of-project form to the Office of Compliance upon completion of your research located on the IRB website. Complete research means that you have finished collecting and analyzing data.

Should you not finish your research within the one (1) year period, you must submit a Progress Report and request a continuation prior to the expiration date. Please allow time for review and requested revisions. Your study expires **October 29, 2014**.

Also, all research materials must be retained by the PI or faculty advisor (if the PI is a student) for at least three (3) years after study completion or be destroyed as evidenced in the application. Should you have any questions or need additional information, please do not hesitate to contact me.

Sincerely,
Charles H. Apigian, PhD.
Chair – Computer Information Systems
Committee Member of IRB
Middle Tennessee State University