

**The Role of Unawareness on Functional Status in Mild Alzheimer's Dementia**

A Dissertation

Submitted to the Faculty

of

Drexel University

by

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In partial fulfillment of the

requirements for the degree

of

Doctor of Philosophy

May 2010

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## **Acknowledgments**

I would like to thank my mentor, Maria Schultheis, Ph.D. You have been a source of support, inspiration, and wisdom as I have found my path in psychology and explored its role in my life. I am forever indebted to Jocelyn Ang and Allison Blasco, who have helped me in recruitment, data collection, and analysis throughout the length of this project. I would like to thank Patricia Shewokis, Ph.D. who helped me through the grueling process of statistical analysis with extreme patience. I am thankful to have such loving friends and family, particularly my husband, who has always supported my pursuits with boundless love and enthusiasm. Thank you to Douglas Chute, Ph.D., J Michael Williams, Ph.D., Tania Giovanetti, Ph.D., and David Libon, Ph.D. who are taking the time to instruct me and foster my growth. Lastly, I would like to thank all the individuals who participated in this project and made it possible.

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**Abstract**

The Role of unawareness on functional status in mild Alzheimer's dementia

Emily C. Roseman

Alzheimer's dementia (AD) is characterized by a progressive decline in memory in addition to decline in at least one other cognitive domain. Integral to the diagnosis is a simultaneous decline in functional abilities such as driving skills, and often an unawareness of this decline. Individuals who are unaware of deficits are often unable to accept the help that they need in completing functional tasks and may put themselves in dangerous situations. For example, individuals with an unawareness of their own deficits may prolong driving cessation. Cognitive status explains some, but not all, of the variability in functional abilities. This study examined the relationship between cognition, unawareness, and functional ability in individuals with mild AD as well as in healthy older adults. Understanding this relationship in healthy older adults will help to establish a baseline prior to disease onset. This baseline is not well understood thereby potentially compromising the safety of even healthy older adults. For example, current driving laws with older adults rely on the assumption that individuals will be able to regulate their driving behaviors as they become aware of age-related changes. This study used a virtual reality driving simulator (VRDS) to assess driving performance in healthy controls with exploratory analyses conducted on individuals with mild AD. Awareness was measured by participant-reliable informant discrepancy scores on the Instrumental Activities of Daily Living (IADL) Questionnaire, as well as discrepancy scores between the participant's perception of performance on the VRDS versus actual performance. Results with healthy controls established no relationship between functional ability and awareness when holding performance on cognitive testing constant. Instead, a relationship was found between functional ability, as measured by the IADL questionnaire, and awareness of functional ability in healthy older adults ( $r = -.747, p <$

.01). As functional ability decreased, awareness of functioning also decreased suggesting that those individuals with greater functional impairments are less aware of such impairments and therefore pose a safety risk. The MMSE was also linked to functional ability in healthy controls, as measured by the IADL, suggesting a relationship continuum between global cognitive status and functioning in healthy older adults from the community. Additionally, trends in the data for individuals with mild AD suggest a correlation between global cognitive status, as measured by the MMSE, and measures of awareness on both functional measures. Findings suggest that unawareness can lead to increased safety risks in healthy older adults. Measurement tools such as the IADL and MMSE may serve to identify those individuals at risk for both healthy older adults as well as individuals with mild AD.

## CHAPTER 1: LITERATURE REVIEW

Alzheimer's dementia (AD) is characterized by a gradual onset leading to a progressive decline in memory as well as impairment in one or more additional cognitive domains. These cognitive deficits result in the decline in the individual's previous level of functioning and are not otherwise accounted for by a central nervous system condition, a systemic condition, a substance-induced condition, or an Axis I disorder (American Psychiatric Association, 2000). AD is the most common cause for dementia, accounting for 50-75% of all late-life dementias which typically occurs after the age of 50 (Welsh-Bohmer & Warren, 2006). In 2000, an estimated 4.5 million Americans were diagnosed with AD, 93% of which were over the age of 74. By 2050, this number is expected to increase three-fold, effecting approximately 13.2 million people in addition to their families and friends (Herbert, Scherr, Bienias, Bennet, & Evans, 2003).

### Neuropathological Presentation of AD

The neuropathological characteristics of AD include the presence of amyloid plaques and neurofibrillary tangles in the cortex. Extracellular amyloid plaque consists of protein and plaque surrounded by glia and dead neurons, which serve as inflammatory markers (Welsh-Bohmer & Warren, 2006). Neurofibrillary tangles exist inside cortical cells and interfere with intracellular transport, ultimately leading to cell death. The distribution of these plaques and tangles as well as the concomitant clinical features characterizes AD (Hyman, Van Hoesen, Damasio, & Barnes, 1984). The progression of AD pathology is understood to start in the parahippocampal region and entorhinal cortex of the medial temporal lobe and eventually spread to other areas of the neocortex (For review, refer to Welsh-Bohmer & Warren, 2006). This presents as gross atrophy in selected regions of the brain on an MRI. A study by Braak & Braak (1997) examined individuals post mortem and found that the distribution of neurofibrillary

tangles began in the entorhinal cortices and spread to temporo-parietal regions, then eventually to the frontal lobes.

Thompson and colleagues (2003) studied the dynamics of gray matter loss in individuals with AD using a 4D method. They used a novel approach of brain mapping examining high resolution MRI scans longitudinally. Individuals with AD were compared with aged matched controls over approximately 2 years (Thompson et al., 2003). They found the trajectory of pathology matched that described by Braak & Braak (1997). Particularly vulnerable to AD pathology were the anterior and ventromedial temporal lobes. These researchers stated that the transition to frontal pathology suggests the degeneration of cortical pathways. Conversely, the neocortical association areas are susceptible because of their integral connection with the limbic structures, where much of the pathology begins (Thompson et al., 2003). They found that individuals with AD had differentially faster left hemisphere atrophy as compared to age matched controls.

### Behavioral and Cognitive Components of AD

The most common method of diagnosing AD is behavioral observations such as that seen on a neuropsychological evaluation, though an autopsy after death serves to confirm this diagnosis (Lezak, Howieson, & Loring, 2004). AD was first described by Alzheimer in 1907, and is now well understood in terms of its clinical presentation. It is degenerative, and among the first symptoms is memory decline, characterized by the inability to encode and consolidate new information into an individual's memory store. As AD progresses, performance also declines on tests of verbal fluency. A diagnosis of AD typically requires a comprehensive neuropsychological evaluation in addition to a functional assessment provided by a reliable informant. Depression is a common symptom in older adults, and often results in cognitive disorders that can mimic dementia. Conversely, symptoms of AD can mimic depression, as individuals become withdrawn, inattentive, and there is often a change in emotional affect (For

review refer to Lezak et al., 2004 p. 207-211). For this reason, diagnosis of AD requires a thorough understanding of an individual's psychiatric history. (Welsh-Bohmer & Warren, 2006).

Scores on the mini mental state examination (MMSE) serve as a reliable global measure of cognitive impairment and are often used clinically (Jefferson et al. 2002). Individuals with AD typically decline by 10% on their MMSE score each year, although this relationship between dementia severity and score on the MMSE is not exactly linear (Morris, 1993). Though the MMSE serves as a global measure of cognitive impairment, specific profiles on this test are more prototypic of an AD profile. For example, Jefferson and colleagues (2002) studied individuals with AD as well as individuals with other types of dementias. They found that individuals with AD scored comparatively worse on measures of temporal orientation and declarative memory, as compared with individuals with other types of dementia. Temporal orientation scores were correlated with performance on a naming test as well as scores on a verbal free recall and delayed recognition memory test.

Although global measures of impairment are used clinically to ascertain the level of dementia, specific areas of cognitive impairment are obtained to differentially diagnose dementia of the Alzheimer's type. Impairment in declarative and semantic functioning in AD is well established (Butters & Miliotis, 1984). Declarative Memory impairments are perhaps the most common and most pronounced evident symptoms. However, this can present itself in very different ways between individuals (Lesak, Howieson, & Loring, 2004, p. 211). For example, due to both impairments in encoding and semantic knowledge, individuals with AD often do not benefit from hearing the gist of the story to serve as a cue for tapping their memory (Nebes, 1992). Additionally, Individuals with AD have smaller learning curves on memory tests, have difficulty encoding new information, and have subsequent low scores on memory tests (Libon et al. 1998). Libon and colleagues (1998) contrasted cognitive test performance and imaging data of individuals with AD and ischemic vascular dementia (IVD). They found that individuals with



AD had a smaller learning curve and performed poorly on a verbal memory test, whereas they had no impairments on a procedural learning test.

Impairment on tests measuring verbal functioning is also evident in individuals with AD. In fact, early in the disease process, deterioration in verbal expression and comprehension is evident. The cause behind this deterioration has been linked to a disruption in semantic knowledge and understanding. This results in difficulty with word generation, loosening of semantic categories, and degradation of concept formation (For review, refer to Lezak, Howieson & Loring, 2004). Passafiume and colleagues examined the disintegration of semantic knowledge in individuals with AD (Passafiume, Di Giacomo, & Carolei, 2006). These researchers conducted their study based on the premise that semantic networks contain information about the world, and are organized hierarchically. These researchers studied the integrity of the semantic networks in AD by giving individuals a word-stem completion task, a task that measures semantic networks and memory. Individuals with both mild and moderate AD performed worse than normal controls on this stem-completion task. The researchers concluded that this performance did in fact represent a disintegration of semantic networks in the brain. Through their work analyzing the responses of individuals with AD on an animal fluency task, Chan, Butters, and Salmon (1997) support this claim. The researchers concluded that semantic knowledge systematically deteriorates as Alzheimer's disease progresses.

Visuospatial abilities in AD are also impaired. Individuals with AD have difficulties with line orientation judgment tasks, constructional tasks such as the WAIS Block Design and the Clock Drawing Test. Additional impairment is seen in object recognition. However, the literature regarding visuospatial functioning in AD is mixed. Though there is undoubtedly a decline in visuospatial ability with AD, this decline is relatively small compared to how individuals with other dementias perform on this cognitive domain (For review, refer to Lezak, Howieson, & Loring, 2004). A study done by Consentino and colleagues (2004) compared

neuropsychological test scores between individuals with AD and individuals with vascular dementia (VaD). Not surprisingly, they found that individuals with VaD scored almost twice as high on tests of lexical/semantic knowledge and delayed recognition memory than did individuals with AD. However, individuals with AD scored almost twice as high on tests assessing the ability to maintain a mental set as well as tests of visuoconstruction. Therefore, although visuospatial impairments may be impaired in individuals with AD, this construct is a relative strength compared with other dementias.

Impairments in executive control have also been linked to individuals with AD. One study has found that 64% of individuals with AD have executive dysfunction (Swanberg, Tractenberg, Mohs, Thal, & Cummings, 2004). Executive functioning impairment in AD presents itself by way of decreased social competence, perseverative and intrusive behaviors, and difficulty with sequencing. Additionally, general cognitive slowing results in slower reaction times (Lesak, Howieson, & Loring, 2004).

In sum, the literature indicates that a constellation of cognitive symptoms are evident in AD. Although global cognitive decline is apparent, discrete cognitive domains are also impacted. Such domains include memory, semantic functioning, visuospatial ability, and executive control. These symptoms generally deteriorate over time and impact an individual's ability to perform functional tasks necessary for daily living.

#### Functional Components of AD

Integral to the diagnosis of AD is a concomitant decline in functional abilities. In fact, approximately 37-49% of individuals with AD who live in the community are dependant on someone else to aid in meeting their daily needs (Aguero-Torres, Fratiglioni, Guo, Vitanen, & Winblad, 1998). Greater functional dependence leads to institutionalization, increased healthcare expenditures, decreased quality of life, disintegration of self-identity, and a burden on caregivers (Yu, Kolanowski, Strumpf, & Eslinger, 2006). Studies show that individuals with mild AD have

difficulty with more complex functional tasks ((Feldman, Van Baelen, Kavanagh, & Torfs, 2005)). Such tasks are often referred to as “instrumental activities of daily living (IADL)”. These tasks include managing finances, taking medications, preparing meals and doing household chores, and driving a car. One study by Yu and colleagues (2006) found that global cognitive scores account for approximately 25-50% of the IADL variance. They found that individuals with mild AD lost the ability to perform more difficult tasks, such as remembering shopping lists, before losing the ability to perform simple activities of daily living (ADL), such as dressing and bathing.

#### *Relationship between Cognition and Function*

Though the relationship between cognitive status and functional status is not absolute, decline in cognitive function typically is accompanied by a decline in IADLs. A study by Feldman and colleagues (2005) demonstrated a correlation between cognitive decline, as measured by the MMSE, and functional decline over a one-year study (Feldman, Van Baelen, Kavanagh, & Torfs, 2005). Additionally, they found that individuals with lower global cognitive scores declined in functional abilities more rapidly. This functional decline also led to an increase in caregiver burden. These researchers found that the loss of functional abilities in AD was hierarchical, beginning with the loss of more complex functional abilities such as organizing finances or driving a car. Basic functional tasks, such as grooming, decline later.

Jefferson and colleagues (2006) studied the relationship between functional abilities, as defined by an individual’s ability to perform IADLs and ADLs, and cognitive abilities on neuropsychological tests. These researchers posited that global cognitive status is the only predictor of IADL and ADL dependence. Despite this, its inclusion in a prediction model obscures the various cognitive components that underlie each functional task. When global cognitive status was removed from the equation individuals were impaired on measures of memory, semantic knowledge, and executive control. However, object recognition measures

were ultimately associated with significant impairment on functional tasks for individuals with AD (Jefferson, Barakat, Giovannetti, Paul, & Glosser, 2006). Conversely, other researchers have found different cognitive domains that predict functional status (Matsuda & Saito, 2005). The conflicting results among studies highlight the mixed opinions regarding the predictive value of the MMSE and various cognitive domains on functional status.

Several studies have highlighted executive function, memory and visuospatial abilities as factors that predict functional performance (For review, refer to Yu et al., 2006). However, in one study by Yu and colleagues (2006), visuospatial abilities were inconsistently related to functional performance. Executive control may also impact functional ability. Yu and colleagues define executive control as the cognitive skills that allow individuals to organize, coordinate, and sequence goal-directed behaviors. In one study, executive dysfunction explained 17% of the variance in IADL performance in people with AD (Boyle, Malloy, Salloway, Cahn-Weiner, Cohen, & Cummings, 2003). The inclusion of memory loss as a factor predicting functional performance in AD is not surprising given that it is a hallmark feature of AD. Still, explicit memory impairments have been linked to behavioral changes, greater dependence on others, and caregiver burden (Avila, Bottino, Carvalho, Santos, Seral, & Miotto, 2004). In fact, one study by Avila and colleagues (2004) demonstrated that implicit memory training can lead to an increase in memory ability on specific functional tasks. This study adds to the conflicting data regarding the link between cognition and functional impairment. However, perhaps this conflict is due to the variability in functional tasks. Some tasks such as bill paying require a great deal of cognitive processing whereas tasks such as grooming are often rote procedures.

The predictive power of global cognitive status on functional ability is both variable and deficient. Yu and colleagues (2006) state that global cognitive impairment accounts for only between 25 and 50% of the variance in instrumental ADLs. Still, a study by Loewenstein and colleagues (1995) found that only 9-34% of the variance in functional measures was accounted

for by cognitive scores (Lowenstein, Rubert, Arguelles, & Duara, 1995). Perhaps this lack of predictive power in functional status can be accounted for by other variables. One consideration is the sizeable differences among functional tasks (e.g. ADL vs. IADL), with each functional task necessitating the use of different cognitive foundations. It is possible that each functional task needs to be examined separately to better understand how it is impacted by cognitive decline. Still, when functional tasks are examined separately, the relationship to cognitive status is unclear. One reason why there might be variability is the measurement tool used to examine function.

### *Measurement of Function*

There are multiple ways of measuring functional capacity, and consequently variation in functional status scores based on the method used to collect the information. The two primary methods of measuring functional ability are using caregiver accounts of patient functioning and directly assessing patient functioning. Caregiver accounts of patient functioning are typically gleaned from a questionnaire such as the Lawton and Brody Instrumental Activities of Daily Living Questionnaire (Lawton & Brody, 1969). Research has shown that caregiver accounts can be confounded by their level of burden in treating the patient as well as their own levels of depression (DeBettignies, Mahurin, & Pirozzolo, 1990). Despite this it is a common approach to functional analysis as it allows for the assessment of activities in day to day life. Family members and caregivers are able to provide accounts of the patient as they perform in their natural environment.

Functional ability is also measured by having patients participate in laboratory controlled simulated activities. While this technique is questioned for its potential lack of ecological validity, it allows for the careful analysis of how patients complete the task and what problems they encounter. This allows for control and manipulation of variables for both qualitative and quantitative assessment of such behaviors. One assessment technique used by Giovannetti and

colleagues (2002) measures the types of errors made by individuals with AD as they complete specific functional tasks such as making coffee and toast (Giovannetti, Libon, & Hart, 2002). Another method used by Schultheis (Schultheis, Himmelstein, & Rizzo, 2002) is to use a virtual reality driving simulator to assess driving performance in a safe manner. This method of assessment is particularly useful because it allows for the interpretation of numerous variables while studying driving behavior in a safe but challenging manner (Schultheis et al., 2002).

One study by Farias and colleagues (2003) studied the relationship between caregiver accounts of functional status and the patient's functional performance scores on a laboratory test (Farias, Harrell, Neumann, & Houtz, 2003). These researchers found that the correlation between these two measurements was  $-.66$ , indicating a moderate but not absolute relationship. These researchers added that beyond the type of measurement, the amount of cognition required in each functional task also creates variability between functional tasks. Functional tasks that have a large cognitive component are more strongly correlated with neuropsychological test scores than those tasks that are more performance driven.

In sum, one challenge in studying functional performance is the variability in measurement tools. Additionally, the link between function and cognitive status is not entirely understood. This relationship is altered by both the cognitive domains that are examined as well as the specific functional task examined. However, even when a single functional task is examined, there is still not a direct relationship to cognitive status. Therefore, the contribution of other factors needs to be considered in order to fully understand the changes in functional ability.

#### Unawareness in AD

Lack of insight and unawareness is a symptom for individuals with Alzheimer's disease (Ready, Ott, & Grace, 2006). In fact, many researchers believe that lack of awareness is one of the clinical features of Alzheimer's disease (Feher, Mahurin, Inbody, Crook, & Pirozzolo, 1991; Green, Goldstein, Sirockman, & Green, 1993). This symptom is perhaps more common in

Alzheimer's disease than it is in other progressive neurological disorders (Ansell & Bucks, 2006). Terms used to describe a lack of awareness of oneself include, 'lack of insight, unawareness, metacognitive unawareness, and anosognosia'. The term 'anosognosia' was first introduced by Babinski (1914) to describe the lack of knowledge about the existence of a neurological disease. These terms are often used interchangeably and refer to the absence of insight into physical, neurological, and/or cognitive deficits (Ansell & Bucks, 2006). For the sake of continuity, it will be referred to as 'unawareness' throughout this paper. Unawareness is understood to be a variable entity, varying according to degree, type, domain effected, temporal stability, and its relationship to the progression of the disease (For review, refer to Ansell & Bucks, 2006).

#### *Variability of Unawareness*

Unawareness can also be characterized in terms of partiality, extension, temporal stability and specificity (Ownsworth, Clare, & Morris, 2006; Schacter & Prigatano, 1991; Weinstein, 1991). Partiality refers to the fact that individuals range in the degree of unawareness in regards to their deficits. Individuals with complete unawareness have no awareness of functional deficit, whereas partial awareness reflects a limited awareness of deficits (Prigatano, 1991). Extension refers to the way in which their awareness is affected. For example, some individuals may understand that they have a specific deficit but they may be unable to understand the consequences. Conversely, they may not be able to monitor the problem in their daily lives (Crosson et al., 1989). Unawareness also varies temporally. Some individuals display unawareness early in the course of the disease when they demonstrate relatively intact cognitive skills. However in some cases, as the disease progresses, their awareness increases (For review, refer to Ownsworth et al., 2006).

Unawareness can also range in 'specificity'. This means that it could be domain-specific and limited to one area of functioning, or it could be global and exist across abilities (i.e. Toglia

& Kirk, 2000). Some researchers believe that the specificity of awareness can be divided into four main levels (Clare, 2004a). The most basic level is when an individual is in a persistent vegetative state or coma, and therefore has no awareness. The next level is domain-specific unawareness which relates to one specific function. Within this level there are indications that there are differences between explicit and implicit awareness in individuals with advanced AD. In one study, individuals with advanced AD looked in the mirror to view their own reflection. Although these individuals did not explicitly recognize themselves, they demonstrated behaviors indicating self-recognition on an implicit level. (Bologna & Camp, 1997).

According to Clare (2004a), the third level of unawareness is termed 'executive' unawareness. Here, the individual is unable to adequately regulate all behaviors, and the awareness of such regulation is disturbed. Finally, general unawareness refers to all areas of functioning. Clare (2004a) posits that any level of unawareness may be present despite normal performance on cognitive tests. The relationship between cognition and unawareness is not well understood. In fact, some individuals report memory deficits but deny any impact of this impairment on functional status. Others avoid specific tasks meanwhile denying that they have any cognitive impairment (Agnew & Morris, 1998).

### *Theoretical Models of Unawareness*

Numerous models provide explanations for unawareness in AD ranging from neurological causes, changes in cognitive functioning (i.e. Agnew & Morris, 1998), and psychological defense mechanisms (i.e. Clare, 2004a). The variability in models serves as evidence that unawareness is still not fully understood. Several models attempt to understand unawareness in AD from a biopsychosocial perspective, addressing defense mechanisms and social roles (For review, refer to Clare, 2004a). Although biopsychosocial models attempt to understand unawareness from a holistic perspective, they have numerous limitations. The primary limitation is that measuring all



of these factors is impractical and unfeasible. Therefore, more parsimonious models attempt to understand unawareness from neuroanatomical and cognitive perspectives.

In 1989, McGlynn and Schacter proposed the dissociable interactions and conscious experience (DICE) model of unawareness. According to this model, the conscious activating system (CAS) in the parietal lobe (Schacter, 1990) is the area of global awareness. Damage to this region results in global awareness deficits. Domain-specific awareness deficits result from a disconnection between the CAS and various cognitive domains, including the central executive system (CES), found in the frontal lobes (Schacter, 1990). This model forms the basis for a subtype of unawareness proposed in a model by Agnew and Morris (1998).

Another model proposed by Agnew and Morris (1998) and later expanded upon by Morris and Hannesdottir (2004) attempted to address the limitations of the DICE model. They believed that the DICE model failed to address the role that memory deficits play on the degree of unawareness. Their model is called the cognitive awareness model (CAM)(For review, refer to Figure 1). The CAM model is used to explain how cognitive impairment might result in unawareness at various stages of cognitive processing. Though memory impairments might sustain unawareness, they are not necessarily causal of unawareness. Morris and colleagues posit that perception of success and failure is based on an appraisal system of behaviors. Unawareness results when this system is disrupted (Agnew & Morris, 1998; Morris & Hannesdottir, 2004).

According to Agnew and Morris (1998) and Morris and Hannesdottir (2004), information enters short term memory where it is experienced as new information and it is consciously processed. It then goes into long term memory where it is again consciously experienced as a personal event. According to this model, new events are fed to a comparator mechanism, an aspect of the central executive system found in the frontal lobes. The comparator mechanism compares this new event to previous events and knowledge from the personal knowledge base, an aspect of semantic memory. If there is a mismatch between the current event and that stored in

the personal knowledge base, the cognitive awareness system in the parietal lobes is then given information about the discrepancy. For example, if an individual experiences new difficulty with their memory and have not previously experienced this problem, the comparator mechanism will note a discrepancy between the new event and the information stored in the personal knowledge base. The conscious awareness system will receive this input and the person will then become aware of this discrepancy.

According to Agnew and Morris (1998), there are three different types of unawareness: Mnemonic, executive, and primary. Though there appears to be variability in the specific type of unawareness typical in Alzheimer's dementia, researchers believe that mnemonic unawareness is the most common type at the mild stage in the disease process (Agnew and Morris, 1998; Ansell and Bucks, 2006). According to Ansell and Bucks (2006), mnemonic unawareness in AD is particularly common for individuals with mild AD due to the medial temporal lobe and hippocampal pathology disrupting semantic memory and therefore an individual's ability to encode new information. Mnemonic unawareness results as a consequence of a disruption between the comparator mechanism in the central executive and the personal knowledge base, a component of semantic memory. When this occurs, a memory error is detected and the individual consciously is made aware of such an error. However, due to a disruption between the comparator mechanism and the personal knowledge base, the individual is not made aware that this memory error is a different and unique event. Their personal knowledge base is not updated and essentially the individual forgets that they are forgetting. According to this model, the comparator mechanism remains connected with implicit memory. As such, individuals can be implicitly aware of the discrepancy between their current and previous state. Agnew and Morris note that the high incidence of depression in mild AD accounts for this implicit knowledge that one's memory is failing.

Support for this model comes from Souchay and colleagues, who add that individuals with mild AD show initial awareness when faced with a lapse in memory (Souchay, Isingrini, Pillon, & Gil, 2003). However, they are not able to form a lasting memory of such difficulty despite often exhibiting symptoms of depression. Findings from a study by Ansell and Bucks (2006) also support this model. Still other researchers would argue that this model of unawareness is incomplete, as it fails to account for the influence of defense mechanisms and social roles on awareness (Clare, 2004a). Despite these potential limitations, this model has many strengths making it the preferred model for this study. The underpinnings of unawareness according to this model are discrete and measurable. Additionally, this model attempts to understand unawareness from a cognitive and neuroanatomical prospective. This is particularly logical when examining AD, which results from brain pathology. Therefore, this study will use the most parsimonious model of unawareness and will therefore avoid addressing social or psychological prospective.

#### *Measurement of Unawareness*

The prevalence of unawareness for people with Alzheimer's disease in the literature is variable. Much of the variability comes from the measurement techniques used to examine unawareness (Agnew & Morris, 1998). The degree of unawareness is typically defined by the measurement technique used to examine it. Whereas some studies have reported the incidence of unawareness to be as high as 80% in a sample of individuals with Alzheimer's disease (Sevush & Leve, 1993), others report a prevalence of 20% (Migliorelli et al., 1995). This variability is at least in part due to the difference in assessment measures used, as each type of measurement taps different features of unawareness (Agnew & Morris, 1998).

The degree of unawareness is typically measured in one of three ways: (1) a clinician rating of patient unawareness; (2) The discrepancy between the patient's self report of functioning and a reliable informant's assessment of their functioning; and (3) on-line

assessments of awareness. This includes the discrepancy between the patient's self rating of their performance and their actual performance on a task, as well as the analysis of error detection and correction. A combination of the aforementioned measurements can also be used. The operational definition of unawareness changes as a function of the measurement type. Therefore, the type of measurement instrument used has an impact on the findings for each study (For review, refer to Clare, 2004b).

Clinical ratings are used as measures of unawareness (i.e. Lopez, Becker, Somsak, Dew, & Dekoshy, 1994). Clinician ratings include structured and unstructured interviews as well as patient chart reviews. One benefit of this technique is that the clinician can explore each area in depth for a greater understanding of the patient (Clare, 2004b). However, this technique assumes that the social interaction between the clinician and the patient does not influence what the patient reports. Another problem with this technique is that it assumes that unawareness is a symptom that can be rated and classified in a straightforward and reliable manner (Clare, 2004b).

Many studies employ the patient versus reliable informant discrepancy approach to measuring unawareness. When using this technique, the definition of unawareness becomes the discrepancy between the patient's ratings of their own functioning compared with their informant's rating of their functioning on the same measure (Clare, 2004a). While many studies have used this technique to examine unawareness for functional tasks, the majority of studies have used this technique to examine memory (For review, refer to Clare, 2004b). These measures are advantageous in that informants such as caregivers give accounts of the patients as they perform in their daily lives. Therefore, this measurement may appear more relevant than measures that are taken in a clinical setting. Additionally, these measures can examine unawareness in the context of a variety of settings so as to better understand a myriad of cognitive and functional domains. This can provide for a more detailed understanding of patient unawareness (Hardy, Oyeboode, & Clare, 2006). Studies have also found that patients tend to

overestimate their performance whereas caregivers tend to underestimate their performance. One drawback to using this approach is that as caregiver burden and depression increase, estimation of the patient performance changes (DeBettignies et al., 1990). Clare (2004b) cautions that this type of measurement requires a careful selection of questions that are given to patients and informants.

Another way of measuring unawareness involves comparing the patient's assessment of performance to their actual performance. This measurement technique examines 'on-line' awareness, or the monitoring of progress as an individual performs a task. Therefore, this technique works under the assumption that individuals are able to monitor their current functioning. Two methods can be used in this approach. Individuals can predict their performance in a task prior to experience with the task or they can predict performance after they have had some experience. One study using this technique found that approximately 50% of individuals with AD studied demonstrated some level of unawareness (Anderson & Tranel, 1989). This approach leads to a high number of individuals with AD that over estimate their performance on a task (Clare, 2004b). Cavanaugh (1989) studied individuals using this method. The results of this study suggest that prediction accuracy is best for everyday tasks rather than laboratory tasks. Accuracy of prediction increased as a function of familiarity with a task. This finding suggests that prediction accuracy will be better for more well known tasks, and the validity of the prediction is questionable for unfamiliar tasks (Clare, 2004b; Hardy, Oyebode, & Clare, 2006). Therefore, when unfamiliar tasks are used, perhaps post task perception of performance should be used as a more accurate assessment of unawareness.

On-line assessment of unawareness can also be done by measuring an individual's ability to recognize their errors. This approach is favored by some researchers because it minimizes the reliance on expressive or receptive language abilities, which are often affected by brain pathology (Hart, Giovannetti, Montgomery, & Schwartz, 1998). Hart and colleagues (1998) describe one

technique which has individuals perform a series of functional activities such as making coffee and toast. Unawareness is measured by the number of errors identified. Although this procedure has been standardized and assessed for ecological validity, the drawback is that these tests do not measure all functional tasks. Therefore, because different measurement techniques assess different types of unawareness, this technique could not easily be used as a comparison of unawareness with another functional task.

Different measurement techniques and therefore different operational definitions of unawareness yield inconsistent findings (Agnew & Morris, 1998). One solution to this problem is to use multiple techniques to measure unawareness. However, these techniques yield different levels of awareness which are often uncorrelated, despite the fact that they presumably measure the same construct (Clare, 2004b). For example, Markova and Berrios (2001) have proposed that the 'object of insight', or the assessment measure used to measure awareness, causes the variation in unawareness. Therefore, careful consideration should be made when selecting the appropriate measurement technique for examining unawareness. The assessment tool selected should match the domain being investigated.

### *Cognition and Unawareness*

The literature is mixed regarding the relationship between unawareness and global cognitive status in AD. Whereas many studies have found a significant relationship between global cognitive status and unawareness (i.e. Kashiwa, Kitabayashi, Narumoto, Nakamura, Ueda, & Fukui, 2005), not all studies have yielded this finding (Hardy et al., 2006). One study by Kashiwa and colleagues (2005) assessed individuals with AD and found that level of awareness correlated negatively with the Mini Mental Status Examination (MMSE). In this study, as cognitive status declined, the level of unawareness increased. Additionally, as the severity of dementia and unawareness increased, functional status declined. Kashiwa and colleagues found that unawareness correlated to specific activities of daily living and specific neuropsychological

assessment measures. They concluded that unawareness is related to global disease progress, but that it is heterogeneous between individuals (Kashiwa et al., 2005). A study by McDaniel and colleagues found similar results (McDaniel, Edland, Heyman, and the CERAD Clinical Investigators, 1995).

Presumably, individuals with more cognitive impairment would have a higher degree of unawareness. However, many studies report findings that are contradictory to this presumption. Hardy and colleagues (2006) examined individuals with mild and moderate AD on the MMSE, memory tests, and on tests measuring unawareness. They found that performance on the MMSE was significantly correlated with performance on the memory tests. However, there was no significant difference between individuals with mild and moderate dementia on measures of unawareness. Therefore, there was no correlation between global cognitive status and level of unawareness. If global cognitive level is not consistently related to unawareness, perhaps other factors impact unawareness.

Rather than the global cognitive score, the degree of memory impairment has been found to correlate with unawareness. However, this memory impairment is associated with a maintenance factor with unawareness rather than a precipitating factor (For review, refer to Agnew & Morris, 1998). Whitlock (1981) posed that individuals with poor episodic memory are less likely to remember that they have memory impairment. Others agree with this proposition, finding that unawareness is significantly associated with one aspect of memory functioning; the number of false positives on a recognition test (Reed, Jagust, & Coulter, 1994). However, others fail to find the association between memory and unawareness. Instead, many researchers highlight the impact of frontal lobe impairment on unawareness (i.e. Reed et al. 1994).

Executive symptoms such as impaired reasoning, problem solving, and mental flexibility have all been implicated in various disorders where individuals demonstrate unawareness, including AD (Lopez et al., 1994). Through a neuroimaging study, researchers have found a

connection between unawareness and the frontal lobes for individuals with AD (Reed, Jagust, & Coulter, 1993). Specifically, individuals who had unawareness for memory loss had hypoperfusion of the right dorsolateral frontal. However, this was not correlated to dementia severity. Findings from Derousne and colleagues (1999) were not as conclusive regarding the role of the frontal lobes on unawareness. They found that patients with mild unawareness had more clinical symptoms of a frontal lobe dysfunction than individuals with no unawareness (32% versus 16%). However, this difference was not statistically significant. These studies add to the literature which suggests an indirect and poorly understood relationship between cognition and unawareness.

Lopez and colleagues (1994) attempted to further understand the relationship between unawareness and frontal lobe impairments as well as other cognitive domains. These researchers ran a stepwise regression to determine what factors are most associated with patient unawareness. Results revealed that age and executive functions were the strongest predictors of unawareness. Executive functions were the best predictors of which individuals would have awareness of their illness. However, conclusions also supported that as disease progressed, level of awareness dropped. The researchers suggest that the lack of awareness seen in some individuals with AD is related to the impairment of CES functioning, or working memory. Lopez and colleagues are clear in their claim that this does not mean that frontal damage is a predominant symptom of AD, rather that there may be a greater distribution of pathology in individuals with higher levels of unawareness (Lopez, Becker, Somsak, Dew, & DeKosky, 1994).

In sum, some research shows a direct relationship between global cognitive status and unawareness, while other studies show contradictory results. Some studies have shown that memory impairments can maintain a greater degree of unawareness. Still other studies highlight frontal lobe impairment as contributory to unawareness. Greater frontal lobe impairment could be indicative of a greater distribution of pathology in the brain. The discrepancy among studies



is an indication that the underlying constructs of unawareness are poorly understood. Perhaps it is more appropriate to examine the impact of unawareness on functional ability in AD.

### *Function and Unawareness*

Individuals with AD have cognitive decline accompanied by a simultaneous decline in functional abilities. The relationship between cognition and function is not direct, suggesting other factors that impact functional ability. Still, research shows that as dementia progresses, activities and independent activities of daily living, such as grooming and meal preparation, decline (Feldman, Van Baelen, Kavanagh, & Torfs, 2005). As previously stated, decline in cognitive status alone does not account for such changes. Unawareness of deficits is associated with increased dependence and safety concerns (Giovannetti, Libon, & Hart, 2002).

Research has shown that unawareness contributes to functional decline (i.e. Wild & Cotrell, 2003; Pachana & Petriwskyj, 2006) however the relationship is not well understood. This is perhaps due to the great degree of variability evident in both unawareness and functional ability measured in individuals with AD. Additionally, one study found that individuals with AD have variable levels of unawareness depending on the domain assessed (Ott et al. 1996). One way to address that limitation is to study functional abilities independently.

One specific functional activity studied extensively in individuals with AD is the ability to drive a car. This is in part due to the importance that individuals place on the ability to drive. Driving provides people with a both a means of necessary transportation, but it also promotes the feeling of independence and identity. Driving is also an activity that requires intact abilities through multiple domains (Pachana & Petriwskyj, 2006). It is therefore a complex activity that becomes troublesome for many older adults. Research on individuals with AD shows that these individuals do not consistently display awareness regarding changes in their ability to drive. In fact in one study 38% of individuals with AD still considered themselves to be safe drivers despite failing a road test. This unawareness can compromise the safety of themselves and others

and has been linked to an eightfold increase in accident rates for individuals with AD compared to healthy controls (Friedland et al 1988). It also decreases the likelihood that these individuals will be able to live independently (Wild & Cotrell, 2003). In addition to cognitive status, researchers posit that individual awareness and willingness to impose driving restrictions is necessary for safe driving. Therefore, unawareness plays a role in safe driving behavior, though it is poorly understood.

#### Comparison of Function and Unawareness in Healthy Older Adults

In contrast to individuals with AD, healthy community dwelling older adults have been found to self impose changes in driving as they deem fit, modifying, restricting, and stopping driving based on their own judgments (Wild & Kaye, 1991). A study by Wild and Kaye (1991) found that older adults reported making modifications to their driving for reasons such as having slower reaction times, being concerned for their safety, or simply feeling too old. The reported changes in driving behaviors implied that these individuals had insight into their functioning, and were consequently maintaining their safety.

Older community dwelling healthy adults have been defined as seniors in the community who may be experiencing age-related changes in vision, range of motion, slowed speed of processing, and medical conditions (Rudman, Friedland, Chipman, & Sciortino, 2006). By the year 2030, the number of seniors aged 65 and older is projected to double and reach 71 million, adding a substantial volume to the number of drivers on the road with potential age-related declines. Despite potential impairments, there is no national policy regulating seniors from driving at a certain age, as a direct relationship between age and traffic safety has not been found. Instead, the current national policy relies on the natural self regulation that appears inherent with healthy aging (in Donorfio, D'Ambrosio, Coughlin, & Mohyde, 2009). Donorfio and colleagues (2009) have defined self regulation as the alteration of driving behavior as one adjusts to changes in health or ability. They note that this self regulation is gradual and common in healthy

community dwelling seniors. Ball and colleagues agree, adding that the majority of seniors they interviewed reported reducing night driving and avoiding high traffic roads over time with increased age (Ball, Owsley, Stalvey, Roenker, Sloane, & Graves, 1998). Other conditions in which self regulation is common include driving in the rain and driving in situations where merging is required (Charlton, Oxley, Fildes, Oxley, Newstead, Koppel, & O'Hare, 2006). When asked why they regulated their driving under certain conditions, seniors in one study most commonly reported that it was their personal preference to do so in response to comfort and confidence level (Charlton et al., 2006).

While age itself is linked to driving ability and self regulation, there is not a direct correlation between age and driving. One study by Donorfio and colleagues (2008) examined other factors that contribute to changes in self regulation in driving as a function of age. Through surveys and focus groups, they found the interaction between one's perceived health and age was the best predictor of self regulation. The researchers concluded that the interaction between age and health directly impacted enjoyment and confidence in driving skills, thus impacting one's driving practices. Work by Anstey and colleagues support this claim, adding that an individual's self-rated health and perceived cognitive abilities were better predictors of driving cessation than documented medical or sensory functioning (Anstey, Windsor, Luszcz, & Andrews, 2006). In sum, a senior's perception of their own health impacts their perception of their driving, and therefore their driving decisions, with age.

In another study, one's perception of the impact of cognitive changes on their driving ability precipitated their decision to self restrict their driving. In this study, Ross and colleagues (Ross, Clay, Edwards, Ball, Wadley, Vance, et al, 2009) measured visual processing speed. They found that individuals at higher risk for crashes due to changes in visual processing speeds regulated their driving to a greater extent than those with lower crash risks. The researchers concluded that individuals with reduced visual processing speeds were aware of such deficits,

and reportedly regulated their driving on their own volition. Results from this study and one conducted by Ackerman, Edwards, Ross, Ball, & Lunsman (2008) suggest that seniors' perceptions of driving behaviors were accurate, as those at higher risk for crashes regulated their driving to greater extent than those at lower risk. Work by Okonkwo and colleagues (2007) also supports this claim. These researchers examined licensed seniors in the community on factors such as driving habits, demographic information, and cognitive measures (Okonkwo, Wadley, Crowe, Roenker, & Ball, 2007). They found that drivers with more impaired visual processing reported restricting their driving to a greater degree than those who did not have such impairments. They concluded that older drivers at increased risks for crashes due to changes in visual attention were more likely to self regulate as a safety measure. In sum, seniors with greater impairments in cognitive abilities such as visual processing were consistently found to self-regulate driving more so than those with less impairments.

Despite research showing that seniors naturally self regulate driving, some seniors in the community as well as researchers express concern about an individual's ability to monitor and self regulate their driving as they age, noting that there are many factors that impact an individual's ability to self regulate driving (Rudman et al., 2006). Freund and colleagues (2004) examined seniors in the community who had been referred for a driving evaluation due to varying but increased safety risks behind the wheel (Freund, Gravenstein, Ferris, Burke, & Shaheen, 2004). Participants in their study were given cognitive tests, underwent a virtual reality driving simulator, and were asked various questions about their driving behaviors. The evaluators found that individuals in their study, despite being at higher risk for crashes as measured by a driving referral as well as performance on the virtual reality driving simulator, rated themselves as being better drivers than their peers. In fact, almost forty percent of the individuals in the study who were deemed 'unsafe drivers' via the driving simulator rated themselves as the same as or better drivers than their peers. This suggests that while many

seniors are able to self regulate their driving and remain safe behind the wheel, those at greater risk may be unaware of any changes in their driving and therefore less likely to self regulate their driving. The researchers suggest that self regulation of driving is mediated by awareness as well as a variety of coping mechanisms meant to preserve ones sense of self-esteem, independence, and mobility.

In attempts to understand the factors that contribute to self regulatory driving behavior in seniors, Donorfio and colleagues (2009) examined surveys from 3,824 healthy seniors above the age of 50 years old in the community. Similar to results from previous studies, they found that seniors viewed driving as a form of maintaining independence that kept them connected to the rest of society. Seniors in their study expressed self awareness regarding changes that occurred over time. They noted that self regulation occurred gradually over time and consisted of both attitudes and behaviors that allowed them to compensate for obvious age-related changes. Four specific variables contributed to this self regulation, the first being the observation that age contributed to changes in driving abilities, which in turn decreased confidence in driving. The second factor that contributed to self regulation was the role that the car played on one's independence and connection with society. Self worth was the third variable, as being able to continue driving added to an individual's perceived independence and perceived worth. Lastly, the practical role that the car plays and the lack of alternative transportation impacted self regulatory behaviors. Results from surveys in this study revealed that physical changes first impacted self regulation, though psychological factors as a result of these physical changes then also impacted driving. The psychological factors such as maintaining self worth, independence, and remaining connected strongly influenced an individual's self regulatory behavior. Rudman and colleagues (2006) conducted a similar study examining pre-seniors, seniors, and ex drivers in the community. Results from information gleaned from focus groups were similar to the

previous study, with themes such as decreased confidence, comfort, and the importance of the car for transportation emerging as important factors impacting self regulation.

In sum, numerous factors appear to impact an individual's awareness and willingness to self regulate driving with age. Perception of one's health status, cognitive functioning, and physical functioning are some motivating factors for self regulating driving. Self regulation in older adults is reportedly common and gradual over time. It underlies the current national policy which relies on seniors naturally self regulating their driving as they deem appropriate. Despite this, numerous factors appear to influence self regulation in seniors, including the important role that driving plays on an individual's self worth and mobility. While the exact relationship between self awareness and self regulation in driving for healthy seniors is not entirely understood, there appears to be a strong link that does not appear evident in individuals with mild Alzheimer's dementia. Understanding self awareness and self regulation in healthy older adults will provide a foundation for which to understanding how brain pathology results in disrupted self awareness and regulation.

#### Measuring Unawareness and Function in AD

Lack of self awareness impacts self regulation in individuals with AD, resulting in potentially unsafe attitudes and behaviors. As such, it is important to be able to measure unawareness in AD. Giovannetti and colleagues (2002) have examined unawareness of deficits through 'on-line' error detection and correction. Awareness is measured as an individual is actively involved in a task, thereby giving researchers greater understanding regarding the relationship between awareness and function. They have found that individuals with dementia identified and corrected significantly less errors on this naturalistic action test than did age matched controls. This finding was true even for individuals with mild AD. These results suggest that individuals with mild dementia make errors in their daily functional tasks, which

they do not consistently identify or correct. This, in turn, compromises their safety and leads to greater dependence on caregivers.

Safe driving behaviors as well as performance on tasks of daily living are crucial for patient independence. The ability to drive is both an important and potentially dangerous practice, and the driving simulator provides a safe format for which to examine this behavior while providing individuals with challenging and realistic driving scenarios. Using an on-line assessment of driving such as a driving simulator provides another way of examining driving beyond using patient/ caregiver discrepancy scores. On-line assessments also allow for direct comparison of the relationship between function and awareness. In this way, researchers can better understand the relationship between cognition, awareness, and function across multiple domains. To date, the literature suggests that cognitive status only explains some of the variability in functional status. Perhaps level of unawareness is another factor that needs to be examined when examining functional ability in AD.

### Conclusion

Individuals with mild AD experience cognitive changes that are well established and understood in the dementia literature. These individuals also experience a change in functional status, which is more idiosyncratic and therefore more difficult to measure. Nonetheless, it is these functional changes that ultimately impact patient safety and independence, causing individuals to become dependant on others. Therefore, it is imperative to understand the variables that predict these functional changes. Research shows that cognitive status and various neuropsychological measures predict some of the variability in functional status, but much of the changes are left unexplained.

Unawareness in AD is also linked to changes in functional status, though the relationship between these variables is not well understood. The lack of understanding between unawareness and functional status is perhaps due to the variability within each construct. Whereas functional

status changes are idiosyncratic and impacted by assessment techniques, the same is true for changes in unawareness. Unawareness is not a global construct, nor is its relationship to cognitive or impact on functional status well understood. In order to examine this relationship, all of the variables have to be explicitly operationally defined. Additionally, understanding the link between unawareness and functional ability in healthy controls is crucial in order to better understand the specific impacts of mild AD on this relationship. As such, this study aimed to examine healthy controls as well as individuals with mild AD on two specific measures of functional ability. One specific measure was driving performance on a virtual reality driving simulator, which was administered in the laboratory. The other measure consisted of the participant's ability to perform independent activities of daily living, as reported by reliable informants. This study therefore utilized two distinct methods of measuring functional abilities and their corresponding measures of unawareness.



### The Current Study

This study aimed to examine the relationship between cognition, unawareness, and functional ability in healthy seniors as well as for individuals with mild AD. The main hypothesis of this study was that controlling for cognitive ability, there was a relationship between unawareness and functional ability. The literature suggests that unawareness varies depending on how functional ability is measured, so this study selected two very different but equally as important measurements of functional abilities. Driving ability on a virtual reality driving simulator measured the functional ability of driving in real time. This task was selected for both the importance that individuals place on this activity as well as for the variety of safety concerns that arise while driving both in seniors as well as for individuals with AD. Driving ability was measured by a virtual reality driving simulator, so as to expose individuals to challenging and realistic driving scenarios while keeping them out of danger. This assessment tool was used as a way of testing driving abilities in real time, so as to better understand the driving behaviors in individuals with AD. Using this technique also allowed for an immediate way of testing individual's unawareness level without relying heavily on memory. Immediately before and after the driving simulator, participants were asked to rate their performance. The primary analysis examined performance following exposure to the driving simulator. This perceived performance was compared to their actual performance to obtain an unawareness score specific to the driving measure.

In a clinical setting, reliable informants are often asked to fill out a questionnaire (IADL questionnaire) which assesses the individual's ability to perform specific functional tasks. Tasks assessed include: Ability to use the telephone, shopping, food preparation, housekeeping, laundry, use of transportation, medication management, and the ability to manage their own finances. This measure is the conventional assessment technique used to glean information about functional ability in clinical settings, and was therefore be used in the present study.

Unawareness scores were obtained by having the participant complete their own form, and then contrasting the participant's total score with the reliable informant's total score.

The literature also suggests that specific cognitive constructs are related to functional ability in individuals with AD. This includes performance on tests of memory, executive function, and visuospatial abilities. As such, this study measured cognitive performance on these domains. This study controlled for the participant's performance on cognitive measures and examined the relationship between unawareness and function. The study design was correlational using first order correlations in a partial correlational model.

### Aims

*Aim 1:* Cognitive scores are typically used in the literature when examining functional abilities.

However, unawareness has also been shown to impact driving performance in both healthy controls as well as for people with AD. The same is true for other functional domains. The primary aim of this study was to examine the relationship between unawareness and functional ability, controlling for performance on specific cognitive tasks. This relationship was examined separately for individuals with AD and healthy controls.

*Aim 2:* The secondary aim of this study was to examine various aspects of unawareness in the context of an on-line functional assessment for both healthy seniors as well as for individuals with mild AD. The virtual reality driving simulator was an unfamiliar task for most if not all of the participants in the study. As such, it provided a way of examining the ability of individuals to change their views about their performance after exposure to a task. Individuals were asked to predict how they would perform on the virtual reality driving simulator after they have been exposed to a practice session but before they start the test itself. They were also asked about their perceived performance after exposure to the test. This study compared predicted performance with actual performance to get a measure of 'predicted awareness'. Performance on the driving simulator was compared to the participant's perceived performance as a task specific measure of

‘unawareness’. Finally, the patient’s predicted performance was contrasted with their perceived performance to get a measure of performance ‘recognition’ (Refer to Figure 3). Analysis of unawareness for healthy controls was used to help establish the proposed relationship between unawareness and function. It was also used to provide a ‘range’ of unawareness in a healthy sample of seniors.

## CHAPTER 2: EXPERIMENTAL DESIGN AND METHODS

Insert Figure 2: Overview of Study Design

### Overview

This main objective of this study was to better understand the role of cognition and unawareness on functional performance in AD. Unawareness is a common symptom of AD, and it is therefore crucial for clinicians to understand how it impacts activities of daily living so as to prolong independence and patient safety. The current study builds on previous research examining the impact of cognition and unawareness on functional ability. Previous research has generally studied cognition and unawareness independently, not accounting for how the combination of variables impact individuals. However clinically, both cognitive decline and unawareness are common symptoms of AD, and need to be examined in conjunction with one another when examining functional tasks.

Another focus of the study was to examine the impact of awareness and cognition on function in healthy seniors. Current laws rely on a healthy seniors' awareness of, and therefore self restriction of, driving in order to maintain safety while also maximizing independence. Despite this, not much is known about the exact relationship between functioning, self awareness, and self restriction in healthy drivers in the community. This study used cognitive measures and task specific measures of unawareness to examine functional ability both performed in the laboratory and as described by reliable informants for both individuals with AD as well as for healthy seniors. To do this the evaluators attempted to recruit a total of 35 individuals with mild AD and 35 healthy controls (HC). However, severe restrictions in enrollment which will be discussed below significantly limited the number of participants in the current study.

All participants were seen for one testing session that lasted approximately one and a half hours. During this session, cognitive tests were administered to all study participants. The selected cognitive tests are commonly used in assessments for AD, and they measure cognitive

constructs thought to underlie functional performance in AD. Driving performance was measured by a virtual reality driving simulator (VRDS). Both before and after this driving test, all participants were asked questions related to their driving performance. The answers provided served as a measure of task specific driving unawareness. Additionally, both participants and their reliable informants completed a traditionally used measure of functional ability, the Instrumental Activities of Daily Living (IADL) Questionnaire. The questionnaire completed by the reliable informant served as a general measure of the participant's functional ability. The discrepancy score between the informant and the participant's total score on the IADL served as a measure of unawareness of IADLs. First order partial correlation analyses were conducted to examine the relationship between unawareness and functional ability, controlling for performance on cognitive tests. A secondary repeated-measures ANOVA examined the various aspects of awareness as they related to the VRDS.

#### Detailed Procedures

##### *Participants*

Study participants were comprised of 4 individuals with mild AD, as determined by NINDS-ADRDA criteria (McKhann et al., 1984) and 30 healthy controls. The University of Pennsylvania's Alzheimer's Disease Research Center and the Department of Neurology through the Drexel College of Medicine acted as the primary recruitment site for individuals with AD in this study. This study adhered to the NIH policy regarding inclusion of minorities and children in research. Therefore, an attempt was made to recruit subjects from diverse ethnic, gender, and age groups. However, AD is considered a disease of the aging, and is typically seen in individuals over the age of 60. A different profile of AD is evident with individuals who are younger than this. Therefore, to avoid age as a confounding variable, individuals younger than 60 years old were not included in this study.

Thirty healthy controls were recruited for this study as a way of examining the relationship between cognition, awareness, and functional status as a function of healthy aging. Healthy controls were recruited from the caregivers and family of the participants in the study. Additional healthy controls were recruited through flyers posted in the community and presentations made to a variety of senior centers in the community. Presumably, all individuals in this study were unfamiliar with all of the evaluation procedures, particularly the virtual reality driving simulator. The healthy controls were included in this study to establish a baseline for individuals with mild AD in order to understand the relationship between cognition, awareness, and functional status. Additionally, they were included to better understand awareness, self regulation, and functioning in healthy aging. An attempt was made to match healthy controls with individuals with AD for age, gender, years of education, and years of driving experience. However, the limited number of participants with AD In this study restricted this matching.

All potential participants had to satisfy specific criteria in order to participate in the current study. Specific areas for inclusion in the study included demographic and medical status as well as driving status.

*Demographic/ Medical Inclusion Criteria:*

- *Age:* All participants were between the ages of 60 and 85 years old. Individuals over the age of 85 were excluded due to the potential confounds of aging on functional status.
- *Neurological history:* Individuals with a significant history of head injury, stroke, seizures, or any other neurological impairment were not included in this study.
- *Psychiatric and substance abuse history:* Individuals with significant psychiatric history (i.e. bipolar disorder, schizophrenia) or documented substance abuse history were not included in the study. In addition to leading to cognitive deficits, the literature suggests that such a history adds to caregiver burden in individuals with mild AD, which could have confounded the report of the reliable informant.

- *Medication:* Individuals were included in the study if they were not on medication that negatively impacted their cognitive status (i.e. steroids, benzodiazepines, neuroleptics, opioids and other narcotic agents).

*Driving Criteria:*

- Individuals had to be considered as ‘active drivers’ at the time of evaluation, which is defined as having a minimum of two driving experiences every two weeks over the last six months. This was to ensure that individuals were familiar with driving, adding to the ecological validity of the data.
- A minimum of one year of driving experience was necessary to be included in this study.
- Individuals who required adaptive driving devices such as steering wheel turn knobs were not included. The driving simulation environment in this study could not accommodate such devices.
- *Simulation sickness history:* Simulation sickness could impact how individuals performed on the virtual reality driving simulator. Therefore, individuals with no/low history of motion sickness as determined by the modified version of the SSQ questionnaire (Kennedy et al., 1993) were included. This questionnaire will be described in detail below.

The current study included 30 healthy controls as well as participants that had been diagnosed with mild AD based on neuropsychologist’s or physician’s reports. Healthy controls were defined as individuals in the community who satisfied inclusion/exclusion criteria and had never received a diagnosis of cognitive impairment or dementia. Four individuals with mild AD were also included in the study. Although initial inclusion criteria necessitated a score of 18-24 on the Mini Mental Status Examination (MMSE; Folstein et al., 1975), problems with enrollment resulted in inclusion with a diagnosis of mild AD from a medical provider. Individuals with moderate to severe AD were not considered, as they are often too impaired to perform

instrumental activities of daily living independently, which is what was examined in this study. Individuals were required to provide a reliable informant who was intimately familiar with the participant's daily functioning. This was defined as someone who knew them and who was familiar with their daily life. A reliable informant was necessary because this study examined unawareness. One way of assessing unawareness was to compare the participant's view of their own functioning with the reliable informant's view of their functioning.

### *Compensation*

Participants were compensated \$35 for their participation in this study. Participants were also compensated for parking at the time of the study. All participants were informed of this before the study began, and were told that their participation would aid in the understanding of awareness in healthy older adults and in people with mild AD.

### *Subject Availability and Appropriateness*

In order to conduct this study with an appropriate power, the evaluators attempted to enroll 70 individuals; 35 individuals with mild AD and 35 healthy controls. However, restrictions in interest resulted in four individuals with mild AD and 30 healthy controls. All individuals with mild AD were recruited from the Department of Neurology at Drexel College of Medicine and the University of Pennsylvania's Alzheimer's Disease Research Center despite efforts from other institutions. The Memory Disorders program through the Department of Neurology at Drexel College of Medicine offers specialized assessment and treatment services to individuals with cognitive and memory disorders through a multidisciplinary team. It is housed in Hahnemann Hospital in central Philadelphia. University of Pennsylvania Alzheimer's Disease Center has been serving patients as a federally supported program since 1991, and has served over 1,100 individuals over the past five years. Through a multidisciplinary team of staff, they offer services to individuals in the community with cognitive and memory impairments that are over 50 years of age. They provide assessment, treatment, and the opportunity to participate in



cutting edge research. Many people who attend these centers for clinical needs sign a form at the onset of their care that they are interested in participating in research studies. Potential participants were identified by the staff at each respective site and were contacted by that site through flyers and mailings. The mailings included the contact information for the investigators in the study. No HIPAA information was released to the study investigators. If an individual responded by calling the study investigator, a telephone screening was conducted to ensure inclusion/ exclusion criteria were met prior to scheduling of the testing session. As previously mentioned, healthy controls were recruited as family members of individuals with AD, through flyers presented in the community and presentations made to a variety of senior centers in the community.

#### *Power Analysis*

The primary analyses in this study involved identifying the relationship between unawareness and specific functional abilities, controlling for performance on each cognitive test. As such, the study design was correlational using first order correlations in a partial correlational model. The relationships were examined independently for individuals with AD and HC for both types of functional abilities measured in this study. The independent variable was participant group (AD and HC). Groups were attempted to be matched on age, gender, years of education, and years of driving experience. The primary dependent variables were performance on cognitive tests (e.g. Judgment of Line orientation, California Verbal Learning Test-II Short Form, and Trail Making Test-B), unawareness level (e.g. performance/perception discrepancies on the VRDS and patient/caregiver discrepancy on the IADL), and functional performance (e.g. performance on the VRDS and score on the IADL questionnaire). To estimate a reasonable effect size for this study, a review of the literature was used. In a similar study measuring cognition and unawareness in individuals with mild to moderate AD yielded a moderate effect size ( $r = .52$ )(Feldman et al., 2005). To obtain a conservative estimate of the

effect size to be used in the apriori power analysis, 95% confidence intervals of the reported effect sizes were calculated. The lower limit of the confidence interval was used ( $r = .44$ ).

Specific power analysis software, G\*Power (ver. 3.0.6) was used to estimate the sample size (Faul, Erdfelder, Lang, & Buchner, 2007). Using a significance criterion of 0.05 with a two-sided test for a moderate effect of ( $r = 0.44$ ) and power of 0.80, yielded a sample size of 35 subjects per group (AD and HC) necessary to determine the relationship between unawareness and each functional task, controlling for performance on cognitive tests.

### *Task Descriptions*

All study participants were administered three brief primary cognitive tests which were included in the partial correlation (Judgment of Line orientation, California Verbal Learning Test-II Short Form, and Trail Making Test-B). Two exploratory tests (Trail Making Test-A and Clock Drawing Test) were added for post-hoc exploratory analysis. All participants underwent one functional evaluation meant to assess driving ability, a functional ability that is often particularly troublesome for individuals with AD and is a topic of concern for healthy seniors as well. Both before and after exposure to this task, participants were asked to answer questions about their predicted and perceived performance on the VRDS. Both participants and their informants were asked to complete an IADL questionnaire. Because all participants were exposed to a virtual reality driving simulator, all participants were also required to complete a questionnaire assessing history of simulation sickness and present symptoms consistent with simulation sickness. Refer to Table 1 for a list of all study variables.

Insert Table 1: Variables in the Study

*Cognitive Evaluation:* Although some researchers have found a relationship between global cognitive status and functional ability in AD, other researchers have highlighted specific cognitive domains as predictive of functional ability. Three specific cognitive domains that have been linked to functional ability include memory, executive functioning, and visuospatial

abilities. Because of their presence in the literature along with the desire to keep the testing session short to eliminate fatigue, these were the only three cognitive domains assessed in the primary analysis. Each cognitive domain was assessed with one neuropsychological test that has been used extensively in AD research. The Trail Making Test-A and the Clock Drawing Test were also included for exploratory purposes, as these test has been linked to driving performance in seniors (Duchek, Hunt, Ball, Buckles, & Morris, 1997; Freund et al., 2004).

*California Verbal Learning Test- Second Edition Short Form (CVLT-II Short Form)*

(Delis, Kramer, Kaplan, and Ober, 2000): This was a 9-word list task containing three semantically related categories of words presented in a semi-randomized order. One list was presented four times, and participants were instructed to try to remember as many words as possible each time. A distracter task was given and then participants were asked to remember as many words as they could from the original word list. After a 10 minute delay, participants were again asked to remember as many words as they could from the original list and were then given cues to aid performance. Finally, participants were presented with a list of words to which they were to respond 'yes' if the word was from the original word list. This test measured verbal learning and memory. The variable of interest from this test was the standardized  $d'$  score, which reflected the difference between a participant's hit rate and false positive rate in standard deviation units. Individuals with AD are differentially impaired on measures of this recognition discriminability (Delis et al., 1991).

*Trail Making Test –parts A & B (TMT-A & B: Army Individual Test Battery, 1944):* For this test participants were asked to connect consecutive numbers in part A, and then to connect consecutive numbers and letters in alternating fashion in part B. The participant was instructed to connect the dots as fast as they could. Scores on both parts A and B were based on time to completion. TMT-B was used in the primary analysis and it assessed visual scanning, motor speed, attention, and cognitive flexibility. This test is sensitive to cognitive decline evident in

dementia. Individuals with AD often have difficulty in dividing and shifting their attention, which can be captured by this test. Difficulty on this task has been linked to difficulties performing instrumental activities of daily living as well. (For review, refer to Lezak et al., 2004, p. 214 & p. 373). The variable of interest from the TMT-B was the standardized time to completion (z-score).

*Judgment of Line Orientation (JLO) (Benton, Sivan, Hamsher et al., 1994)*: This test examined visuospatial perception, analysis, and judgment. Here, individuals were asked to match angled line pairs to eleven numbered lines that formed a semi circle. This test began with five practice items followed by a thirty item test. The total score (0-30) was the number of items in which both lines were correctly matched. Hamsher, and colleagues (1994) note that scores of 21 and higher reflect average performance. Individuals with AD have demonstrated impairment on this test, though performance has varied from failure to slightly low performance (Ska, Poissant, & Joannette, 1990). Scores were converted into age and gender corrected scores, adapted by Benton, Sivan, Hamsher and colleagues (1994). The variable of interest on this test was the total age-corrected score.

*Clock Drawing Test (CDT)(exploratory)*: For this test, participants were instructed both verbally and in writing to draw the face of a clock with all of the numbers, and place the hands set to ten minutes after eleven. Participants were given a blank space for which to draw the clock, and performance was untimed, though typically takes less than five minutes for completion. The evaluator was not allowed to give cues during the test, though the participant was allowed to self-correct. The Freund scoring system was used, where participant could earn a total of 0-7 points based on number placement, indication of time on the clock, and spacing (Freund et al., 2004). Using this scoring system, Freund and colleagues (2004) have found that a score of 4 or less is predictive of unsafe driving in seniors. They found that incorrect time setting was the most significant predictor of unsafe driving. The CDT has also been linked to executive

functioning in Alzheimer's dementia (Royall, Cordes, & Polk, 1998). The variable of interest on this test was the total score (0-7).

### *Functional Measures*

*Novel Functional Measure of Driving:* Driving ability is a major concern both for healthy older adults as well as for individuals with mild AD due to the importance individuals place on this ability as well as the tremendous safety issues that potentially arise. Behind the wheel driving evaluations have numerous limitations as well as safety concerns, while cognitive tests are not ecologically valid ways of assessing driving ability. Because of that, this study employed a virtual reality driving simulator as a way of measuring driving performance. Driving simulation has been used in this clinical population by a variety of researchers (i.e. Cox, Quillian, Thorndike, Kovatchev, & Hanna, 1998; Shua-Haim & Gross, 1996; Szlyk, Myers, Zhang, Wetzel, & Shapiro, 2002). Driving simulation has also been used to study driving in healthy older adults (Freund et al., 2004).

*Virtual Reality Driving Simulator (release 1.0)(VRDS):* This study used the current version of the Virtual Reality Driving Simulator (release 1.0). This system was developed through collaboration by Digital MediaWorks Inc. and Maria Schultheis, Ph.D. The system delivered pre-programmed environments to expose individuals to simulated real world driving experiences. Various actions were made by navigating through and interacting with various objects and environments through the use of artificial intelligence behavior algorithms. Medium resolution geometry and high resolution textures provided for high quality visuals, which when paired with the realistic environments, created a believable driving experience. Individuals controlled their environment by a commercially available steering wheel and foot pedals. While individuals drove through the environment, information about their performance was simultaneously tracked and stored in the computer. Such information included raw steering and brake-pedal input, vehicle position, and speed. This system was designed to operate on an

equivalent single processing system to the Pentium 4 class PC. The information was projected to three, flat screen 30-inch monitors.

The driving system included four types of driving zones: a residential, school, highway, and commercial zone. Each zone flowed into one another, thereby enabling drivers to drive through every zone during a 15-minute drive. These zones were specifically selected from clinical driving specialists, in an attempt to capture real life driving situations. This study required the individuals to drive through every zone once. Prior to driving in these zones, individuals were asked to drive in practice residential and highway zones for several minutes in order to familiarize themselves with the machine, controls, and virtual environment. Directions were given by the computer as the driver drove through the environment. However, an experimenter was also there to provide the instructions if the individual was unable to hear the original instructions. Information was generated by the computer and sampled every 200 ms during driving, though no filtering was performed. Specific variables sampled included speed (mph), lane deviation (in feet), acceleration and deceleration rates (average mph), and stopping behavior.

A total of seven measures were sampled throughout the driving route and were used as measures of driving performance (for a detailed description, refer to Table 2). Each of these measures were then converted into a final score of one through five so that driving performance could be explicitly compared with scores gleaned from an unawareness measure described below. Two such measures were driving behaviors at stop signs embedded within the residential section and at traffic lights found in the commercial section of the driving environment. Specifically, driving behavior was sampled and averaged from three stop signs and three traffic lights. This behavior included if the individual stopped, the distance stopped from each stop sign or traffic light, and the length of time an individual waited before resuming driving.

Speed was another important measure to consider when examining driving behavior. Speed was sampled from the highway portion of the driving environment, as this portion of the environment allowed for measurement over a continuous period of time during which an individual was not required to stop or turn. Two specific highway zones were selected for speed sampling based on the relative straightness of the road and lack of extraneous environmental challenges. Lane management was another measure sampled from two predetermined zones of the highway in the driving environment as well as overall deviation from the lane throughout the entire highway portion. The two zones selected to measure lane management were picked due to the curviness of the road, necessitating more conscious control of the vehicle. In addition to measurement of lane management during these two zones, the number of times that an individual deviated, or drove out of the lines demarcating the lane throughout the entire highway portion of the environment was also calculated.

Three driving measures were calculated based on environmental challenges encountered by each individual. The first challenge was encountered on the highway where an individual was asked to follow behind a target vehicle at a safe distance for an allotted amount of time as the target vehicle's speed varied slightly. Measurements were taken based on the individual's attempt to follow the target, success at remaining behind the target, and control over their own lane management as they attempted to follow the target. Another challenge was also measured during the highway portion of the environment, and included an individual's driving behavior during a construction zone. The construction zone was preceded by a sign indicating that the individual needed to move to the left-hand lane. Throughout the construction zone, the right lane was barricaded off by cones, and a sign read that the speed limit was changed to 30 mph. Here, the individual's driving behavior was measured based on response to road signs and barriers in the road, speed during the construction zone, and change in speed after the zone when an individual was to return back to an appropriate highway speed.

The third environmental challenge was measured by an individual's reaction to unexpected objects on the road. One unexpected object occurred in the residential zone where a kid and his ball unexpectedly came out into the middle of the street, necessitating the participant to stop the car in order to avoid an accident. Here, driving behavior was measured by an individual's lane management and stopping behavior to the kid and ball. Another way of measuring driving behavior to unexpected objects was measuring the number of crashes and near-crashes experienced by each individual as they navigated the driving environment and encountered other cars and objects on the road. Response to the kid and the ball as well as overall reaction to unexpected objects throughout the environment was converted into one score.

Each of the seven driving measures was sampled using very specific criteria outlined on Table 2. Measurements of such behaviors were compared to scores from a sub section of a normative sample collected on the same VRDS. This normative sample was collected with the intention of creating normative data for studies such as the current one. The current study utilized a sample of 10 individuals from the normative study, ranging in age from 33-58 years old. The statistics from the normative study were used as standards for which to compare each participant's performance during the current study.

Insert Table 2: Virtual Reality Driving Simulator Variables in the Study

Simulation sickness was a potential adverse reaction for certain individuals when exposed to a virtual environment. Simulation sickness had the potential to become both a confounding variable for the study as well as frustrating for the individual. Therefore, at screening, individuals were asked to complete a screening version of the Simulation Sickness Questionnaire (SSQ)(Kennedy et al., 1993). Individuals with a pronounced history of motion or simulation sickness were considered a high risk for developing simulation sickness in this study, and were therefore excluded. An individual was considered high risk if they answered "always" in response to "how often would you say you get" sick under a specific condition. Those who were



at low/no risk were included in the study. Before exposure to the VR environment, individuals completed the Pre-Exposure Symptom Checklist of the SSQ (Appendix A) as a measure of how they were feeling prior to being exposed to the virtual environment. Following exposure to the VRDS, individuals were administered the Post-Exposure Symptom Checklist of the SSQ to compare symptoms prior to and following virtual reality exposure.

*Traditional Functional Measure of Instrumental Activities of Daily Living (IADL):* The research shows that individuals with AD have functional impairments along with cognitive impairments. These impairments are what ultimately lead to greater dependency and institutionalization for many individuals.

*Instrumental Activities of Daily Living (IADL) questionnaire (Lawton & Brody, 1969):* This questionnaire assessed independent living skills in eight functional domains (Appendix B). Such domains included the ability to use the telephone, shop, prepare food, maintain the home, launder clothes, use transportation, manage medication, and handle finances. Individuals were scored according to their highest level of functioning in each domain. The total score ranges from 0-17, with 0 reflecting low functioning and 17 reflecting virtual independence in all areas assessed. Both individuals with mild AD and healthy controls were required to complete this questionnaire. Reliable informants were asked to complete this form for both groups of participants in the study, as this was its intended use. This measure is commonly used when assessing functional ability for individuals with AD (i.e. Farias et al., 2003; Feldman et al., 2005; Matsuda & Saito, 2005). A study by Farias and colleagues (2003) found the inter-rater reliability of this questionnaire to be .85.

*Unawareness Measures:*

In this study, unawareness was measured in two ways: participant/reliable informant discrepancy scores and participant perception/performance scores. This study did not employ clinical ratings scores based on their subjectivity as well as the limited time in which the

clinicians had to assess each participant. Measures of unawareness were gleaned from discrepancy scores for both the VRDS and the IADLs.

*Measure of Unawareness on a Novel Functional Task:* This study assessed the participant's perception of their own functioning both before and after completing the VR Driving Simulator (See Appendix C and D). However, only the individual's perception of performance post-VRDS exposure was used in the primary analysis, as individuals were relatively new to this driving technique and therefore may have had difficulty predicting performance. The individual's post-VRDS perception of performance was compared with their actual performance on the VRDS to yield an 'unawareness' score for the task. This was a task specific and novel measure of unawareness, as a participant's perception was being compared to actual performance on the VRDS. This study used a self-rating questionnaire similar to one created by Hart, Giovannetti, Montgomery, and Schwartz (1998) who created a self-rating questionnaire to assess unawareness in individuals with traumatic brain injury on a task assessing naturalistic action. The questionnaire asked participants how they thought they performed on specific demands of the naturalistic action task. Questions were answered on a 1 (Wasn't able to do) to 5(Did with ease) scale. A total score was then calculated (range 9-45). The specific questions on this questionnaire were changed to suit the VR Driving Simulator task. All seven driving behaviors sampled on the VR task were explicitly addressed on the unawareness questionnaire. For example, one question on the unawareness questionnaire necessitated the participant to score themselves from one through five on how they thought they did at managing stop signs. The total score on the unawareness questionnaire was contrasted to the total score on the VRDS to get a task specific unawareness score.

Secondary analyses examined the qualitative aspects of unawareness. Here, individuals' predictions of their performance were contrasted to both their actual performance as well as their post-VRDS exposure perceived performance. The pre-performance predictions were assessed

just after the practice trial of the VRDS and right before the actual VRDS test. This afforded participants some exposure to the VRDS so that they could better predict performance. This assessment included the same questions as asked on the post-VRDS exposure questionnaire, though here participants were asked to predict how they would do on cognitive, physical, and specific task specific VRDS measures. Refer to figure 3 for a better understanding of the unawareness variables gleaned from the VRDS exposure.

*Measurement of Unawareness on a Traditional Functional Tool:* A traditional measurement of unawareness was gleaned from the discrepancy score between the participant and their reliable informant on the IADL questionnaire. This score is considered ‘traditional’ because it has been used in the literature to assess awareness. Additionally, the IADL is a well known measure of functional assessment. This discrepancy score is labeled “IADL discrepancy” score.

### *Methods*

Participants with a clinically verifiable history of mild AD and healthy control participants were recruited through various hospitals, centers, and community organizations. Recruitment was described above. Interested potential clinical participants were given the contact information of the principal investigator and underwent a structured screening to determine eligibility if they expressed interest in participating in the study. Healthy older adults in the community similarly contacted the principal investigator if they were interested in participating in the study. If individuals satisfied criteria, they were scheduled for a formal testing session.

At the start of the experimental session, all participants were required to sign an informed consent that had been approved from the Institutional Review Board of Drexel University. All participants with mild Alzheimer’s dementia also signed a medical release form giving the researchers in the study access to their medical history for medical verification. All participants

then received a thorough structured interview to ensure eligibility. The testing session lasted approximately one-and-a-half hours. All testing took place at Drexel University's Bossone Research Enterprise Center, room 630A. All participants were required to provide a reliable informant to be involved in the study. All reliable informants signed an informed consent and were asked to complete the IADL form describing their interpretation of the participant's functioning in the community. A caregiver burden questionnaire was given to reliable informants for the participants with mild AD to eliminate the possibility of burden as a covariant to the informants' responses. Reliable informants for individuals with mild AD were also required to be present for the structured interview to ensure accuracy of personal information. All participants in this study underwent a structured interview, completed all cognitive testing, completed forms pertaining to functioning in daily life, and underwent the VRDS and all related forms. Participants completed the VRDS unawareness measures before and after exposure to the virtual environment. The order of administration of the cognitive testing, completion of forms, and VRDS were counterbalanced.

Both the healthy controls and the participants with AD were exposed to the VRDS. Prior to being tested on the VRDS, all participants completed the modified SSQ (Pre-Exposure Symptom Checklist) to assess physical symptoms prior to VRDS exposure. They then completed practice trials on a simplified virtual highway and residential environment in order to become familiarized with the VR simulator, the steering wheel, and the brake pedals. Participants next completed the pre-test unawareness questionnaire predicting performance on the upcoming driving task. Participants were asked to do this after the practice drive in order to have some familiarity with the environment for which to predict performance. Each participant then completed the VRDS driving route, involving exposure to the residential, highway, commercial, and school virtual driving zones. The participants drove through the environment while voice commands and the evaluator guided them through the virtual route. If any participant began to

feel the effects of simulator sickness, they were strongly encouraged to discontinue the study with no negative consequences to them. Several participants were discontinued at this time due to unanticipated simulation sickness. Following exposure to the driving route, all participants completed the post-test unawareness questionnaire assessing how they thought they performed on the task. Each participant then completed the modified SSQ (Post-Exposure Symptom Checklist) to assess for symptoms of simulation sickness. If symptoms of simulation sickness were present, participants were observed by the researcher until these symptoms subsided. They were then debriefed about the study, compensated for their time, and thanked for their participation.

### Planned Statistical Analysis

Recruitment for the study was severely restricted due to unanticipated confounding factors. Preliminary power analyses for the study revealed that 35 individuals with mild AD and 35 healthy controls were needed in order to reach appropriate power. The current study contains 4 individuals with mild AD and 30 health controls due to difficulty with enrollment. The primary hypotheses and study aims were changed slightly to better reflect the study sample.

Before the final analysis of all the variables, tests were run to determine if the data met all the necessary parametric assumptions. Data was analyzed using non-parametric analyses, as transformation did not work to normalize the data. Descriptive statistics were calculated. This included a 95% confidence interval for all significant correlations to better reflect the population parameters. Specific analyses for each hypothesis will be examined below.

*Aim I:* The primary aim of this study was to examine the relationship between unawareness and functional ability, controlling for performance on specific cognitive tests. Data from healthy controls were examined quantitatively. Results from individuals with mild AD were examined in an exploratory nature, due to the limited sample size.

*Hypothesis 1a.* Controlling for performance on a verbal memory test (CVLT-II), there will be a relationship between unawareness and performance on the virtual reality driving simulator in healthy controls.

*Hypothesis 1b.* Controlling for performance on an executive control test (TMT-B), there will be a relationship between unawareness and performance on the virtual reality driving simulator in healthy controls.

*Hypothesis 1c.* Controlling for performance on a visuospatial cognitive test (JLO), there will be a relationship between unawareness and performance on the virtual reality driving simulator in healthy controls.

Three first order partial correlations were used to determine how much variability in VR driving performance was determined by unawareness of the task, holding performance on each cognitive test constant. This study used a two-tailed hypothesis test with a significance criterion set to .05. Diagnostics, analysis of residuals, and standard errors were used to assess variability and goodness of fit in this statistical model. Assumptions such as recursivity, linearity, additivity, interval level data, correlation of residual variables, and multicollinearity were checked and resulted in the use of nonparametric tests.

*Hypothesis 1d.* Controlling for performance on a verbal memory test (CVLT-II), there will be relationship between unawareness and functional ability as measured by a discrepancy measure from the Independent Activities of Daily Living Questionnaire in healthy controls.

*Hypothesis 1e.* Controlling for performance on an executive control test (TMT-B), there will be relationship between unawareness and functional ability as measured by a discrepancy measure from the Independent Activities of Daily Living Questionnaire in healthy controls.

*Hypothesis 1f.* Controlling for performance on a visuospatial cognitive test (JLO), there will be relationship between unawareness and functional ability as measured by a discrepancy measure from the Independent Activities of Daily Living Questionnaire in healthy controls.

Three partial correlations were used to determine how much variability in general functional performance as measured by discrepancy scores in the IADL questionnaire was determined by unawareness, holding performance on each cognitive test constant. This study used a two-tailed hypothesis test with a significance criterion set to .05. Diagnostics, analysis of residuals, and standard errors were used to assess variability and goodness of fit in this statistical model. Assumptions such as recursivity, linearity, additivity, interval level data, correlation of residual variables, and multicollinearity were checked and resulted in the use of non-parametric tests.

*Aim 2:* The secondary aim of this study was to examine various aspects of unawareness in the context of a novel functional assessment. This study compared predicted performance with actual performance on the VRDS to get a measure of ‘predicted awareness’. Performance on the VRDS was compared to each participant’s perceived performance after their exposure to the VRDS as a task specific measure of ‘unawareness’. Each participant’s predicted performance was also contrasted with their perceived performance for a measure of performance ‘recognition’ (refer to Figure 3). Analysis of unawareness for healthy controls was used to help establish the proposed relationship between unawareness and function on the VRDS. A quantitative analysis could not be run with individuals with mild AD due to the small sample size.

*Hypothesis 2a.* There is a significant difference between at least one type of unawareness on the VRDS in healthy controls: the prediction unawareness score, recognition unawareness score, and unawareness score.

Differences between unawareness scores were evaluated using a repeated-measures ANOVA using the Greenhouse-Geisser estimates of sphericity due to non-normally distributed data. A two-tailed hypothesis test was conducted using a significance criterion of .05.

### CHAPTER 3: RESULTS

After approximately 19 months of recruitment, the current study contains four individuals with mild AD and 30 health controls. Several sites throughout and neighboring Philadelphia agreed to act as recruitment sites for participants with AD including University of Pennsylvania's Alzheimer's Disease Research Center, the Department of Neurology through the Drexel College of Medicine, The Center for Neuroscience at Riddle Memorial Hospital, the New Jersey Institute for Successful Aging at the University of Medicine and Dentistry of New Jersey, Jefferson Hospital for Neuroscience, the Alzheimer's Association, and the Outpatient Neuropsychology Laboratory of Cooper University Hospital. Four participants were successfully enrolled from University of Pennsylvania's Alzheimer's Disease Research Center and the Department of Neurology through the Drexel College of Medicine. The recruitment of healthy controls was expanded to include postings in the community and various senior centers with the result of 30 healthy controls. The evaluators were met with unanticipated resistance from individuals to be included in the study. Many potential participants expressed extreme hesitance regarding having their driving and cognition tested, despite the confidential nature of the study. These concerns lead to many individuals cancelling appointments before their scheduled dates. In many cases, they were reluctant to reconsider rescheduling, citing their numerous concerns. Additionally, a higher proportion of simulation sickness as a result of exposure to the VRDS resulted in incomplete VRDS data collection, as multiple individuals were discontinued from the VRDS prior to completion (n=8, 24%). The primary hypotheses and study aims were modified to better reflect the smaller study sample.

Prior to conducting primary analyses, data was evaluated for normality and descriptive characteristics. Sample characteristics were defined, and data was compared to performance by individuals from normative studies. Several modes of analyses were conducted to test the primary hypotheses. Results were examined separately for healthy controls and individuals with



mild AD. Data from the healthy controls in the study were examined quantitatively. The number of participants with mild AD was too low to conduct quantitative analysis. Thus, results will be presented through case analysis and use of cut scores below.

### Sample Characteristics

#### *Healthy Controls*

Thirty-five individuals completed this study; thirty healthy controls and four individuals with mild AD. One healthy control participant met inclusion criteria and was enrolled in the study. However, due to simulation sickness during the practice session of the VRDS, no VRDS data was collected on this individual. All of the remaining information from this participant is included in the study. Demographic information for all 30 healthy controls is presented in Table 3. Thirty healthy controls ranged in age from 60 to 84 with a mean age of 73.57 years ( $SD=7.70$ ). Healthy control participants had a range of education from 12 to 21 years, with a mean of 16.23 years ( $SD=2.99$ ). Sixteen females and 14 males were included in the study. Though the study attempted to include individuals from all ethnic backgrounds, 24 Caucasians and 6 African Americans acted as controls in this study. Twenty-eight were right-handed while two were left-handed. Thirty-three percent of healthy control participants used a spouse as a reliable informant, 23% used a child, 17% used a romantic partner, and 13% each used a friend or sibling. On average, these participants reported knowing their reliable informants for 37.65 years ( $SD=23.36$ ).

Insert Table 3: Demographic Variables for Healthy Controls (n=30)

Driving characteristics (Table 4), including current and past driving habits, were collected to understand possible factors that might influence the VRDS. Healthy control participants ranged in driving experience from 32 to 77 years with a mean of 55.10 years ( $SD=10.20$ ). Currently, participants ranged from driving two to 30 days per month, with a mean of 22.37 days per month ( $SD=8.50$ ). Mileage per drive ranged from 2.5 to 160, with a mean of 32.58 ( $SD=$

40.95) miles. Twenty percent of participants reported an accident or ticket within the past year while 30% of participants reported restricting their driving in some way within the past year.

Twenty-one percent of participants reportedly were the only drivers in their household.

Insert Table 4: Driving Characteristics for Healthy Controls

#### *Clinical Case Examples*

Four participants with mild Alzheimer's dementia were included in the study.

Although initial inclusion criteria necessitated a score of 18-24 on the Mini Mental Status Examination (MMSE; Folstein et al., 1975), problems with enrollment resulted in inclusion with a diagnosis of mild AD from a medical provider. Demographic and driving information from each clinical participant are presented qualitatively below and important demographic information is presented in Table 5.

Insert Table 5: Demographic Information for Clinical Sample

*Alzheimer's Dementia Case #1 (AD1)*. The first clinical participant was a right-handed 73 year old female with 16 years of education with an MMSE score of 21. She had been retired for approximately 12 years at the time of the study. This participant had bilateral cataract surgery and reported that her vision is currently 'fine', occasionally necessitating the use of reading glasses. Her husband, whom she had known for 51 years and with whom she interacted daily, acted as her reliable informant. They noted that she was diagnosed with mild Alzheimer's dementia approximately 18 months ago by way of blood work and cognitive testing conducted at a regional hospital's memory center. At the time of her participation in the study, AD1 was currently taking Aricept daily. As per the participant and her reliable informant, she experienced problems with her memory including forgetting what day it is and misplacing things around the house. She had been driving for 57 years and currently reported driving approximately six times per month, traveling 10 miles each drive. She denied receiving any tickets or being involved in any accidents within the last year and reported that over the past eight months she had only

driven when accompanied by another person. She reported being more careful when driving. She was not the only driver in her household, as her husband also drove. AD1 had no history of exposure to virtual reality or motion sickness.

*Alzheimer's Dementia Case #2 (AD2).* A 75 year old right handed male, this participant scored 25 on the MMSE. He had 19 years of education and had been diagnosed with mild Alzheimer's dementia approximately 9 months prior to participation in the study at a regional hospital's memory center. The participant's wife acted as his reliable informant, with whom he lived with and interacted with on a daily basis. He noted that he became concerned about memory problems when he had difficulty remembering the names of familiar streets and could not remember the players' names from his favorite sports team. No other cognitive problems were reported. The participant was on Aricept and Namenda since he was diagnosed with mild AD. He has reportedly been driving for 59 years and remains the primary driver in his household despite the fact that his wife also drives. He reported driving over 60 miles each weekend and an average of 10 miles during the week. Both he and his wife had not noticed any changes in his driving, and he had not restricted his driving in any way. The participant had not received any tickets or been in any accidents within the last year. He noted that he had played a virtual reality golf game once before, but he had no previous exposure to a virtual reality driving simulation, nor did he have any history of simulation or motion sickness.

*Alzheimer's Dementia Case #3 (AD3).* The third clinical case was a right-handed 69 year old male with 12 years of education who had retired from work approximately 8 years ago. He was right-handed and scored 17 on the MMSE. The participant's wife, whom he had known for 39 years and with whom he currently resided, acted as his reliable informant. They reported that he was diagnosed with depression one year prior to his diagnosis of mild Alzheimer's dementia. Upon diagnosis of depression, his family doctor prescribed him Prozac, which he used to date (current GDS=0). He later received a comprehensive evaluation at a regional hospital's memory

center, resulting in a diagnosis of mild AD approximately 24 months ago for which he was currently taking Aricept. He and his wife reported difficulty remembering people's names, a slight decline in concentration, and a propensity for repeating himself and misplacing things. He had been driving for 53 years and currently reported driving approximately 30 miles every day. He did not restrict his driving despite the fact that his wife also drove, and noticed no differences in his driving abilities though his wife reported that he was less patient than he once was. He had received no tickets and had not been any accidents within the last year. The participant had no history of virtual reality exposure and no history of motion sickness.

*Alzheimer's Dementia Case #4 (AD4).* The last clinical case is a 78 year old right-handed male with 16 years of education. He received a 29 on the MMSE. AD4 had a history of alcohol abuse, but was reportedly sober for the past 21 years. The participant lived with his wife, whom he had known for 25 years and acted as his reliable informant. He had reportedly suffered from a stroke to his brainstem approximately 11 years ago, from which his wife notes he fully recovered with no need for rehabilitation. He is currently on Prozac, though did not meet criteria for geriatric depression (GDS=1). The participant was diagnosed with mild AD approximately 18 months prior to participation in the study by his primary care doctor. He is currently involved in Alzheimer's support groups in the community. The participant endorsed daily problems with his memory. He had been driving for 62 years and currently drove 10 miles every day. Although his wife also drove, the participant reportedly did not restrict his driving, though noted that he preferred not to drive at night due to limited night vision. He had no prior exposure to virtual reality, and had no history of simulation sickness.

## Data Processing

### *Primary Cognitive Variables*

The CVLT (short form), TMT-B, and JLO were used as primary cognitive variables for the current study. Upon completion, scores from these tests were converted into standardized

scores for the purposes of comparing across participants with varying backgrounds. The 'yes/no' forced recognition subsection of the CVLT was converted into a standardized  $d'$  score which controlled for a participant's age and gender. This  $d'$  score was the difference between a participant's hit rate and false positive rate in standard deviation units. Results from the TMT-B were converted into T-scores (using normative data from Heaton, Grant, & Matthews, 1991), which accounted for age, education, gender, and ethnicity. T-scores were then converted into  $z$ -scores so that they could be directly compared to performance on the CVLT. Performance on the JLO was converted into age and gender corrected scores, adapted by Benton, Sivan, Hamsner and colleagues (1994). This test does not utilize normative scores, relying instead on cutoff scores.

#### *Functional Variables*

*Traditional Functional Measure:* The IADL questionnaire was given to all participants and reliable informants. The IADL score (0-17) from the reliable informant was used as the participant's measure of functioning.

*Novel Functional Measure:* The VRDS was given to all participants as a novel measure of one instrumental activity of daily living: driving. Raw data from the VRDS were analyzed and converted into scores based on pre-determined measurements of variables. Seven key variables were examined (described in detail in Table 2): Behavior at stop signs, behavior at traffic lights, speed maintenance at various sections of the route, lane management during various sections of the driving route, behavior when following a target vehicle, behavior at a construction zone, and response behaviors to unexpected objects. Raw data was contrasted to scores from a normative database of 10 healthy controls ranging in age from 33-58 years old. The normative database was collected for another study in attempts to norm variables using this VRDS. The data from the normative group reflects scores that are slightly divergent from real-life driving criteria. For example, the mean driving speed for individuals in this normative group during a construction

zone was 34.74 mph despite the fact that the speed limit was posted at 30 mph. Despite being over the posted limit, this mean score was used as a standard for the current study.

An unexpected limitation of the current study was the high incidence of simulation sickness, resulting in discontinuation of the VRDS for 8 participants. This was 23% of the study. The final VRDS score was the total score for each participant for only the variables that were completed for that individual. For example, if a participant never made it to the residential zone and therefore was never exposed to stop signs due to simulation sickness, a total score for stop sign behavior was not calculated into the total score.

#### *Unawareness Variables*

Unawareness was measured in multiple ways for a comprehensive understanding of this experience. The tool used to measure unawareness reflected the function being assessed.

*Traditional Unawareness:* One unawareness score was the difference between the participant's score and the reliable informant's score on the IADL. This yielded a traditional unawareness score for general activities of daily living called "IADL discrepancy score".

*Novel Unawareness:* The other unawareness score related to the VRDS and was generated by way of the unawareness questionnaire completed after exposure to the VRDS. This post-assessment questionnaire asked participants questions about their performance that directly compared to performance being measured on the VRDS (i.e., speed management). The score for each participant was calculated only for those variables that were completed on the VRDS. For example, if the participant was never exposed to stop signs due to simulation sickness, that variable was not factored into the total score for that questionnaire. Using the total score on that questionnaire, the VRDS "unawareness score" was the post-assessment unawareness total score minus the participant's total VRDS score. A score of zero meant that the person's perception of their performance was the same as their score on the VRDS, indicating accurate awareness. A

higher positive score reflects a participant's overestimate of driving performance. A lower negative score reflects a participant's underestimation of their performance.

Aim II of this study examined two additional forms of novel VRDS-related awareness: 'prediction awareness' and 'recognition awareness'. Prediction awareness was the total score on the unawareness questionnaire that a participant completed prior to the testing portion of the VRDS and after the practice trial. This questionnaire asked the participants how they thought they were going to perform on the VRDS, and is directly comparable to the post-assessment VRDS unawareness questionnaire. The total prediction awareness score included only those variables which the participant completed in the VRDS. The recognition awareness score was the difference between the prediction score and the post-assessment unawareness score. The recognition awareness score attempted to identify if a participant changed their assessments of themselves based on their perceived driving performance.

#### *Analyses of Covariates*

Primary variables were evaluated at three different levels to assess for potential covariates. All variables were correlated with demographic information to assess for covariates. Additional information about driving behaviors was correlated with study-related driving variables. Finally, information about participant relationships with their reliable informants was correlated with scores from the IADL for potential covariates.

##### *1. Covariates to Demographic Variables*

Demographic variables were evaluated as potential covariates to the primary variables. Spearman's rho correlations were used to evaluate continuous variables and Mann Whitney U tests were used to determine significant differences in medians between categorical variables (Table 6 below). Age was significantly related to the standardized performance on the TMT-B, despite the fact that standardization corrected for age,  $r=.349$ ,  $p<.05$ . As age increased, the TMT-B  $z$ -score improved. Education was significantly correlated with the age-corrected

performance on the Judgment of Line Orientation test,  $r = .382, p < .05$ . As education increased, the age-corrected score on the JLO improved. Education was also significantly related to performance on the VRDS,  $r = .489, p < .01$ . Higher education was correlated with greater performance on the VRDS. There was a significant difference in the median CVLT  $d'$  scores between Caucasian participants and African American participants,  $U = 22.50, z = -2.61, p < .01$ . On average, Caucasian participants scored higher on the CVLT  $d'$  than did African American participants. There was also a significant difference in the median CVLT  $d'$  score between male and female participants,  $U = 37.50, z = -3.14, p < .01$ . The median score for males on the CVLT  $d'$  was 1.0 while the median score for females was -0.5. Gender differences existed despite normative corrections for this factor. Lastly, education was significantly negatively correlated with the recognition awareness score,  $r = -.368, p < .05$ .

Insert Table 6: Relationship between Demographics and Primary Variables in Healthy Controls

## 2. *Covariates to Driving Variables*

Additional driving variables were evaluated as potential covariates with the VRDS and VRDS awareness measures. Spearman's rho correlations were used to evaluate continuous variables and Mann Whitney U tests were used to determine significant differences in the medians between categorical variables. Variables examined included the number of years a participant had been driving, the number of days a participant currently drove per month, the number of miles driven each outing, tickets and accidents received within the year, if the participant was the only driver in their household, and if they had restricted their driving. No driving variables were significantly correlated with performance on the VRDS or awareness scores. Relationships between each variable are described in Table 7 below.

Insert Table 7: Relationship between Driving Variables and VRDS-Related Measures in Healthy Controls



### 3. *Covariates to IADL Scores*

Additional factors had the potential to impact scores on the IADL for the participant and the reliable informant. The length of time the participant had known their reliable informant was compared to the IADL score ( $r = -.07, p = \text{ns}$ ) and IADL discrepancy score ( $r = .019, p = \text{ns}$ ) using Spearman's rho correlations. Kruskal-Wallis tests were used to determine if there were any significant differences in IADL and IADL median discrepancy scores based on the type of relationship the participant had with the reliable informant. There were no significant differences between groups. For complete statistics, refer to Table 8.

Insert Table 8: Relationship between Demographic Variables and IADL's in Healthy Controls

#### Preliminary Analyses

##### *Statistical Power*

A power analysis for the current study was based on a literature review for a similar study examining individuals with mild AD, which yielded a moderate effect size (Feldman et al., 2005). The present study aimed to be conservative, and therefore used the lower of the 95% confidence interval of the effect size, yielding an effect size of  $r = .44$ . Though the study aimed for power of .80, this yielded a total of 35 participants needed in each group to test Aim I in this study (G\* Power: Faul, Erdfelder, Lang, & Buchner, 2007). The current study had complete results for 30 healthy controls. With an effect size of  $r = .44$  and an alpha level of .05, this yielded a power of 0.69. Given the reduced sample size, it is likely that the study had insufficient power to detect a minimal meaningful effect. As this is one of the first studies to examine the relationship between awareness and performance on a VRDS, estimates of the effect were used to ensure a 95% probability of a true population parameter in future studies. This was done for significant relationships for only the primary variables. This study conducted exploratory work to better understand cognition, function, and awareness in older adults. As such, it is likely that

one or more of the significant correlations may be spurious given the inflated type I error for the number of correlations calculated.

Individuals with mild AD were not examined quantitatively for the original hypothesis due to the small sample size ( $n=4$ ). This sample size resulted in insufficient power to determine a minimal meaningful effect. Rather, each individual was analyzed as a separate case, yielding a case series.

### *Healthy Controls*

Primary variables were evaluated for normality, distribution, and descriptive statistics. The distribution of data across variables was not normally distributed, as performance across cognitive, functional, and unawareness tests were skewed. Logarithmic and linear transformation of the data was attempted, though it did not result in the data being normally distributed. Therefore, nonparametric analyses were conducted. Table 9 displays the means, standard deviations, quartiles, minimum, and maximum scores for each variable for a more complex understanding of each variable.

Insert Table 9: Cognitive and Functional Characteristics for Healthy Controls

A Spearman's rho correlation matrix of primary variables was conducted and is presented on Table 10. Scores from the TMT-B and JLO were significantly and positively related,  $r=.411, p<.05$  as well as the JLO and the CVLT,  $r=.373, p<.05$ . As the standardized score on the TMT-B increased, the age-corrected score on the JLO also increased. Similarly, as scores on the JLO improved, performance on the CVLT also improved. A significant correlation existed between the VRDS and the CVLT,  $r=.563, p<.01$ . As performance on the VRDS improved, similar performance was noted on the CVLT. A significant correlation was also evident between the VRDS and the JLO,  $r=.452, p<.05$ . Higher performance on the VRDS was associated with better performance on the JLO. The IADL was significantly correlated with the IADL discrepancy score,  $r=-.747, p<.01$ . An increase in IADL score was correlated with a decrease in

the discrepancy between the participant and the reliable informant on the IADL (IADL discrepancy score). The predicted awareness score was significantly, negatively correlated with both the scores on the CVLT,  $r=-.471$ ,  $p<.01$  as well as with the TMT-B,  $r= -.378$ ,  $p<.05$ . As these cognitive scores improved, the participant tended towards underestimating their predicted performance on the VRDS. There was also a significant and negative correlation between the TMT-B and the recognition awareness score,  $r= -.380$ ,  $p<.05$ . As the  $z$ -score for the TMT-B increased, there was a tendency for a participant to minimize perceived performance from pre- to post- VRDS. There was a significant and negative relationship between the predicted awareness score and performance on the VRDS,  $r= -.433$ ,  $p<.05$ . Better performance on the VRDS was associated with an underestimation of VRDS performance. There was also a significant and negative correlation between the VRDS and the recognition awareness score,  $r= -.440$ ,  $p<.05$ . Better scores on the VRDS were associated with a tendency to minimize perceived performance from pre- to post- VRDS. Lastly, there were significant correlations found between recognition awareness and both predicted awareness ( $r=.697$ ,  $p<.01$ ) and unawareness post VRDS exposure ( $r=-.507$ ,  $p<.01$ ). Table 11 shows the 95% confidence intervals for significant correlations which may be helpful for future studies to have estimations of the relationship between the measures. If there were multiple random samples taken of the measures from the same parent population, the true population correlation coefficient would be between the lower and upper limits of the confidence interval. It is unlikely (5%) that the true value of the correlation coefficient would be outside the confidence limits. The lower limit of the confidence intervals also provide important information as estimates of the population effect size for apriori power analyses.

Insert Table 10: Spearman's rho Correlation Matrix for Primary Variables for Healthy Controls

Insert Table 11: 95% Confidence Intervals for Significant Correlations

*Analyses of Hypotheses*

*Aim 1:* The first aim of this study was to examine the relationship between unawareness and functional ability for healthy controls, controlling for performance on each cognitive task. Functional ability was measured by the IADL, a traditional questionnaire of daily functioning as well as by performance on the VRDS, a more novel on-line measure of one specific functional task: driving performance. Unawareness was measured in two ways, the first being the discrepancy between a participant's score on the IADL and their reliable informant's score on the IADL. The second measure of unawareness was the discrepancy between the participant's actual performance on the VRDS and their perception of their performance following VR exposure. Cognitive tasks that this study controlled for included the CVLT ( $d'$  score), the TMT-B ( $z$ -score), and the JLO (age-corrected score). See Table 12 for a list of partial correlations among variables.

*Hypothesis 1a.* Controlling for performance on the CVLT, a verbal memory test, there was not a significant covariance between performance on the VRDS and unawareness of performance,  $r = .33, p = .08$ . Controlling for performance on the CVLT, unawareness accounted for 11% of the variance in VRDS performance. When performance on the CVLT was not controlled for, unawareness shared 3% of the variance with performance on the VRDS.

*Hypothesis 1b.* Controlling for performance on an executive control test, the TMT-B, there was not a significant covariance between unawareness and performance on the VRDS,  $r = .14, p = .48$ . Unawareness accounted for 2% of the variance of performance on the VRDS, controlling for performance on TMT-B. Unawareness shared 3% of the variance with performance on the VRDS when not controlling for performance on the TMT-B. The TMT-B is a suppressor variable in the relationship between unawareness and performance on the VRDS.

*Hypothesis 1c.* There was not a significant covariance between unawareness and performance on the VRDS when controlling for performance on a visuospatial test, the JLO,  $r = .184, p = .35$ . Controlling for performance on the JLO, unawareness accounted for 3% of the

variance of performance on the VRDS. When not controlling for performance on the JLO, unawareness accounted for 3% of the variance in VRDS performance. The JLO did not clarify the relationship between unawareness and performance on the VRDS.

*Hypothesis 1d.* There was a significant covariation between unawareness and functional ability, as measured by the IADL when controlling for performance on the CVLT,  $r = -.662$ ,  $p < .0001$ . Controlling for performance on the CVLT, unawareness of one's functional ability accounted for 44% of the variance on the IADL score. When not controlling for performance on the CVLT, unawareness accounted for 44% of the variance on the IADL score. Therefore, although there is a significant covariance between unawareness and IADL score when controlling for CVLT, it appears that controlling for the CVLT does not clarify the relationship between the two variables.

*Hypothesis 1e.* A significant covariation exists between unawareness of functional ability and score on the IADL when controlling for performance on the TMT-B,  $r = -.656$ ,  $p < .0001$ . Controlling for performance on the TMT-B, unawareness of functional ability accounted for 43% of the variance on the IADL. Although this is significant, unawareness accounted for 44% of the variability in IADL score when not accounting for score on the TMT-B. Therefore, controlling for the score on the TMT-B does not clarify the relationship between IADL and unawareness of functional ability.

*Hypothesis 1f.* There is a significant covariation between unawareness of functional ability and score on the IADL when controlling for performance on the JLO,  $r = -.661$ ,  $p < .0001$ . Unawareness of functional ability accounted for 44% of the variance on IADL score when controlling for performance on the JLO. When not controlling for performance on the JLO, unawareness also accounted for 44% of the variability on the IADL score.

Insert Table 12: Partial Correlations for Primary Variables for Healthy Controls

*Aim 2:* The second aim of the study was to evaluate different types of awareness of a more novel functional assessment, the VRDS. Participants were asked to predict their performance prior to driving in the VRDS, and after a practice trial. This score was called “predicted awareness”. They were then asked to rate their perceived performance (unawareness score) upon completion of the VRDS. This comparison served as the primary unawareness score for Aim I of this study. Perceived awareness and unawareness were contrasted to better understand if participant’s views about themselves change upon exposure to a task. Perceived awareness and unawareness after exposure to the VRDS were contrasted in a ‘recognition awareness’ score. This score reflects the change in unawareness scores from prior to post VRDS exposure.

*Hypothesis 2a:* A repeated-measures ANOVA using the Greenhouse-Geisser estimates of sphericity show that there was not a significant difference in the type of awareness used for the VRDS,  $F(1.18, 32.92) = .591, p > .05$ . There was no significant difference between predicted awareness, unawareness, and recognition awareness.

*Hypothesis 2b:* Due to the restricted clinical sample size of participants with mild AD, a repeated-measures ANOVA could not be run.

#### *Results for Clinical Case Examples*

There were four participants with mild Alzheimer’s dementia in the study. Quantitative measures were not appropriate for analysis of the original hypotheses. Instead, the scores for each clinical case example were contrasted to the mean of the healthy controls for each primary variable. This comparison is displayed graphically in Figures 4-12 below. In addition, cut scores were introduced for each primary variable, and results from each clinical case example were contrasted to these cut scores. Therefore, the four clinical cases will be described qualitatively and quantitatively below.

*Cut Scores:* Normative data from both the CVLT (CVLT-Short form normative data in Delis et al, 2000) and TMT-B (Heaton et al., 1991) allowed for conversion of scores into  $z$ -scores. Cut

scores of both 1 and 2 standard deviations were used for each test for a comparison of how each clinical participant scored in contrast to both the normative data as well as to the healthy controls, which served as the normative data for this clinical sample. Although there was no normative data for  $z$ -score conversions on the JLO, normative data from Benton, Sivan, Hamsher, and colleagues (1994) provided cut scores at which point scores reflect mild to moderate impairment (scores between 17 and 20) and at which point scores reflect severe impairment (below 17).

The remaining primary variables were scores on the IADL, the IADL discrepancy score, performance on the VRDS, the unawareness score, the predicted awareness score, and the recognition awareness score. These variables were compared to the performance from the healthy controls by converting scores into  $z$ -scores using the healthy controls from this study as the normative population. Cut scores of 1- and 2- standard deviations from the mean were used as comparisons for each clinical case. Scores for the clinical sample are presented in Table 13.

*ADI:* With scores well below the 2-standard deviation cut score on both the CVLT ( $d' = -5.50$ ) and TMT-B ( $z = -2.30$ ), this participant had difficulty with cognitive tests measuring verbal memory and executive functioning. In contrast, she performed within normal limits on the JLO. Her IADL score (10/16) was well beyond 2 standard deviations from the mean of the healthy controls in the study, indicating difficulty on functional tasks. The IADL discrepancy score of 6 indicates a degree of unawareness related to these instrumental activities of daily living. She significantly overestimated her functional abilities as compared to what her reliable informant reported. In contrast, the participant scored above the mean for the healthy controls on the VRDS, an on-line test of functional ability. Whereas the participant had overestimated her functional ability on instrumental activities of daily living on the IADL questionnaire, she underestimated her ability on the VRDS both when predicting how she would do (within one standard deviation from the healthy control mean), and following exposure to the test (greater

than one standard deviation from the healthy control mean). Therefore, her awareness of functional ability is not accurate both for traditional and more novel functional measures.

*AD2:* This participant demonstrated the greatest difficulty on the CVLT, scoring below 2 standard deviations from the normative mean ( $z = -4.0$ ). Performance on the TMT-B was less than one standard deviation from the normative mean ( $z = -1.70$ ), while performance on the JLO was substantially above the cut score. This participant's IADL score indicated mild difficulty on functional tasks, and his score was greater than 1 standard deviation lower than the mean for the healthy controls. His IADL discrepancy score was over 1 standard deviation from the healthy controls' mean from this study, indicating a degree of unawareness in overall traditional measures of functioning. In contrast, his performance on the VRDS was above the healthy controls' mean from this study, and both his predicted awareness as well as his unawareness score after exposure to the test was within one standard deviation to the mean, indicating a degree of accuracy when measuring performance on the more novel functional task. His awareness therefore differed between traditional and more novel functional measures.

*AD3:* While his score on the TMT-B was above the cut score and within normal limits, his performance on the CVLT was below 2 standard deviations from the normative mean ( $z = -3.5$ ), indicating difficulty with verbal memory. His score on the JLO was in the range considered mild to moderately impaired, evidencing difficulty with visuospatial perception. The IADL score indicated significant difficulty on functional tasks (beyond 2 standard deviations below the healthy control's mean), and there was a substantial discrepancy from his and his reliable informant's perception of his functioning. This discrepancy was beyond 2 standard deviations from this study's healthy controls' mean, indicating problems in awareness on traditional measures of daily functioning and a tendency for him to overestimate overall functioning. He also demonstrated unawareness on the VRDS both prior to and following exposure to the task (beyond 1 standard deviation from the mean). Although his performance on the VRDS was



within normal limits, he significantly overestimated his performance on both occasions.

Therefore, he demonstrated limited awareness on both traditional and novel functional tasks.

*AD4:* This participant scored within normal limits on tests measuring verbal memory and executive functioning. His score of 20 on the JLO was in the mild to moderate impairment range. His reliable informant indicated difficulty on several aspects of instrumental activities of daily living (scoring 12/17). There was a discrepancy of two points between his score and his reliable informant's score on this measure, which was beyond 1 standard deviation from this study's mean. While he tended to overestimate his general functional abilities, he demonstrated intact awareness of performance on the VRDS. His actual performance on the VRDS was within normal limits.

Insert Table 13: Cognitive and Functional Characteristics for Clinical Sample

#### Exploratory Analyses

##### *Simulation Sickness*

One of the major unanticipated findings in this study was the number of participants who experienced simulation sickness as a result of VRDS exposure. Eight of the participants in this study experienced symptoms consistent with simulation sickness requiring the discontinuation of the driving environment. This is equivalent to approximately 24% of the study sample. One participant experienced symptoms after exposure to the training session which lasted less than five minutes, and therefore was never exposed to the VRDS for testing. In attempts to understand factors that may have been significantly correlated to simulation sickness, the data from all 34 participants were examined. Chi squared analyses were conducted to determine a significant association between the presence of simulation sickness during the study (yes/no) and other categorical variables such as gender and ethnicity. Mann Whitney tests were conducted to determine if there were significant differences in the mean age, days per month a participant drove, miles driven each drive, history of past simulation sickness, and cognitive and IADL

variables for all the participants who got simulation sickness versus those who did not. Chi squared analyses yielded no significant associations, and Mann Whitney tests yielded no significant differences between groups of people who experienced simulation sickness and those who did not. To further clarify potential factors that may relate to simulation sickness, the total score on the post-VRDS SSQ was also compared to all of the variables mentioned above through Spearman's rho correlations and Mann Whitney tests with no significant findings.

#### *Other Cognitive Variables*

The MMSE was given to all participants to screen for inclusion criteria. Additionally, the Clock Drawing Test and Trail Making Test- Part A (TMT-A) were also given as exploratory tests, due to their link to functional performance in previous studies (Duchek, Hunt, Ball, Buckles, & Morris, 1997; Freund et al., 2004). Exploratory correlation analyses were run to identify any significant relationships between these cognitive measures and performance on the VRDS, IADL, or unawareness scores in healthy controls. A significant correlation was found between the MMSE and the IADL score,  $r = .509, p < .01$ . As the score on the MMSE increased, the score on the IADL also increased. The raw score on the Clock Drawing Test was significantly correlated with the score on the IADL,  $r = .391, p < .05$ . As performance on the Clock Drawing Test improved, the score on the IADL also increased.

#### *Exploratory Partial Correlations*

Correlational analyses revealed significant relationships between several measures of cognition and performance on the VRDS with predicted awareness scores and recognition awareness scores. Because of this, exploratory partial correlations were run using this variable in place of the previously used unawareness score when examining the first aim of the study for healthy controls. No significant relationships were found between performance on the VRDS and predicted awareness, when controlling for performance on the CVLT, TMT-B, or JLO. While significant relationships were found between performance on the VRDS and recognition

awareness controlling for each cognitive variable, controlling for such variables did not clarify the relationship between the VRDS and recognition awareness. In fact, controlling for such variables resulted in less variation explained between VRDS and recognition awareness.

When exploring the primary aim of the study for healthy controls, partial correlations were run between performance on the VRDS, unawareness, and performance on several cognitive measures. Holding performance on cognitive measures constant, there was no significant relationship between performance on the VRDS and unawareness score. However, holding unawareness constant, significant relationships were found between performance on the VRDS and performance on cognitive tests which warrant discussion. The results for healthy controls are presented in Table 12 below. Controlling for unawareness, there is a significant relationship between performance on the VRDS and CVLT, as measured by the  $d'$ ,  $r=.610$ ,  $p<.001$ . Controlling for unawareness, performance on the CVLT accounted for 37.3% of the variance in VRDS performance. When unawareness was not controlled for, the CVLT shared 31.7% of the variance with performance on the VRDS. Controlling for unawareness, there is a significant correlation between performance on the VRDS and the JLO,  $r=.453$ ,  $p<.05$ . When holding unawareness constant, performance on the JLO accounted for 20.5% of the variance in VRDS. However, when not holding unawareness constant, performance on the JLO shared 20.4% of the variance in VRDS. Therefore, though there was a significant relationship, controlling for unawareness did not serve to clarify the relationship between VRDS and performance on the JLO. See Table 14 for additional partial correlations.

Insert Table 14: Additional Partial Correlations for Primary Variables for Healthy Controls

## CHAPTER 5: DISCUSSION

The intended focus of the present study was to examine the relationship between unawareness and functional ability holding cognitive factors constant in individuals with mild AD. Enrollment challenges resulted in a total of four individuals with mild AD who completed the study, making the originally proposed quantitative analyses within this group inappropriate. Instead, the majority of the participants in the study included healthy older adults from the community. Thus, the originally proposed study design was examined quantitatively for healthy controls only, and its importance is two-fold. Understanding this relationship in healthy controls will serve as a baseline for which to compare results for individuals with mild AD in future studies. Additionally, due to the importance placed on driving as well as the inconsistent policies restricting driving as adults age, it is crucial to understand the factors that lead to unsafe driving in older adults. Current policies rest on the assumption that healthy older drivers are able to restrict their own driving as they become aware of sensory, functional, and cognitive age-related changes (in Donorfio, D'Ambrosio, Coughlin, & Mohyde, 2009). These policies thus rely on an individual's awareness of any driving changes. Studies conducted on older adults have also shown that individuals report less accurate awareness of driving difficulties as problems in cognition arise (Freund et al., 2004). In sum, understanding the relationships between unawareness, cognition, and functional ability can help to establish safer driving laws as well as promote greater safety as individuals age.

## Examining Functioning in Healthy Older Adults

Two most commonly used methods of measuring functional ability in individuals with mild AD are by way of caregiver accounts of performance and by directly assessing individuals in laboratory settings. Studies examining functioning in older adults have also relied on response to questionnaires as well as performance in laboratory settings. The current study measured function using both methods in order to gain a more comprehensive understanding of

functioning. The study used the Lawton and Brody Instrumental Activities of Daily Living Questionnaire (IADL questionnaire), which is one traditional measurement of functional performance by way of caregiver account. The study also used the virtual reality driving simulator (VRDS), a novel method of functional. Farias and colleagues (2003) have found a correlation of  $-.66$  between the more traditional caregiver assessment of functioning and the more novel laboratory assessment of function. Specifically, they used the IADL questionnaire and the Direct Assessment of Functional Status Scale, which measures the individual's performance in a laboratory setting on a variety of tasks, such as dialing a telephone and writing a check. They posit that the level of cognition involved in a functional task contributes to the variability in measurements. In contrast to their study, the current study found a weak correlation of  $r = .145$  between the traditionally used IADL questionnaire and the novel VRDS in assessing functional performance. The VRDS functional score showed a strong relationship to measures of cognition, unlike the IADL functional score.

In order to better understand these findings, it is important to consider the difference between these functional measures. First, the VRDS provides an objective measurement of specific functional behavior while the IADL is a subjective measurement which assesses general functional performance on a variety of tasks. The VRDS allowed for the carefully controlled measurement of functional performance in real-time, thereby allowing for observation of driving performance under specific and challenging conditions. In contrast, the IADL relied on a caregiver or reliable informant's assessment of functioning in daily functioning over a variety of conditions. Although the scoring on the VRDS was objective across all participants in the study, the normative data used to assess driving performance was based on a small sample size of individuals and was specific to the virtual environment used in the present study. Conversely, the IADL is a heavily utilized instrument in both clinical and research settings with more established psychometrics (i.e. Farias et al., 2003). In sum, the two measures of functional assessments used

in this study were distinct from one another in numerous ways, and were minimally correlated. The distinct qualities of each assessment measure have implications for their relationship with measures of cognition and awareness, and will be described below.

### Examining Awareness in Healthy Older Adults

One of the primary aims of the present study was to examine unawareness in individuals with mild AD as well as in healthy older adults. The literature suggests that the operational definition of unawareness changes as a function of the technique used for measurement (Agnew & Morris, 1998). Because of this, different measures of unawareness are often uncorrelated (Clare, 2004b). Despite this relationship, studies suggest that using multiple techniques for which to measure unawareness will result in a more comprehensive understanding of this construct. Additionally, studies suggest using measures of unawareness that are appropriate for the domain being assessed. The present study examined awareness of functioning as measured by both the IADL questionnaire as well as performance on the VRDS, which are vastly different constructs of functioning. As such, the use of the term 'unawareness' throughout is defined as a score an individual received on one of two measurement techniques. While the study attempted to equate this score to an individual's level of insight into their own functioning, it is important to understand that the 'unawareness' scores used in the study are a narrow measurement of a broad and complicated construct.

In examining functional ability by way of the IADL questionnaire, unawareness was defined as the discrepancy between the participant's reports of their own functioning versus their reliable informant's assessment of their functioning. While it allows for an account of a participant's functioning in their daily lives, it is potentially influenced by the relationship between the reliable informant and participant. The current study found no significant differences in IADL scores by the reliable informants as a function of length or type of relationship with the participant. Studies involving both individuals with mild AD (Clare, 2004b)

as well as healthy older adults (Freund et al., 2004) have also found that individuals tend to overestimate their functional performance in their daily lives as well as in their driving abilities. Findings from this study support these claims. Participants tended to rate themselves with higher IADL scores than did their reliable informants, although the discrepancy between participants and their reliable informants was much greater for individuals with mild AD.

Awareness was also examined in relation to performance on the VRDS. Three measures of VRDS-awareness were examined. 'Predicted awareness' was the participant's assessment of their predicted performance minus their actual performance on the VRDS. 'Unawareness' was the participant's perception of their performance minus their actual performance on the VRDS. Finally, 'recognition awareness' was their predicted awareness score minus their unawareness score, or the amount of change in perception after exposure to the VRDS. Studies have shown that accuracy of predicted awareness changes as a function of an individual's familiarity to a task (Cavanaugh, 1989). As the study relied on a virtual driving environment which was novel to most participants, predicted awareness was not used as the primary unawareness variable. Instead, the primary variable used in the study was 'unawareness', or the participant's perception of their performance on the task after exposure.

Results from the present study found no significant relationship between post-assessment unawareness of driving ability and performance on the VRDS. There were significant relationships between performance on the VRDS and both predicted awareness as well as recognition awareness. However, the significance of this relationship is minimized as research suggests that the validity of awareness measures change as a reflection of task familiarity. As participants in the study were unfamiliar with the virtual environment, their predicted awareness score is therefore deemed less valid than their assessment after exposure to the environment. Additionally, when comparing the three types of unawareness measures, no differences were found, suggesting a spurious significance. The lack of relationship between the VRDS and

unawareness score can be considered in light of the cognitive awareness model (CAM) outlined by Morris and Hannesdottir (2004) and described by Ansell and Bucks (2006).

The CAM model of unawareness was developed for individuals with mild AD, and explains different types of unawareness based on disruption of information processing as a result of brain pathology. The assumption in the given study was that the healthy controls did not have the brain pathology evident with individuals with mild AD. However, this model posits that unawareness results when an individual's appraisal system of success and failure is disrupted. Healthy controls in the study may not have had an accurate appraisal of their performance on the VRDS due to the novelty of the virtual reality instrument. According to the model, new events and information are processed by the central executive system in the frontal lobe. A comparator mechanism in the executive system compares this new event to knowledge from the individual's personal database. Any mismatch between a new event and personal knowledge is processed by the cognitive awareness system in the parietal lobe, which ultimately results in an individual's awareness of that discrepancy. Healthy controls in the study had no past knowledge for which to compare their current level of functioning on the VRDS. As such, there was no mismatch between the new VRDS event and previous performance. This may have resulted in an individual's inability to assess their current performance. This model may also account for the lack of significant changes in awareness over time (i.e. no significant difference between predicted awareness, unawareness, and recognition awareness). Participants in the study were more likely to be consistent with their original hypothesis about their performance in such a novel environment. For this reason, some researchers suggest that the validity of certain awareness measures is questionable for unfamiliar tasks (Clare, 2004b; Hardy, Oyebode, & Clare, 2006). Thus, using virtual technology with older adults might be a limitation in accurately assessing awareness of function.



Controlling for scores on cognitive tests did not serve to clarify the relationship between function and awareness of function in healthy controls. This was seen in both traditional and novel assessments of functioning. The individual relationships between function, awareness, and cognitive variables differed based on the construct examined. Results warrant further discussion.

#### *Function, Awareness, and Cognition Using Traditional Measures*

Controlling for cognition did not clarify the relationship between functioning, as measured by the traditional IADL questionnaire, and unawareness, as measured by the participant-reliable informant discrepancy score. This discrepancy score had low variability for healthy controls (the maximum discrepancy score was five points). This may have been due to the fact that the IADL questionnaire was designed for individuals with dementia, and is therefore not as sensitive to functional changes in healthy older adults. Despite this, the study did find a relationship between function and awareness using the IADL, not controlling for cognition. Significant findings are based on a maximum five-point discrepancy between the participant and the reliable informant, and should therefore be interpreted with caution. One possible interpretation of these scores is the suggestion that higher functional status, as reported by a reliable informant, is related to greater awareness of functional ability. Likewise, awareness declines as functioning declines. This relationship was not seen when using the VRDS to assess awareness and function.

The relationship between IADLs and awareness of functional status, as measured by the discrepancy score, in this study suggests that those healthy older adults with intact functional abilities demonstrate more awareness regarding these abilities. The reverse relationship is also true, though should be interpreted with caution due to the low variability in scores as well as lack of sensitivity of the IADL questionnaire for healthy older adults. However, an individual's ability to self regulate is likely to decline as their awareness of ability declines. Current policies regarding driving rely on the individual to restrict their driving as they deem necessary in order to

avoid any potentially unsafe driving practices. While this policy may maintain the safety for those individual with intact awareness, it may put those at risk who lack the awareness to regulate their own driving as a result of functional changes. While the current study used a questionnaire that was designed for individuals with dementia, results suggest a relationship between function and awareness. Future studies should further examine this relationship using instruments designed specifically for healthy older adults.

Exploratory analyses for the healthy controls revealed significant and positive relationships between both the MMSE, a global measure of cognition, and the Clock Drawing Test, a measure of visuospatial processing and executive functioning, with scores on the IADL. This is not surprising, as research has linked higher scores on the MMSE with higher functional status in both healthy older adults as well as for people with dementia (i.e. Ford, Haley, Thrower, West, & Harrell, 1996). Studies have also established a relationship between the Clock Drawing Test and IADL's, particularly in individuals with Alzheimer's dementia (Freund et al., 2004). In fact, some suggest that the Clock Drawing Test is so predictive of activities of daily living in individuals with Alzheimer's dementia that it might even work to take the place of the IADL questionnaire (Fukui & Lee, 2008).

Although neither the MMSE nor the Clock Drawing Test were correlated to unawareness of IADL scores in this study, the correlation between them and IADL scores in healthy controls is important. Both the MMSE and Clock Drawing Test are well established cognitive tests, quick to administer, and well known to geriatric healthcare providers. In fact, the Clock Drawing Test has been shown as useful for predicting driving in older adults (Freund et al., 2004). Higher scores on the MMSE and Clock Drawing Test were correlated with greater functioning, which in turn was associated with greater awareness of functioning and potentially greater safety due to appropriate self restriction. Conversely, lower scores were associated with lower IADL scores, which were associated with less awareness and therefore potential safety concerns due to the

decreased likelihood of appropriate self regulation. Future studies should further examine this relationship.

### *Function, Awareness, and Cognition Using Novel Measures*

Controlling for cognition did not further clarify the relationship between functioning and awareness on the VRDS, a novel functional task. Significant relationships were found between performance on the VRDS and several cognitive tests, which is not surprising as researchers posit that functional tasks that require a great deal of cognitive capacity such as driving are more strongly correlated with performance on neuropsychological tests (Farias et al., 2003). There was a significant relationship between performance on the VRDS and scores on a test measuring visuospatial processing (JLO). A significant relationship between driving performance and scores on visuospatial tests is well established in the literature both in individuals with mild AD (Yu et al., 2006) as well as in healthy older adults (Okonkwo et al., 2007). In fact, numerous driving studies have linked impairments in visuospatial processing with worse driving performance and therefore greater self-restricted driving practices in otherwise healthy older adults (Okonkwo et al., 2007). The relationship between performance on the VRDS and visuospatial processing was not linked to awareness of one's performance. A lack of awareness corresponding with increased visuospatial problems could possibly result in unsafe driving in those individuals with visuospatial impairments.

### Clinical Findings

With four clinical participants in the study, quantitative analyses were not appropriate. Rather, each clinical participant's findings were compared to results from normative data or results from the healthy controls if normative data was unavailable. Trends in the data suggest that scores on the MMSE were related to awareness of both IADL's and VRDS performance, as operationally defined by way of discrepancy scores. This relationship was not seen in healthy controls, though the MMSE was linked to functional performance.

The MMSE currently serves as the gold standard for which to summarize cognitive status in individuals with dementia, and has been correlated with functional ability in individuals with dementia (Feldman et al., 2005). The MMSE has also been linked to functional status in older healthy adults both in previous studies (ie., Ford et al., 1996) and in the current study. This instrument is widely used, quick and easy to administer, and well known to numerous geriatric healthcare professionals. Some researchers argue that the MMSE is too general an instrument to measure the exact cognitive mechanisms underlying function in individuals with mild AD (Jefferson and colleagues, 2006). However, the association between MMSE score and measures of awareness in individuals with mild AD in the current study merits examination.

Determination of disease stage is often made based on the MMSE score. Individuals with Alzheimer's are generally considered to be mild in the disease process if they score between 18 and 24 on this test (MMSE; Folstein et al., 1975). Lower scores are associated with lower cognitive functioning whereas higher scores are associated with higher cognitive functioning. As such, lower scores are reflective of greater disease involvement. Lower MMSE scores in this study were also associated with a general trend towards more unawareness on both traditional and novel functional tasks. Conversely, greater MMSE scores are reflective of less disease involvement and were associated with a general trend towards less unawareness on both traditional and novel functional tasks.

Taken together, data from this study suggests that the MMSE may be a useful tool for understanding changes in awareness as the AD disease process progresses. Although the MMSE measures global cognitive functioning, it reflects disease progression in mild AD that is known to originate in the medial temporal lobes and hippocampus (Welsh-Bohmer & Warren, 2006). As such, mnemonic unawareness as described by the CAM model may explain the progression of unawareness as scores on the MMSE decline (Agnew and Morris, 1998; Ansell and Bucks, 2006; Morris and Hannesdottir, 2004). Lower MMSE scores reflect greater disease progression, which

in turn reflects greater pathology in the medial temporal lobes and hippocampus in individuals with mild AD. According to Ansell and Bucks (2006), this pathology disrupts an individual's ability to update or accurately access their personal knowledge database, an aspect of semantic memory that contains knowledge of one's self. As such, an individual is therefore not able to encode changes in cognitive or daily functioning. Thus, they are unable to accurately compare present performance to their personal knowledge of oneself. Therefore, no discrepancy is detected between present and past performance, resulting in an unawareness of functional or cognitive changes. As AD evolves, unawareness evolves because an individual becomes less able to encode new information and compare new information to previous information about oneself.

Additional support for mnemonic unawareness as suggested by the CAM model comes from qualitative examination of unawareness scores on both traditional and novel functional tasks for participants with mild AD. Consistent with the literature (Clare, 2004b), clinical participants in this study tended to overestimate their daily functioning, as measured by the IADL. Although healthy controls in the study also overestimated their daily functioning, individuals with mild AD did so to a far greater degree. A tendency to overestimate present functioning is fitting with the model in that individuals are not able to encode new functional capabilities, nor are they able to accurately compare present abilities to past abilities. This results in a self construct that reflects past functional abilities, thus overestimating current functional capacity as disease progress leads to decreased functional capacity.

The CAM model describing mnemonic unawareness is further supported by the pattern of awareness scores regarding performance on the VRDS in clinical participants. Similar to performance from the healthy controls, clinical participants tended to maintain the same level of awareness both pre- and post- VRDS exposure. Both groups of participants had virtually no exposure to a VRDS, and therefore had no prior knowledge for which to compare their present

performance. In both groups of individuals, it follows that individuals therefore could not accurately appraise their present performance with past performance, leading to a tendency to be consistent with their original hypothesis about their performance in this novel environment.

The lack of a relationship found between memory measures and unawareness scores in individuals with mild AD are not fitting with the CAM model of unawareness. It is possible that the sample size used in this study was too small to find a minimal meaningful result. Another possibility is that global cognitive measures, such as the MMSE, are more sensitive to overall awareness levels at the earlier stages of Alzheimer's dementia. Future studies should further explore the relationship between memory and awareness in individuals with mild AD.

### Unanticipated Findings

#### *Difficulty with Enrollment*

Perhaps the most interesting and unanticipated finding of the current study was the extreme hesitance for individuals to enroll in the study. As difficulty with enrollment emerged, a total of seven clinical sites in the community agreed to aid in recruitment for the study. Additionally, postings and presentations in the community were introduced as methods for recruitment of healthy controls. Feedback from these sites over time revealed that potential participants were hesitant to have their driving and cognition assessed despite the confidential nature of the study.

Several theories emerged underlying hesitation for study enrollment particular to individuals with mild AD. Numerous individuals were informed about the study during their feedback session from a neuropsychological evaluation, an evaluation deemed appropriate due to the individual's cognitive and/or functional decline. As such, these individuals may have already felt anxious about these changes. The current study examined cognition and function, thus serving to further increase anxiety. Additionally, feedback sessions are generally a time when an

individual is first told about their diagnosis of mild AD. This diagnosis is a great deal for an individual to process, leaving the importance of participation in the study of low priority.

Healthy controls were also hesitant to enroll in the study, necessitating recruitment from community centers throughout the Philadelphia County in addition to recruitment from the seven clinical sites. When approached about the study, three factors emerged as reasons for resistance to participate in the study. Several individuals noted the inconvenience of the study location. Inconvenience was largely due to distance from the individuals' homes or the preference of individuals to avoid navigating in the city. A second factor that emerged was the hesitancy individuals expressed about participating in a study that assessed cognitive functioning. Lastly, numerous individuals conveyed reluctance towards having their driving assessed. Speculation about the resistance could be the relationship between driving and self worth, independence, and one's link to the community (Donorfio et al., 2009). This could be a reason why individuals might not self regulate driving as they age, which could in turn lead to unsafe driving practices.

#### *Simulation Sickness:*

An unanticipated negative side effect of the study was the high percentage of people who experienced simulation sickness symptoms severe enough to warrant discontinuation of the VRDS. Eight of the 34 participants in the study discontinued the VRDS due to such symptoms, which was approximately equivalent to 24% of the study sample. Several other participants in the study experienced symptoms consistent with simulation sickness that were mild, not interfering with their completion of the VRDS. The high rate of discontinuation due to simulation sickness was surprising, because although research suggests that up to 60% of individuals can develop some symptoms of simulation sickness upon exposure to a virtual environment (Lawson, Graeber, & Mead, 2002), these symptoms are reportedly typically mild and do not warrant discontinuation from the environment (in Nichols and Patel, 2002).

Additionally, steps were taken in the design of the study in attempts to minimize simulation sickness. These steps are described below.

Simulation sickness, also known as cybersickness, includes symptoms such as nausea, sweating, increased salivation, disorientation, headache, and dizziness (Nichols & Patel, 2002). Although simulation sickness is not clearly understood, one popular theory to explain the constellation of symptoms is based on sensory conflict (Reason & Brand, 1975; in Nichols & Patel, 2002), and posits that the virtual environment creates a disconnect in the sensory system. While the eyes indicate that the person has moved, both the vestibular and proprioceptive systems indicate otherwise. Factors that influence simulation sickness include individual characteristics, system characteristics, and the interaction between the individual and the task (Nichols & Patel, 2002). Age has been linked to simulation sickness, with a peak in simulation sickness between age 2 and 12 years old. Reason and Brand (1975) have reported that susceptibility to simulation sickness gradually wanes after 12 years old and those around 50 years of age are much less prone to such symptoms. Additional individual characteristics influencing simulation sickness include gender, with females being more susceptible to sickness due to a wider field of vision, experience with virtual environments, anxiety, coping strategies, and perceptual styles (Biocca, 1992).

System characteristics thought to impact simulation sickness include the mode of visual presentation. For example, virtual environments presented through a head mounted display are associated with a greater degree of sickness than are environment presented by way of a flat screened monitor (In Nichols & Patel, 2002). Additionally, the feeling of motion is associated with greater simulation sickness due to the disconnection between visually represented motion and the absence of motion experienced through the vestibular systems (in Nichols & Patel, 2002). One study by Mourant and Thattacherry (2000) found that greater perceived vehicle velocity in the virtual environment was associated with greater symptoms of simulation sickness.



In general, the incidence of simulation sickness is hard to predict and not well understood. One model found a complicated relationship between gender, age, mental rotation ability, and postural stability (Kolasinski, 1996). Nichols & Patel (2002) have also reported a relationship between past history of motion sickness and simulation sickness susceptibility. Numerous factors impact simulation sickness and the exact underlying mechanisms of this phenomenon are incompletely understood. Therefore, controlling for simulation sickness in virtual reality is difficult.

Despite the inability to completely avoid simulation sickness, this study attempted to control for as many factors as possible to minimize the onset of sickness. The modified SSQ was given to all potential participants in the current study, and those with a past history of severe motion sickness were excluded from the study. Additionally, as research has shown that older adults are less likely to get simulation sickness (Reason & Brand, 1975), it was predicted that the incidence of sickness would be low. Holland and Rabbit (1992) conducted research on older drivers and found that visual problems for older adults are evident due to the shrinkage of the visual field. Research on simulation sickness posits that wider field of views are associated with greater simulation sickness (Nichols & Patel, 2002). Therefore, it was predicted that simulation sickness would be lower in the current study due to the smaller field of vision and less visual perception of peripherals in older adults. Lastly, the study attempted to avoid simulation sickness by presenting the virtual environment through three flat screen monitors versus a head mounted display. Despite this, a high incidence of simulation sickness was reported.

In attempts to understand potential factors that correlated with the presence and intensity of simulation sickness symptoms, exploratory analyses examined numerous individual factors including past history of motion sickness, driving history, age, cognitive, and functional status. No significant correlations were found. Anecdotally, several participants who discontinued the VRDS in the current study appeared quite anxious in the driving trial. While this study was not

designed to properly examine the impact of anxiety and coping strategies on simulation sickness, future studies should examine this relationship in greater detail.

### *Implications*

The present study served as one of the first to examine awareness and function in both healthy older adults and those with mild AD by way of a VRDS. The results serve as a baseline for which to understand cognition, unawareness, and function for these individuals. It should be noted that ‘unawareness’ in this study was defined by discrepancy scores between the participant’s perception of functioning and either their actual performance on a driving simulator or their reliable informant’s perception of their functioning. Although these are common ways of measuring awareness, they reflect insight into a very specific functional construct and by an equally specific measurement tool. Interpretation using such methods should be taken with caution.

Enrollment issues that emerged resulted in an inability to quantitatively examine individuals with mild AD. However, these enrollment issues served to bring to light the hesitation that many older adults possess regarding having their cognition and functional abilities examined. Particularly noteworthy is the resistance many individuals exhibited regarding having their driving assessed despite both the confidential nature of the study as well as the lack of implications the study had on driving privileges. This highlighted the importance many individuals place on the ability to drive, and it supports theories suggesting that driving serves to promote a sense of connection with society, feeling of independence, and self worth. While it is essential to foster positive self worth and mood as people age, it is also essential to maintain their safety. Future studies should examine whether hesitation in having driving assessed is linked to a greater likelihood of unsafe driving behavior and lack of self regulation.

### *Novel Measures of Functioning*

The current study was one of the first to evaluate cognition, function, and awareness through virtual reality in individuals with AD as well as healthy older adults. As such, the resulting correlations can serve as estimates of population parameters for future studies. The use of VRDS in examining driving for older adults is not well established and this study serves to better understand the factors that impact this type of assessment in the given population. Results suggest that measuring awareness by way of a VRDS is challenging due to the novel nature of the environment. The validity of the awareness measures related to the VRDS were questionable, as participants in the study had no prior knowledge for which to compare their performance on the VRDS.

An additional challenge when using a VRDS was the incidence of simulation sickness. Although some studies posit that simulation sickness is less likely in older adults, the high incidence of sickness in the current study suggests that the factors underlying simulation sickness are still not well understood. Exploratory analyses revealed no significant correlations between simulation sickness and demographics, driving experience, cognitive or functional status. Although the study was not developed to examine the relationship between both anxiety and coping strategies with simulation sickness, anecdotal observations suggest a possible relationship that should be examined further.

Despite the drawbacks of using the VRDS, multiple strengths in using this method of functional assessment also became evident throughout the study. The VRDS allowed for the examination of driving in a safe and controlled environment, in which limits of driving behavior could safely be examined. In fact, 24% of the study sample collided with another object while 18% almost collided with either another vehicle or object on the road. Twelve percent of the study sample lost control over the vehicle at some point in their drive, and 6% drove the wrong way on a one-way street. These are factors that could not have been studied on a behind the wheel test due to safety concerns. In addition to objectively measuring driving behaviors in a

safe manner, the VRDS has the benefit of challenging individuals in ways that could mimic real life situations while studying the types of errors and accidents that older adults might be prone. Given the lack of understanding about the factors that impact driving in adults as they age, this is a viable, inexpensive, and safe manner for which to study this impact. A solid understanding of this population will serve as a foundation for which to understand the functional and awareness changes that result as a function of mild AD. The significant relationship between the VRDS and measures of visuospatial processing (JLO) is consistent with previous studies examining driving behavior (i.e. Okonkwo et al., 2007). These studies suggest a link between driving abilities with visuospatial processing, attention, and speed of processing in older adults. Results suggest that these cognitive measures may have predictive value in determining safe driving practices in older adults.

#### *Traditional Measures of Functioning*

Two significant findings emerged as a result of using a traditional measure of functioning, the IADL questionnaire on healthy controls. The first finding is the significant correlation between functioning and awareness of functioning, as operationally defined by this study. Though much is known about the lack of awareness in individuals with mild AD, intact awareness in healthy older adults appears assumed. In fact, current driving policies regarding older adults rely on the assumption that individuals have awareness of driving abilities enough to self regulate when they deem appropriate. The relationship between functioning and awareness in this study suggests that those individuals with less functional independence have less awareness of such. However, noteworthy is the lack of variation in IADL and IADL discrepancy scores, reflective of the lack of sensitivity of this tool for the use of healthy older adults. Despite this, the significant relationship found in the study raises possible concerns about the likelihood that an individual will demonstrate awareness if self regulation of driving behavior becomes necessary in order to maintain safety. Awareness of functional ability and therefore restriction of

potentially unsafe behaviors should not be assumed in healthy older adults. Effective measures may be necessary to ensure proper regulation of driving as adults age.

The second significant finding is the link between specific cognitive measures with scores on the IADL. Both the MMSE and the Clock Drawing Test were correlated with the IADL in healthy controls, and suggest a relationship between general cognitive functioning and functional ability for healthy older adults. Although this relationship has been established in individuals with mild AD, it suggests a relationship continuum between cognition and functioning that is present without the existence of a dementing illness. This finding lends support for the educated use of both cognitive tools by healthcare providers as screeners for older adults who might have safety risks or have greater needs for assistance in accomplishing daily functional tasks.

#### *Individuals with Mild AD*

Although the number of clinical participants was too small to run quantitative analyses, a trend was seen between global cognitive functioning, as measured by the MMSE, and awareness of functioning. This relationship was seen in awareness measures of both traditional and novel functional measures. As the MMSE serves as a tool to capture global cognitive status, results suggest that disease progression is accompanied by progression of unawareness of functioning. A trend was present for individuals with lower cognitive capacity due to disease progression to score lower on measures of awareness, which might lead to additional safety concerns as individuals lack the awareness to regulate their behaviors. Examination of individuals with AD, as well as healthy controls in the study, support the CAM model which posits that mnemonic unawareness results from an inability to accurately appraise one's behaviors.

#### *Limitations*

When conducting the study, a number of unforeseen difficulties were encountered, and several limitations are reported that have implications on future research. The major limitation was the lack of an adequate sample size to be able to run quantitative analyses on individuals

with mild AD. The primary focus of this study originally was to better understand the factors that impact awareness and functional ability in individuals with mild Alzheimer's dementia. As problems with enrollment emerged, inclusion criteria became less stringent, thereby resulting in several participants with potentially confounding factors impacting mood, cognition, and function. A strength of making criteria less stringent is that the clinical population in this study may better reflect and generalize to other individuals with mild AD in the community. However, despite the difficulty in recruiting clinical participants, the study was able to recruit healthy older adults, which can serve as a baseline for which to understand awareness and functional ability in cognitively intact individuals.

This study's original purpose was to investigate individuals with mild AD while healthy older adults served as a control group. Because of this, the study was designed to measure unawareness using methods common to examining this clinical population: using a participant-reliable informant discrepancy score as well as using a participant perception versus actual performance discrepancy score. Using such scores is less common for healthy older adults, and would not have been the method employed had healthy adults been this study's target population. Instead, the study would have focused on self-regulatory practices related to driving and activities of daily living. The current study used the IADL questionnaire to assess functional activities such as driving. However, this questionnaire is designed for individuals with dementia and is not sensitive to the functional changes of healthy older adults. Questionnaires pertinent to healthy aging, such as those related to sensory functioning, cognition, and physical functioning would have been employed instead. Information would have been collected to assess the importance of driving and independence in each individual's daily lives. A limitation of this study is the lack of information gathered about these changes, attitudes, and behaviors in healthy controls. Future studies should aim to examine the link between self regulation and unawareness in older healthy adults, as it relates to driving and functional ability.

A strength of this study was the ability to examine driving behavior in a safe and manageable way by using a VRDS. However, the size and lack of portability of this instrument resulted in the necessity for participants to come into the lab for complete assessment. Throughout recruitment, several individuals declined to participate in the study due to distance, hesitation of traveling to an unknown destination, or fear of commuting into the city of Philadelphia by way of car, train, or public transportation. The current study only included individuals that were both willing and able to navigate to the lab.

Transportation difficulties resulted in a biased study sample. Additional factors contributed to a biased sample, including the fact that individuals could only participate if they were able to provide a reliable informant who had known them for at least a year. While this did not appear to impact participation, it may have acted as a deterrent for those individuals who could have been uncomfortable stating they could not provide a reliable informant. Still other factors that resulted in a biased sample were the fact that this study assessed people on several cognitive factors as well as driving factors. Difficulties in enrollment reflects the fact that many individuals expressed discomfort with assessment of both factors, and some chose not to participate because of this. The resulting sample reflects a group of individuals that were more comfortable in being assessed on such measures. This sample is more highly educated than the average individual in Pennsylvania, and most likely reflects a group of individuals who are intrigued by research and academia. In fact, the mean education level for healthy controls in the study was approximately 16 years. The minimum level of education for participants in this study was 12 years and almost 62% of the study held at least a bachelor's degree. This is in contrast to the approximately 22% of individuals in Pennsylvania over the age of 25 who were reported to hold bachelor's degrees or higher in the United States census conducted in 2000 (Census, 2000). This may limit the ability to generalize findings to other healthy older adults in the community or individuals with mild Alzheimer's dementia.

Additionally this study is correlational, and therefore cannot make any statements regarding causation. Correlational studies typically require approximately 50 cases for ample power. The small sample size of individuals with mild AD as well as healthy controls may have been insufficient to detect a meaningful effect. Future studies should attempt to further understand the specific relationships between functional status, cognitive status, and awareness as they relate to individuals with mild AD. A broader understand of this relationship could help in treatment planning and possible implications for behavior changes as the disease progresses.



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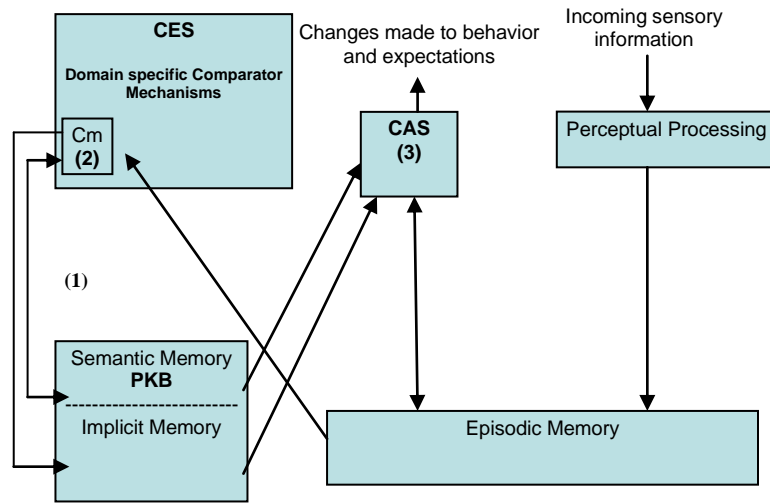
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Figure 1. Cognitive Awareness Model (CAM) (Agnew and Morris, 1998)



(1) = Mnemonic anosognosia; (2) = Executive Anosognosia; (3) = primary anosognosia

CAS: Conscious Activating System

CES: Central Executive System

Cm: Mnemonic Comparator

PKB: Personal Knowledge Base

Figure 2: Overview of Study Design

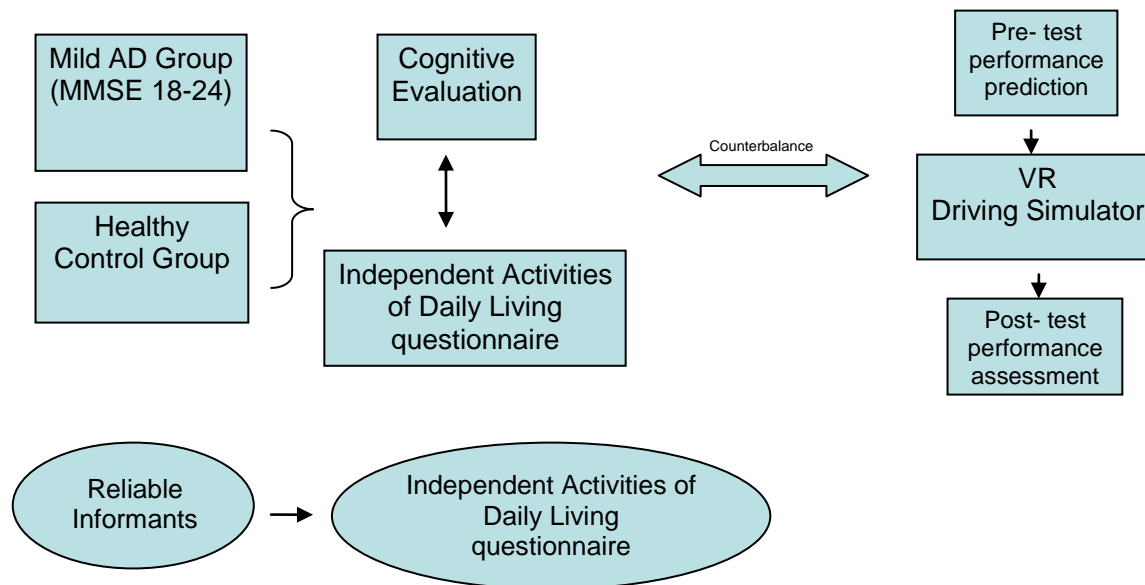


Figure 3: Virtual Reality Driving Simulator Unawareness Variables

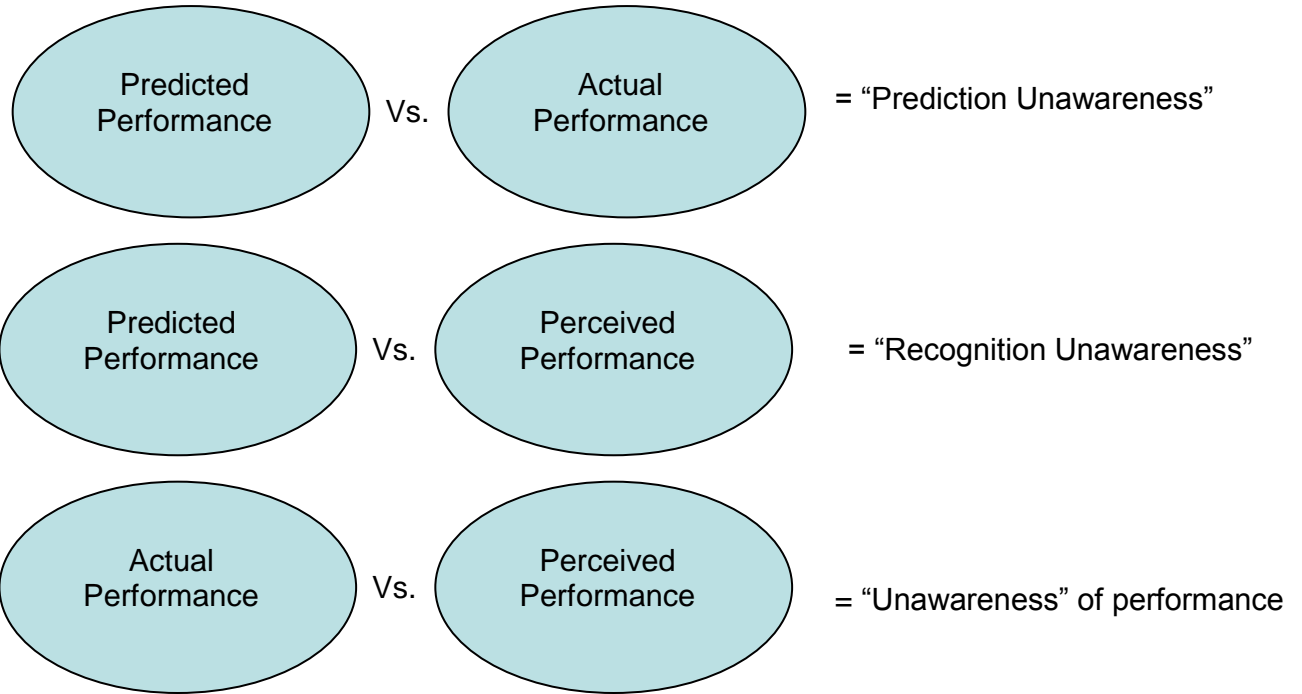
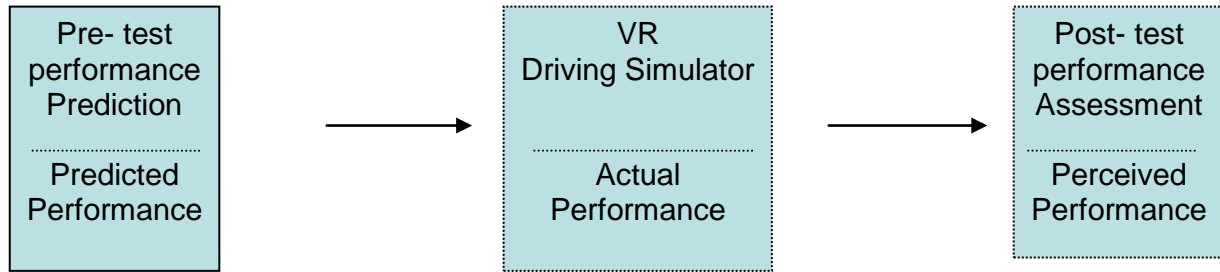


Figure 4: CVLT  $d'$  Scores for Clinical Participants

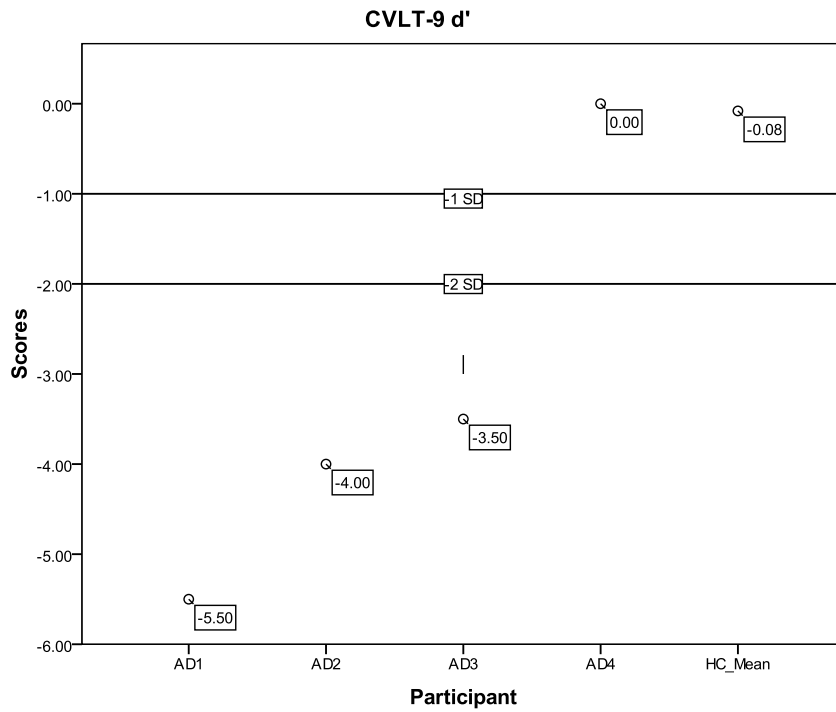


Figure 5: TMT-B Scores for Clinical Participants

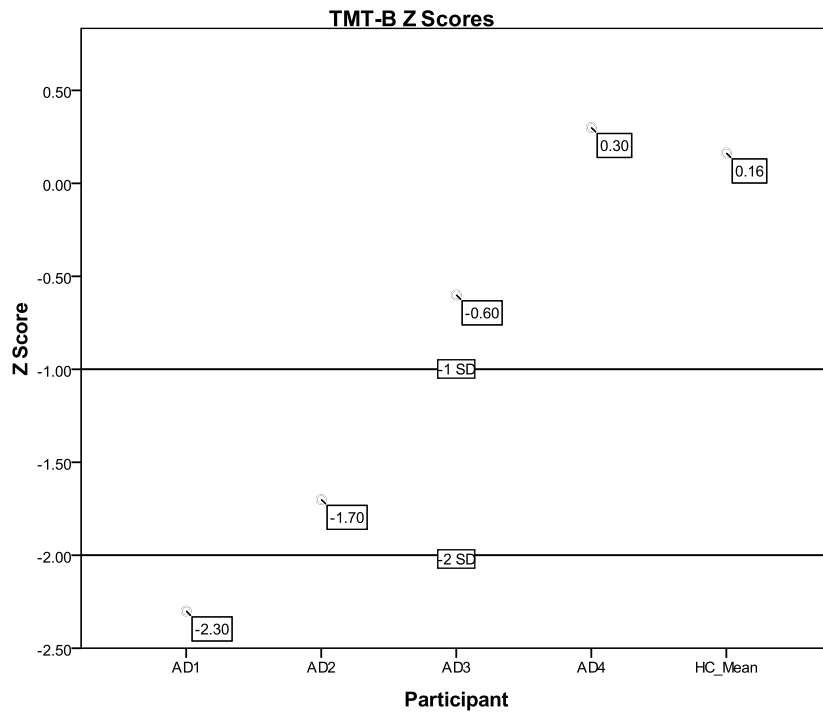


Figure 6: JLO Correction Scores for Clinical Participants

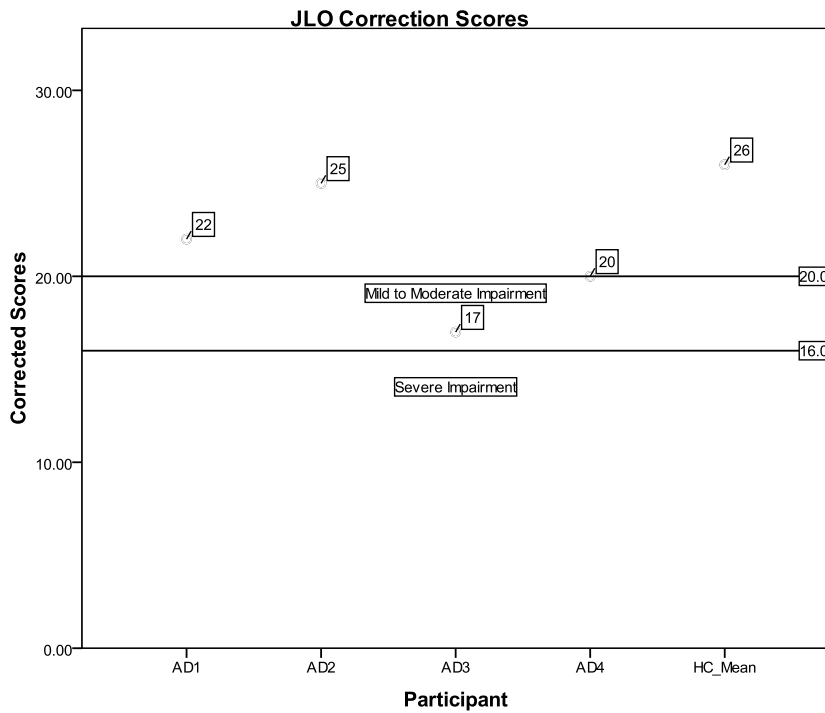


Figure 7: VRDS Scores for Clinical Participants

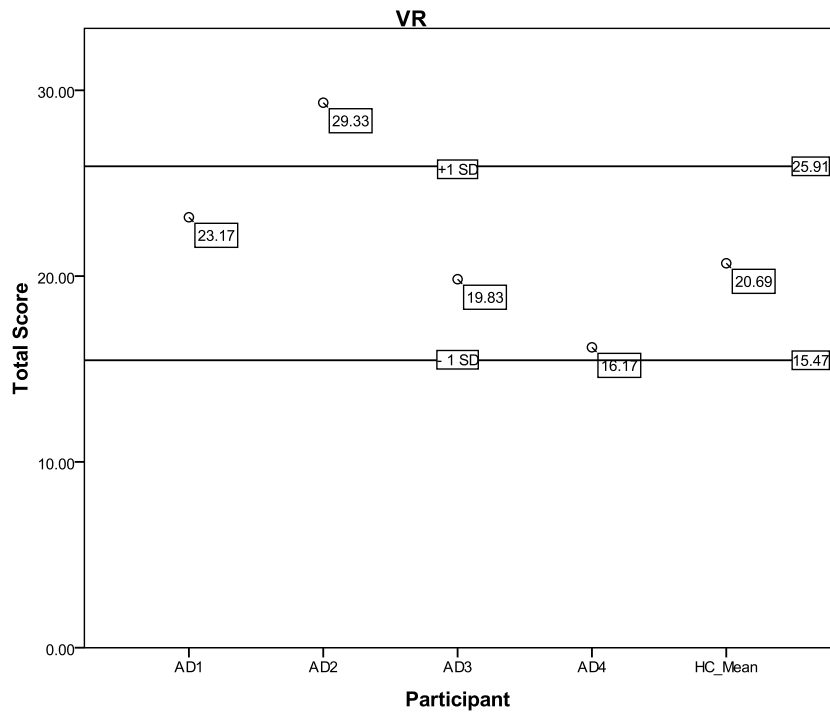




Figure 8: Unawareness Scores for Clinical Participants

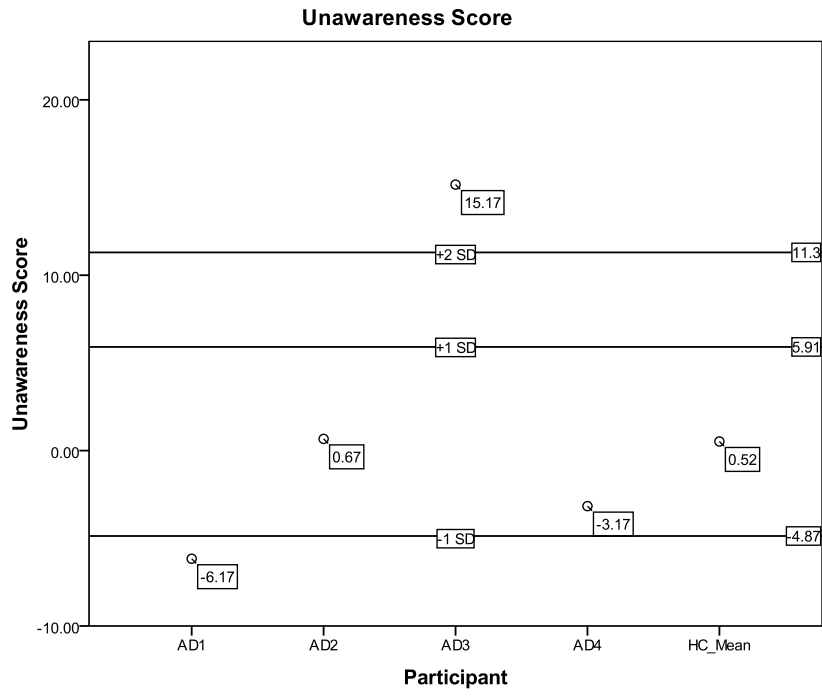


Figure 9: Predicted Awareness Scores for Clinical Participants

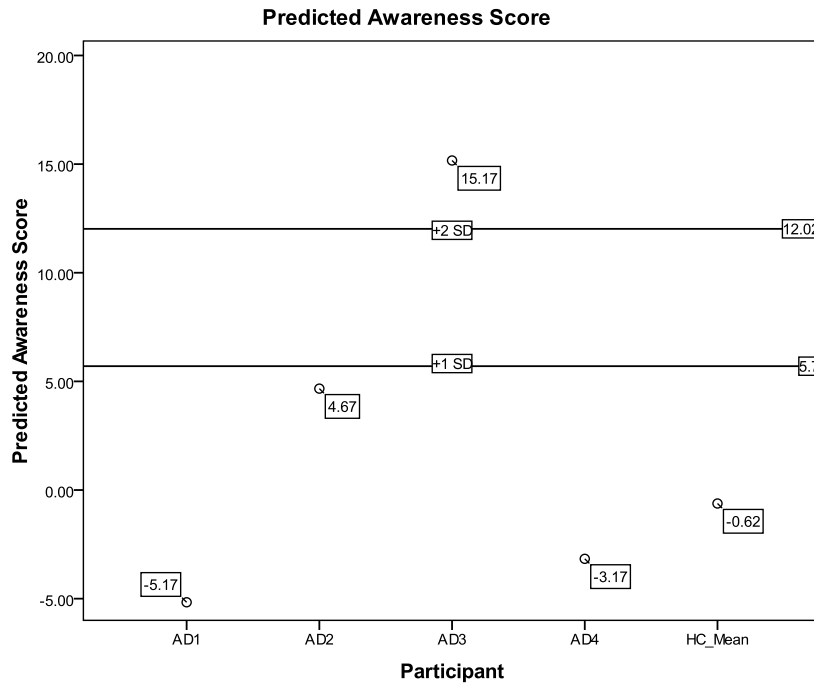


Figure 10: Recognition Awareness Scores for Clinical Participants

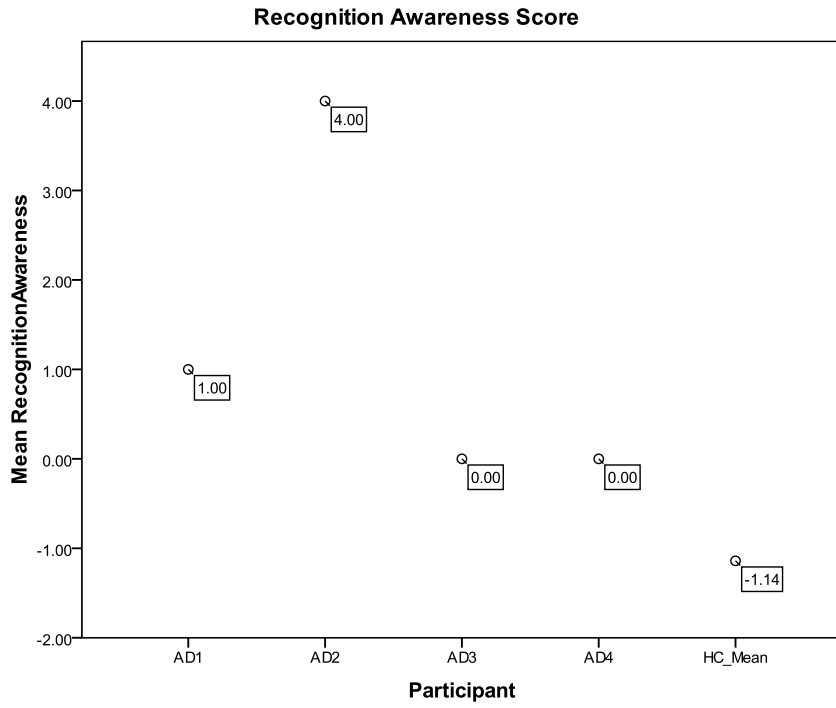


Figure 11: IADL Scores for Clinical Participants

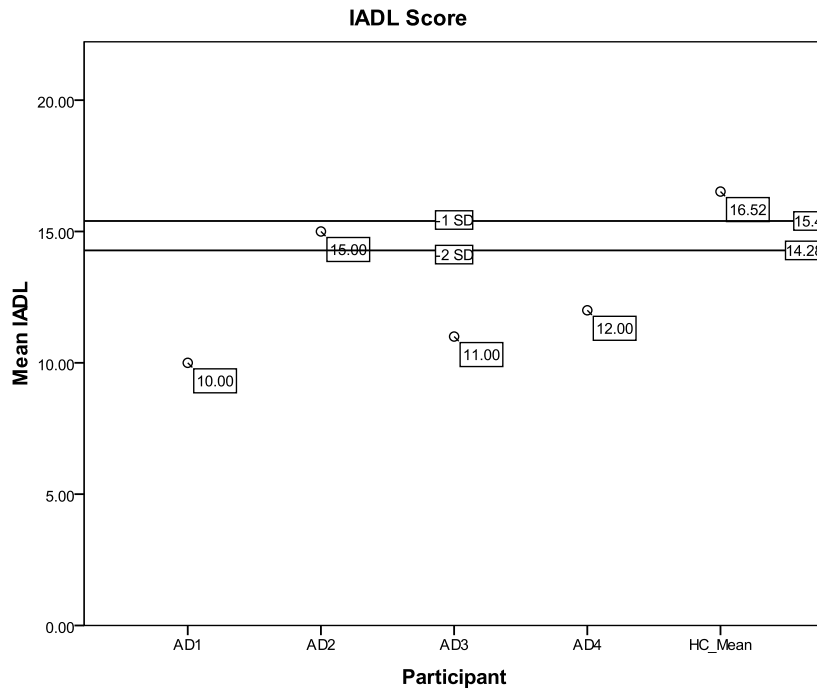


Figure 12: IADL Discrepancy Scores for Clinical Participants

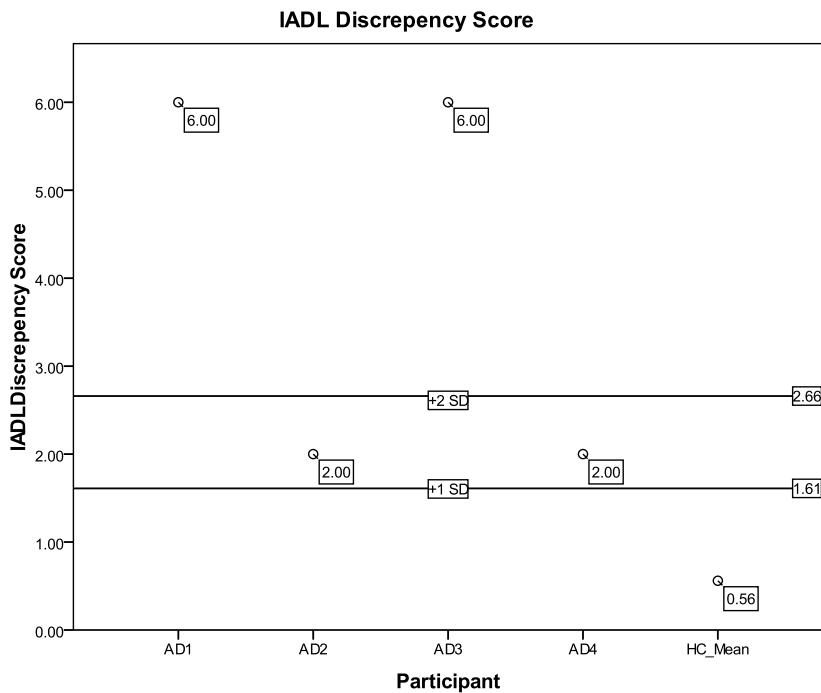


Table 1: Variables in the Study

Measure	Variables collected	Manipulation to the Variables	Studies that have used this technique	Final Variable
<b>Cognitive Measures</b>	CVLT-II Short Form: Recognition Discriminability Score	Hit rate minus false positive rate in standard deviation units	Reviewed in Delis et al., 2005	CVLT-II $d'$ Recognition Discriminability Score
	TMT-B: Time to completion in seconds	Age, gender, education, and ethnicity corrections	No manipulation	TMT-B $z$ -score
	JLO- Total correct out of 30	Age and gender corrections	Benton, Sivan, Hamsher, Varney, & Spreen, 1994	JLO Corrected Score
<b>Virtual Reality Driving Simulator</b>	Distance from Stop Signs Traffic light behavior Mean Speed: residential and highway zones Mean Lane Deviation in residential and highway zones Following a vehicle Responding to construction Responding to something in the road	All measures will be converted to a Z score. These Z scores will be added together to form a total global driving score.	Schultheis, Simone, Roseman, Nead, Rebimbas, & Mourant, 2006	VRDS Total Score for sections completed
<b>VRDS Unawareness Measure</b>	9-item questionnaire measuring patient perception of their performance using a 5-point scale	This questionnaire will be correlated with the contrasted with actual performance on the VR task.	Hart et al., 1998	VR Unawareness= Correlation Score
<b>Instrumental Activities of Daily Living Questionnaire</b>	8-item questionnaire measuring patient functioning on various domains. This is completed by a reliable informant, and scores range from 0-17.	Total score (0-17)	Derouesne et al., 1999 Salmon et al., 2005	IADL Total Score
<b>Instrumental Activities of Daily Living Unawareness Measure</b>	8 question scale for patient 8 question scale for caregiver	Difference score between the caregiver and the patient.	Cotrell & Wild, 1999 Ott et al., 1996	Traditional Unawareness Score

Secondary Analyses: Exploratory: VRDS Unawareness Measures			
<b>Pre- VRDS exposure questionnaire</b>	9-item questionnaire measuring patient prediction of their performance using a 5-point scale	Difference score between pre-exposure questionnaire and actual performance on the VRDS	“Prediction Unawareness”
<b>Pre- VRDS exposure questionnaire</b>	9-item questionnaire measuring patient prediction of their performance using a 5-point scale	Difference score between pre exposure questionnaire and post-exposure questionnaire	“Recognition Unawareness”
<b>Post-VRDS exposure questionnaire</b>	9-item questionnaire measuring patient perception of their performance using a 5-point scale	This questionnaire will be correlated with the contrasted with actual performance on the VR task.	“VR Unawareness”

Table 2: Virtual Reality Driving Simulator Variables in the Study

Driving Performance Recording Sheet							
	Topic	Sub-Topic	Criteria	Points	Total Points		
1	Stop Sign (SS)	(residential)	Stop Sign 1	They Stopped	3		
			(res1)	Did not stop	1		
				<i>old highway exit</i>	-15.84 to 6.24 ft from stop sign (-2 - 2 SD from norm mean)	1	
			> -15.84 ft from the stop sign		0		
			> 6.24 ft from stop sign		0		
			Wait ≥ 1.55 seconds before driving (normative mean)		1		
					Wait < 1.55 seconds before driving	0	
			Stop Sign 2	They Stopped	3		
			(res3)	Did not stop	1		
				<i>2nd stop after residential start</i>	-15.84 to 6.24 ft from stop sign (-2 - 2 SD from norm mean)	1	
			> -15.84 ft from the stop sign		0		
			> 6.24 ft from stop sign		0		
			Wait ≥ 1.55 seconds before driving (normative mean)		1		
					Wait < 1.55 seconds before driving	0	
			Stop Sign 3	They Stopped	3		
			(res4)	Did not stop	1		
				<i>turn to school</i>	-15.84 to 6.24 ft from stop sign (-2 - 2 SD from norm mean)	1	
			> -15.84 ft from the stop sign		0		
			> 6.24 ft from stop sign		0		
			Wait ≥ 1.55 seconds before driving (normative mean)		1		
		Wait < 1.55 seconds before driving	0				
Stop Sign Behavior (Total SS1 + SS2 + SS3)/3							
2	Traffic Light (TL)	(commercial)	Traffic Light 1	They stopped	2		
			(Comm 1)	Did not stop	1		
				<i>1st traffic light</i>	-13.62 to -6.93 ft from traffic line (-2 - 2 SD from normative mean)	2	
			>-13.62 or <-6.93 from traffic line		0		
			Wait ≥ 9.51 seconds before driving (normative mean)		1		
			Wait < 9.51 seconds before driving		0		
			Traffic light 2	They stopped	2		
			(Comm 2)	Did not stop	1		
				<i>2nd traffic light</i>	-13.62 to -6.93 ft from traffic line (-2 - 2 SD from normative mean)	2	
			>-13.62 or <-6.93 from traffic line		0		
			Wait ≥ 9.51 seconds before driving (normative mean)		1		
			Wait < 9.51 seconds before driving		0		
			Traffic light 3	They stopped	2		
			(Comm 3)	Did not stop	1		
				<i>3rd traffic light</i>	-13.62 to -6.93 ft from traffic line (-2 - 2 SD from normative mean)	2	
			>-13.62 or <-6.93 from traffic line		0		
Wait ≥ 9.51 seconds before driving (normative mean)	1						
Wait < 9.51 seconds before driving	0						



Traffic Light Behavior (Total TL1 + TL2 + TL3)/3				
3	Speed			
	Highway 1 (55 mph) (zone 23-24) <i>min/max mph</i>	45.82 - 50.9 mph	(-1/2 SD to 1/2 SD from mean)	5
		43.29-45.81 mph OR 51-53.43 mph	(-1 to 1 SD from normative mean)	4
		38.22-43.28 mph OR 53.43-58.5 mph	(-2 to 2 SD from normative mean)	3
		33.15-38.21 mph OR 58.51-63.57 mph	(-3 to 3 SD from normative mean)	2
		≤ 33.14 OR ≥ 63.58	(> 3 SD from normative mean)	1
	Highway 2 (55 mph) (zone 27-28a) <i>min/max mph</i>	45.82 - 50.9 mph	(-1/2 SD to 1/2 SD from mean)	5
		43.29-45.81 mph OR 51-53.43 mph	(-1 to 1 SD from normative mean)	4
		38.22-43.28 mph OR 53.43-58.5 mph	(-2 to 2 SD from normative mean)	3
		33.15-38.21 mph OR 58.51-63.57 mph	(-3 to 3 SD from normative mean)	2
		≤ 33.14 OR ≥ 63.58	(> 3 SD from normative mean)	1
	Highway 3 (55 mph) (zone 29b-30) <i>min/max mph</i>	45.82 - 50.9 mph	(-1/2 SD to 1/2 SD from mean)	5
		43.29-45.81 mph OR 51-53.43 mph	(-1 to 1 SD from normative mean)	4
		38.22-43.28 mph OR 53.43-58.5 mph	(-2 to 2 SD from normative mean)	3
		33.15-38.21 mph OR 58.51-63.57 mph	(-3 to 3 SD from normative mean)	2
		≤ 33.14 OR ≥ 63.58	(> 3 SD from normative mean)	1
Speed (HW1 + HW2 + HW3)/3				

4	Lane Management			
	Highway 1 (zone 25a-25b)	≤ 199.41 inches from middle of road	1 SD from mean of the min and	1.5
		≥ 78.23 inches from middle of road	max lane deviation of norm	0
	Highway 2 (zone 26a-26b)	≤ 199.41 inches from middle of road	1 SD from mean of the min and	1.5
		≥ 78.23 inches from middle of road	max lane deviation of norm	0
	Lane Busts	Total highway lane busts < 7	Approximate normative mean	2
		Total highway lane busts ≥ 7		1
Lane Management Behavior: Total Highway 1 + Highway 2 + Lane Busts				

5	Target Vehicle	(zone 24-27)		
		Attempts to follow entire time		2
		Attempts to follow part of the time		1
		No attempt to follow		0
		Stays with vehicle entire time		2
		Stays with vehicle until zone 26		1
		Looses vehicle before zone 26		0
		Remains in control of vehicle	(< 2 lane busts, no crashes)	1
		Poor control of vehicle	(≤2 lane busts or crashes)	0
Following behavior: Total Attempts + Stays + Control				

6	Construction Zone	(zone 28a-28b)		
		Move to left lane at sign and avoid barriers		2
		Don't respond appropriately		1
	(zone 28a-28b)	27.32-42.16 mph	(-1 - 1 SD from normative mean)	2
		19.9-27.31 mph OR 42.17-49.58 mph	(-2 - 2 SD from normative mean)	1
		≤19.89 mph OR ≥ 49.59 mph	(>2 SD from normative mean)	0

Role of unawareness 130

	(zone 28b-29a)	Mean(28b-29a) $\geq 11.02$ mph mean(28a-28b)	(Mean speed difference from normative sample)	1	
		mean difference < 11.02 mph		0	
Total Construction behavior					

7	Unexpected objects	Kid/Ball	Stays on the road when sees kid	LbN=0	2	
			Swerves off of the road	LbN > 0	1	
			Stops when sees kid		1	
			Does not stop		0	
		Throughout environment	No accident risk with other vehicles/objects	(Over entire course)	7	
			Accident risk with others		3.5	
			Accident with others		0	
Reaction to unexpected objects: (Stay on road + Stops + Accident Risk)/2						

Table 3  
Demographic Variables for Healthy Controls (n=30)

Demographic Variables	Number of Subjects	%
Gender		
Female	16	53
Male	14	47
Ethnic Identity		
Caucasian	24	80
African American	6	20
Handedness		
Righty	28	93
Lefty	2	7
Relationship with reliable informant		
Husband/Wife	10	33
Child	7	23
Partner	5	17
Friend	4	13
Sibling	4	13
Demographics Variables	Mean/ Standard Deviation	Min/Max
Age	73.57 (7.70)	60/84
Education Level	16.23 (2.99)	12/21
Reliable Informant length	37.65 (23.36)	1/74
Mini Mental Status Examination	28.97 (1.19)	25/30

Table 4  
Driving Characteristics for Healthy Controls

Driving Characteristics	Number of Subjects	%
Self restrictions on driving		
Yes	9	30
No	21	70
Only driver in the household		
Yes	7	23
No	23	77
Accidents/ tickets in the past year		
Yes	6	20
No	24	80

Driving Characteristics	Mean/ Standard Deviation	Min/Max
Days driven in the month	23.37 ( 8.50)	2/30
Miles driven each time drive	32.58 (40.95)	2.5/160
Length of time with license	55.10 (10.20)	32/77

Table 5  
Demographic Information for Clinical Sample

	AD1	AD2	AD3	AD4
Gender	Female	Male	Male	Male
Ethnicity	Caucasian	Caucasian	Caucasian	Caucasian
Age	73	75	69	78
Education	16	19	12	16
Time Since Diagnosis (months)	18	9	24	18
MMSE	21	25	17	29

Table 6  
Relationship between Demographics and Primary Variables in Healthy Controls

	Age	Education	Ethnicity	Gender
	Spearman's rho Correlation		Mann-Whitney test	
CVLT d'	$r = -.037$	$r = .275$	U=22.50, $z = -2.61^{**}$	U=37.50, $z = -3.14^{**}$
TMT-Z	$r = .349^*$	$r = .156$	U=71.00, $z = -0.59$	U=131.00, $z = -0.47$
JLO Corrected	$r = .206$	$r = .382^*$	U=55.00, $z = -0.89$	U=97.00, $z = -0.63$
VRDS	$r = -.036$	$r = .493^{**}$	U=44.00, $z = -1.35$	U=81.00, $z = -1.05$
IADL	$r = -.120$	$r = -.118$	U=34.00, $z = -1.13$	U=77.00, $z = -0.94$
IADL Discrepancy	$r = -.032$	$r = .067$	U=44.00, $z = -0.16$	U=58.50, $z = -1.85$
Unawareness	$r = .104$	$r = .284$	U=49.00, $z = -1.08$	U=90.50, $z = -0.63$
Predicted	$r = -.272$	$r = -.344$	U=45.00, $z = -1.29$	U=75.50, $z = -1.29$
Awareness	$r = -.156$	$r = -.368^*$	U=66.00, $z = -0.16$	U=80.00, $z = -1.09$
Recognition Aware.				

\*  $p < .05$ , \*\*  $p < .01$

Table 7  
 Relationship between Driving Variables and VRDS-Related Measures in Healthy Controls

	# yrs driving	Days/month driving	Miles driven	Tickets/Accidents	Any Restrictions	Only Driver
	Spearman's rho Correlation			Mann-Whitney test		
VRDS	$r = .045$	$r = .159$	$r = .068$	U=62.00, $z = -0.38$	U=74.00, $z = -0.49$	U=61.50, $z = -0.40$
Predicted Awareness	$r = -.273$	$r = -.098$	$r = .140$	U=46.50, $z = -1.21$	U=76.00, $z = -0.39$	U=54.00, $z = -0.81$
Unawareness	$r = .035$	$r = -.186$	$r = -.146$	U=59.00, $z = -0.54$	U=78.50, $z = -0.27$	U=47.00, $z = -1.19$
Recognition Aware.	$r = -.102$	$r = .129$	$r = .262$	U=58.50, $z = -0.57$	U=70.50, $z = -0.66$	U=55.00, $z = -0.76$

Table 8  
 Relationship between Demographic Variables and IADL's in Healthy Controls

	Length of relationship with RI	Type of relationship with RI
	Spearman's rho correlation	Kruskal-Wallis test
IADL	$r = -.10$	$H(4) = 2.25$
IADL Discrepancy	$r = .019$	$H(4) = 0.931$



Table 9  
Cognitive and Functional Characteristics for Healthy Controls

Variable	Mean (SD)	Median	1 <sup>st</sup> /3 <sup>rd</sup> quartile	Min/Max
CVLT d' Score	-0.08 (1.75)	0.50	-.50/ 1	-7/2
TMT-B Z Score	0.16 (1.17)	0.60	-1/ .93	-2.6/2.3
JLO Correction Score	26.0 (5.34)	28	24.50/ 29.25	5/30
IADL Score	16.52 (1.12)	17	17/17	12/17
IADL Discrepancy Score	0.56 (1.05)	0	0/ 1	0/5
VRDS Score	20.69 (5.22)	21.25	17.67/ 24.33	7/31.33
Predicted Awareness Score*	-0.62 (6.32)	-2.58	-5.67/3.88	-9.5/17.17
Unawareness Score*	0.52 (5.39)	0	-3.04/ 4.79	-9.33/15.67
Recognition Score†	-1.14 (7.39)	-1.00	-8.50/4.00	-13/19

\*Greater positive scores reflect an over-inflation of perceived performance. Greater negative scores reflect a participant thought they performed worse than they actually performed.

†Greater positive scores reflect a participant's minimizing their perceived performance over time. Greater negative scores reflect a participant's perceived performance is inflated over time.

Table 10  
Spearman's rho Correlation Matrix for Primary Variables for Healthy Controls

Variable	CVLT d'	TMT-B z	JLO Corr.	IADL	IADL Discrep.	VRDS	Pre. Aware	Unaware	Recog. Aware
CVLT d'	1	.264	.373*	.223	-.077	.563**	-.471**	-.163	-.228
TMT-B z	.264	1	.411*	.109	-.149	.274	.378*	.173	-.380*
JLO Correction	.373*	.411*	1	.018	-.065	.452*	-.339	.036	-.178
IADL	.223	.109	.018	1	-.661**	.145	-.007	.345	-.249
IADL Discrepancy	-.077	-.149	-.065	-.661**	1	-.096	-.072	-.269	-.068
VRDS	.563**	.274	.452*	.145	-.096	1	-.433*	.180	-.440*
Pre. Awareness	-.471**	-.378*	-.339	-.007	-.072	-.433*	1	.124	.697**
Unawareness	-.163	.173	.036	.345	-.269	.180	.124	1	-.507**
Recog. Aware	-.228	-.380*	-.178	-.249	-.068	-.440*	.697**	-.507**	1

\* $p < 0.05$ , \*\*  $p < 0.01$

Table 11  
95% Confidence Intervals for Significant Correlations

Variables Correlated	Lower Limit	Upper Limit
CVLT d' - JLO Corr.	.016	.768
CVLT d' - VRDS	.261	1
CVLT d' - Predicted Awareness	-.887	-.135
TMT-B z - JLO Correction	.061	.813
TMT-B z - Predicted Awareness	.022	.774
TMT-B z - Recog. Aware	-.776	-.024
JLO Corr. - VRDS	.111	.863
IADL - IADL Discrepancy	-1	-.395
VRDS - Predicted Awareness	-.809	-.088
VRDS - Recog. Aware	-.848	-.090

Table 12  
 Partial Correlations for Primary Variables for Healthy Controls

Partial Correlation	r	r <sup>2</sup>	t	p
r(VRDS)(Unawareness).CVLT	.333	.111	1.80	.084
r(VRDS)(Unawareness).TMT	.140	.020	0.72	.478
r(VRDS)(Unawareness).JLO	.184	.034	0.95	.351
r(IADL)(IADLDiscrepancyScore).CVLT	-.662	.439	-4.33	<.0001
r(IADL)(IADLDiscrepancyScore).TMT	-.656	.430	-4.26	<.0001
r(IADL)(IADLDiscrepancyScore).JLO	-.661	.437	-4.32	<.0001

Table 13  
Cognitive and Functional Characteristics for Clinical Sample

Variable	AD1	AD2	AD3	AD4
MMSE	21	25	17	29
CVLT d'	-5.50	-4.00	-3.50	0.0
TMT-B z	-2.30	-1.70	-0.60	0.30
JLO Correction	22	25	17	20
TMT-A z	0.60	-0.70	0.70	-0.60
Clock	7	4	6	5
IADL/ Z Score using study norms	10/ -5.82	15/ -1.36	11/ -4.93	12/ -1.89
IADL Discrep./ z score using study norms	6/ 5.18	2/ 1.37	6/ 5.18	2/ 1.37
VRDS/ Z Score using study norms	23.17/ 0.47	29.33/ 1.66	19.83/ -0.16	16.17/ -0.87
Predicted Awareness/ z score using study norms	-5.17/ -0.72	4.67/ 0.84	15.17/ 2.50	-3.17/ -0.40
Unawareness/ z score using study norms	-6.17/ -1.24	0.67/ 0.03	15.17/ 2.72	-3.17/ -0.68
Recognition Aware./ z score using study norms	1/ 0.29	4/ 0.70	0/ 0.15	0/ 0.15

Table 14  
 Additional Partial Correlations for Primary Variables for Healthy Controls

Partial Correlation	r	r <sup>2</sup>	t	p
r(VRDS)(CVLT).Unawareness	.610	.373	3.93	.0006*
r(CVLT)(Unawareness).VRDS	-.325	.106	-1.75	.092
r(VRDS)(TMT).Unawareness	.251	.063	1.32	.198
r(TMT)(Unawareness).VRDS	.131	.017	.670	.509
r(VRDS)(JLO).Unawareness	.453	.205	2.59	.016*
r(JLO)(Unawareness).VRDS	-.052	.003	-.260	.797
r(IADL)(CVLT).IADLDiscrepancy	.230	.053	1.16	.258
r(CVLT)(IADLDiscrepancy).IADL	.096	.009	.470	.643
r(IADL)(TMT).IADLDiscrepancy	.014	0	.070	.945
r(TMT)(IADLDiscrepancy).IADL	-.103	.011	-.510	.615
r(IADL)(JLO).IADLDiscrepancy	-.033	.001	-.160	.874
r(JLO)(IADLDiscrepancy).IADL	-.071	.005	-.350	.729

Appendix A: Simulation Sickness Questionnaire

**MODIFIED- SIMULATOR SICKNESS QUESTIONNAIRE (M-SSQ)**

Subject ID # \_\_\_\_\_ Age \_\_\_\_\_ Gender ( M / F ) Date \_\_\_\_\_

1. *Previous Simulator Experience*

Have you had any prior exposure to simulators? **YES** **NO**

If yes, how long has it been since your last exposure in a simulator? \_\_\_\_\_ Days

Did you experience any sickness from your simulator experience? **YES** **NO**

If yes, please describe: \_\_\_\_\_

**Is sickness same or different as prior to injury or illness? SAME**

2. *Previous Flying Experience*

How long has it been since your last flight in an aircraft? \_\_\_\_\_ days

Did you experience any sickness from your flying experience? **YES** **NO**

If yes, please describe: \_\_\_\_\_

**Is sickness same or different as prior to injury or illness? SAME**

**How often would you say you get airsick?**  
**Always**\_\_\_\_\_ **Frequently**\_\_\_\_\_ **Sometimes**\_\_\_\_\_ **Rarely**\_\_\_\_\_ **Never**\_\_\_\_\_

3. *Previous Shipboard Experience*

How long has it been since your last voyage at sea? \_\_\_\_\_ days

Did you experience any sickness from your shipboard experience? **YES** **NO**

If yes, please describe: \_\_\_\_\_

**Is sickness same or different as prior to injury or illness? SAME**

**How often would you say you get seasick?**  
**Always**\_\_\_\_\_ **Frequently**\_\_\_\_\_ **Sometimes**\_\_\_\_\_ **Rarely**\_\_\_\_\_ **Never**\_\_\_\_\_

4. *Previous Virtual Environment (VE) Experience*

Number of exposures/hours in a VE \_\_\_\_\_ number of exposures \_\_\_\_\_ approximate hours

How long has it been since your last exposure in a virtual environment? \_\_\_\_\_ days

Did you experience any sickness from your VE experience? **YES NO**

**Is sickness same or different as prior to injury or illness? SAME**

5. Do you get sick while riding in a car? **YES NO**

If yes, please describe: \_\_\_\_\_

**Is sickness same or different as prior to injury or illness? SAME**

**How often would you say you get carsick?**

**Always** \_\_\_\_\_ **Frequently** \_\_\_\_\_ **Sometimes** \_\_\_\_\_ **Rarely** \_\_\_\_\_ **Never** \_\_\_\_\_

6. Do you get sick when riding on roller coasters? **YES NO**

If yes, please describe: \_\_\_\_\_

**Is sickness same or different as prior to injury or illness? SAME**

**IN GENERAL, HOW SUSCEPTIBLE TO MOTION SICKNESS ARE YOU?**

**Extremely** \_\_\_\_\_ **Very** \_\_\_\_\_ **Moderately** \_\_\_\_\_ **A little** \_\_\_\_\_ **Not at all** \_\_\_\_\_

**PRE-EXPOSURE PHYSIOLOGICAL STATUS INFORMATION**

1. Are you in your usual state of fitness? (Circle one) **YES NO**  
If not, please indicate the reason:

2. Have you been ill in the past week? (Circle one) **YES NO**  
If "Yes", please indicate:

a) The nature of the illness (flu, cold, etc.):

b) Severity of the illness: Very Mild-----Very Severe

c) Length of illness: \_\_\_\_\_ Hours / Days

d) Major symptoms:

e) Are you fully recovered? **YES NO**

3. How much alcohol have you approximately consumed during the past 24 hours?

\_\_\_\_\_ 12 oz. cans/bottles of beer \_\_\_\_\_ ounces wine \_\_\_\_\_ ounces hard liquor

4. Please indicate all medication you have used in the past 24 hours. If none, check the



first line:

- a) NONE \_\_\_\_\_
- b) Sedatives or tranquilizers
- c) Aspirin, Tylenol, other analgesics
- d) Anti-histamines
- e) Decongestants
- f) Other (specify):

5. a) Approximately how many hours of sleep did you get last night? \_\_\_\_\_ hours

b) Was this amount sufficient? (Circle one) **YES** **NO**

6. Please list any other comments regarding your present physical state which might affect your performance on our test battery.

## PRE-EXPOSURE SYMPTOM CHECKLIST

Instructions: Circle how much each symptom below is affecting you right now.

1. <u>General discomfort</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
2. <u>Fatigue</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
3. <u>Boredom</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
4. <u>Drowsiness</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
5. <u>Headache</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
6. <u>Eye strain</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
7. <u>Difficulty focusing</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
8. <u>Changes in Salivation</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
9. <u>Sweating</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
10. <u>Nausea</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
11. <u>Difficulty concentrating</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
12. <u>"Fullness of the Head"</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
13. <u>Blurred vision</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
14. <u>Dizziness with eyes open</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
15. <u>Dizziness with eyes closed</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
16. <u>*Vertigo</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
17. <u>**Visual flashbacks</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
18. <u>Faintness</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
19. <u>Changes in breathing</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
20. <u>Stomach discomfort</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
21. <u>Decreased appetite</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
22. <u>Increased appetite</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
23. <u>Desire to move bowels</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
24. <u>Confusion</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
25. <u>Burping</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
26. <u>Vomiting</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
27. <u>Yawning</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
28. <u>Light-headedness</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
29. <u>Other</u>	_____			

\* Vertigo is experienced as loss of orientation with respect to vertical upright.

\*\* Visual illusion of movement or false sensations of movement, when not in the simulator, car, or aircraft.

\*\*\* Stomach awareness is usually used to indicate a feeling of discomfort which is just short of nausea.

## POST-EXPOSURE SYMPTOM CHECKLIST

Instructions: Circle how much each symptom below is affecting you right now.

1. <u>General discomfort</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
2. <u>Fatigue</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
3. <u>Boredom</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
4. <u>Drowsiness</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
5. <u>Headache</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
6. <u>Eye strain</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
7. <u>Difficulty focusing</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
8a. <u>Salivation increased</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
8b. <u>Salivation decreased</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
9. <u>Sweating</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
10. <u>Nausea</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
11. <u>Difficulty concentrating</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
12. <u>Mental depression</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
13. <u>"Fullness of the Head"</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
14. <u>Blurred vision</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
15a. <u>Dizziness with eyes open</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
15b. <u>Dizziness with eyes closed</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
16. <u>*Vertigo</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
17. <u>**Visual flashbacks</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
18. <u>Faintness</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
19. <u>Aware of breathing</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
20. <u>***Stomach awareness</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
21. <u>Loss of appetite</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
22. <u>Increased appetite</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
23. <u>Desire to move bowels</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
24. <u>Confusion</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
25. <u>Burping</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
26. <u>Vomiting</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
27. <u>Yawning</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
28. <u>Light-headedness</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>
29. <u>Other</u>	<u>None</u>	<u>Slight</u>	<u>Moderate</u>	<u>Severe</u>

- \* Vertigo is experienced as loss of orientation with respect to vertical upright.
- \*\* Visual illusion of movement or false sensations of movement, when not in the simulator, car or aircraft.
- \*\*\* Stomach awareness is usually used to indicate a feeling of discomfort which is just short of nausea.

### POST-EXPOSURE INFORMATION

Instructions: Please fill out this page AFTER you have completed your virtual environment experience.

1. While in the virtual environment, did you get the feeling of motion (i.e., did you experience a compelling sensation of self motion as though you were actually moving)?  
(Circle one)  
YES                      NO                      SOMEWHAT
  
2. a. Did any unusual events occur during your exposure? (Circle one) YES NO  
b. If YES, please describe \_\_\_\_\_
  
3. a. Time spent in VE \_\_\_\_\_ b. The time now
  
4. On a scale of 1 (POOR) to 10 (EXCELLENT) rate your performance in the virtual environment:
  
5. Virtual Reality Device: \_\_\_\_\_ Visual scene:

## Appendix B: Questions from Instrumental Activities of Daily Living Questionnaire

### **A.) Ability to use the telephone**

- 1.) Operates the phone (3).
- 2.) Dials a few well known numbers (2).
- 3.) Answers the telephone, but does not dial the phone (1).
- 4.) Does not use the telephone at all.

### **B.) Shopping**

- 1.) Takes care of all shopping needs independently (1).
- 2.) Shops independently for small purchases.
- 3.) Needs to be accompanied on any shopping trip.
4. Completely unable to shop alone.

### **C.) Food Preparation**

- 1.) Plans, prepares, and serves adequate meals independently (1).
- 2.) Prepares adequate meals if supplied with ingredients.
- 3.) Heats and serves prepared meals, but does not maintain adequate diet.
- 4.) Needs to have meals prepared and served.

### **D.) Housekeeping**

- 1.) Maintains house alone or with occasional assistance (4).
- 2.) Performs light daily tasks, i.e., dish washing and bed making (3).
- 3.) Performs light daily tasks, but cannot maintain acceptable level of cleanliness (2).
- 4.) Needs help with all home maintenance tasks (1).
- 5.) Does not participate in any housekeeping tasks.

### **E.) Laundry**

- 1.) Does personal laundry completely (2).
- 2.) Launders small items, i.e., stockings etc. (1).
- 3.) All laundry must be done by others.

### **F.) Mode of Transportation**

- 1.) Travels independently on public transportation or drives own car (3).
- 2.) Arranges own travel via taxi, but does not otherwise use public transportation (2).
- 3.) Travels on public transportation when accompanied by another person (1).

- 4.) Travel limited to taxi or automobile with assistance of another person.
- 5.) Does not travel at all.

**G.) Responsibility of Medication**

- 1.) is able to take medication in correct dosage at the correct time (1).
- 2.) Takes responsibility for medication if it is prepared in advance such as using a weekly pill container.
- 3.) Is not capable of dispensing own medication.

**H.) Ability to Handle Finances**

- 1.) Manages financial matters independently, i.e., writes checks, pays bills, goes to the bank, etc. (2).
- 2.) Manages day-to-day purchases, but needs help with banking, major purchases (1).
- 3.) Is incapable of handling money.

Appendix C: Pre- VRDS Questionnaire

**Pre- Virtual Reality Driving Simulator Questionnaire**

Prediction of Performance

Please use the following scale to answer the questions below:

- 1 Will do badly
- 2 Will have some trouble
- 3 Will do ok/ don't know/ average
- 4 Will do ok, but not my best
- 5 Will do very good

1. How will you do with the physical demands of this activity, such as using the steering wheel, using the foot pedals, coordinating these movements, and being able to see what is presented on the screen? \_\_\_\_\_

2. How will you do with the overall mental demands of the activity, such as monitoring your speed, planning your movements, remembering everything, and following directions? \_\_\_\_\_

3. How will you do with:

- a.) managing the stop signs \_\_\_\_\_
- b.) managing the traffic lights \_\_\_\_\_
- c.) managing your speed \_\_\_\_\_
- d.) your ability to manage the lanes \_\_\_\_\_
- e.) following another vehicle \_\_\_\_\_
- f.) managing a construction zone \_\_\_\_\_
- g.) responding to unexpected objects in the street \_\_\_\_\_

Total Score \_\_\_\_\_

Appendix D: Post- VRDS Questionnaire

**Post- Virtual Reality Driving Simulator Questionnaire**

Perception of Performance

Please use the following scale to answer the questions below:

- 1 Did badly
- 2 Had some trouble
- 3 Did ok/ don't know/ average
- 4 Did ok, but not my best
- 5 Did very well

1. How did you do with the physical demands of this activity, such as using the steering wheel, using the foot pedals, coordinating these movements, and seeing what was presented on the screen? \_\_\_\_\_

2. How did you do with the overall mental demands of the activity, such as monitoring your speed, planning your movements, remembering everything, and following directions? \_\_\_\_\_

3. How did you do with:

- a.) managing the stop signs \_\_\_\_\_
- b.) managing the traffic lights \_\_\_\_\_
- c.) managing your speed \_\_\_\_\_
- d.) your ability to manage the lanes \_\_\_\_\_
- e.) following another vehicle \_\_\_\_\_
- f.) managing a construction zone \_\_\_\_\_
- g.) responding to unexpected objects in the street \_\_\_\_\_

Total Score \_\_\_\_\_

Adapted from the questionnaire created by Hart, Giovannetti, Montgomery, & Schwartz, 1998