THE RELATIONSHIP AMONG ATTENTION, DAILY BEHAVIOR AND DISEASE SEVERITY IN PATIENTS WITH ALZHEIMER'S DISEASE

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Abstract

THE RELATIONSHIP BETWEEN ATTENTION, DAILY BEHAVIOR AND DISEASE SEVERITY IN PATIENTS WITH ALZHEIMER'S DISEASE

by

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Introduction: Complex instrumental activities of daily living (IADL) and basic activities of daily living (BADL) are typically impaired in Alzheimer disease (AD). It is unclear, however, how attention versus global cognitive impairments selectively impact functional decline. We hypothesized that performance on attention tasks would predict functional impairment, and specifically be predictive of IADL. **Method:** Twenty-seven newly-diagnosed participants with AD were assessed on (1) global cognition: Mattis Dementia Rating Scale-2 (DRS-2); (2) attention: a) RT on simple detection, b) covert orienting, c) speed and errors on executive attention, D-KEFS Trail Making Test (TMT) Condition-4; (3) a) caregiver ratings of IADL/BADL: Modified Lawton-Brody, Neuropsychiatric Inventory (NPI). **Results:** Forty eight percent of the participants had only IADL impairment, while the remaining participants had both IADL and BADL deficits. There were no differences in demographics or cognitive status between those with and without BADL deficits. Hierarchical regression revealed that errors on the TMT Condition- 4 accounted for the majority of IADL variability. After accounting for the TMT Condition-4 errors, the changes in variability of IADL associated with DRS-2 and NPI were minimal. Neither global cognitive scores nor attentional measures predicted BADL performance. **Conclusions:** IADL impairments are primary deficits at the time of diagnosis of AD, and as hypothesized, a measure of executive attention best

predicted the variable daily demands of IADL. As global cognitive scores did not predict the more variable IADL impairment, these findings suggest that measures of higher executive attention are more sensitive to IADL, and may better inform clinicians and caregivers of potential difficulty with daily tasks faced by patients with early AD.

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This dissertation is in honor of those teachers who instilled in me intellectual curiosity and a love of learning. While there have been many along the way, three stand out at this juncture: Ruth and Julius Kaplan, my parents and Gita Porway, my first clinical/professional mentor.

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LITERATURE REVIEW

Introduction

Deficits in cognition are associated with functional declines in patients with Alzheimer's disease (AD), (Atchison, Massman, & Doody, 2007; Baum, Edwards, Yonan, & Storandt, 1996; Giovannetti, Libon, Buxbaum, & Schwartz, 2002) and impairments in both domains are necessary for diagnosis (McKhann et al., 1984). Memory deficits are identified by clinicians and caregivers as being associated with early AD; however, concurrently identified problems with daily living skills (Bouwens et al., 2008; Tekin, Fairbanks, O'Connor, Rosenberg, & Cummings, 2001) are often the impetus for families and patients to seek diagnosis and treatment. Successful performance of most life activities (e.g., employment, life roles such as being a grandparent) requires the ability to generate a variety of responses to changeable conditions and events, and does not rely heavily on memory or automatic response processes. Tasks involving a novel or previously experienced but variable situation appear difficult for patients with AD, interfering with work, leisure and independence, while tasks that rely on the similarity of daily routines and have more automaticity (e.g., making breakfast, dressing, calling well known phone numbers), and are typically not as impaired. Thus, patterns in the types of daily tasks impaired in the early and later stages of AD have emerged in the literature but have not been linked to specific domains of cognition. The ability of caregivers to anticipate living needs and safety in those with early AD becomes problematic as impairments in a patient's performance vary across environmental conditions (T. M. Gill, Richardson, & Tinetti, 1995).

Clinically, the relationship between functional and neuropsychological measures has not been consistent (Chaytor & Schmitter-Edgecombe, 2003). While association was demonstrated in some studies of patients with AD (Matsuda & Saito, 2005; Nadler, Richardson, Malloy, Marran, & Hosteller Brinson, 1993; Richardson, Nadler, & Malloy, 1995), others have shown a relationship only between cognitive measures and more complex instrumental activities of daily living (IADL) (Bouwens, et al., 2008), while yet others show little relationship at all (Derouesne et al., 2002). Simple, routine, basic activities of daily living (BADL) that remain intact until later stages, have been found to be unrelated to scores on cognitive measures in some samples of patients with AD (Baum, et al., 1996; Lechowski et al., 2008; K. P. Liu et al., 2007) but related in others (Atchison, et al., 2007). Characteristics differentiating complex/IADL versus simple/BADL daily tasks are often unstated, defined by the items on the functional measure used or inconsistent across studies of patients with AD. Definitions of task complexity/simplicity have traditionally hinged on amount of sequential steps in a task; however, other characteristics such as ‘organization’ (the degree to which steps of a sequence are dependent or interrelated) and ‘variability’ (the degree of change in conditions during performance) add demands on the performer (Magill, 2010) and must be included. Without defined task characteristics and performance conditions, parsing cognitive deficits that contribute to early versus later patterns of functional decline in patients with AD remains obscure.

To investigate how cognitive deficits contribute to functional decline, four areas will be reviewed.

(1) *Neuropathology*. The pathological, structural, and neurochemical changes ongoing in AD will be discussed relative to impairments in neuropsychological processes.

(2) *Cognition and neuropsychiatric status.* The relationship between impaired cognition, neuropsychiatric behavior, and decline in functional behavior will be explored. Typically, disease severity is described by 'global' measures of cognition (with or without delineated subdomains) and neuropsychiatric function. Measures of global cognition have been found to account for a significant amount of the variability in activity of daily living (ADL) scores in patients with AD (Jefferson, Barakat, Giovannetti, Paul, & Glosser, 2006). Additionally, neuropsychiatric symptoms (e.g., apathy, depression, aggressiveness, agitation, disinhibition, delusions) will be explored relative to cognitive testing (Cummings, 1997a) and functional performance (Gallo, Schmidt, & Libon, 2008).

(3) *Analysis of ADL tasks.* An analysis of daily task characteristics and requirements can identify how cognition is important to specific types of tasks. Awareness of the relationships between task requirements and cognitive resources would enable clinicians and caregivers to better understand and predict fluctuations in patient behavior. Thus, the third area of exploration will explore ADL relative to performance requirements and to the environments and conditions in which they take place. ADL categorization can be summarized from three perspectives; the *environment* the *performer*, and from a *resource-based* perspective. The classical environmental categorization divides daily tasks into: (1) basic activities of daily living (BADL), which are involved in physical self care centered on the bathroom or kitchen of the home; and

(2) instrumental activities of daily living (IADL) occurring in extended home (e.g., basement laundry area) or community environments (e.g., grocery, bank) (Lawton & Brody, 1969). ADL can also be categorized by the perspective of the intrinsic skills of the *performer* (Oakley & Sunderland, 1997) and grouped according to 'cognitive' or 'motor' demands placed on the individual. Neither of these two classifications accounts for the ability to adapt to changes in conditions, which are typical of real-life situations. Daily life has a great deal of variability, and the omission of taking variability into account will be highlighted in the review of these ADL categories. Thus, the *resource-based* category, adopted from Gentile's (2000) taxonomy differentiates tasks as a function of the variability and novelty that occur during performance. Gentile's taxonomy will be adapted to differentiate daily tasks as a function of the variability that occurs during task performance. Changes in timing and spatial characteristics during performance or in subsequent attempts create variability and heighten demands on attentional resources and adaptability. Several current ADL tests will be reviewed, emphasizing benefits and limitations of these theoretical perspectives as applied to the lives of patients and their caregivers.

(4) *ADL and attention.* Lastly, the features and environmental contexts that appear to distinguish daily living tasks (i.e., those that are, and are not, prone to automaticity) and their relationship to attentional impairment in AD will be reviewed. Surprisingly the cognitive domain of attention has rarely been associated with changes in daily task performance (Rosenbaum, 2005). Schwartz et al. (1998) proposed a resource theory of daily task impairment, which posits that everyday actions are resource demanding and that errors emerge when resources (defined as attention, effort or activation of cognition)

are limited. A relationship between attention resources and daily task performance has been implied by studies of healthy (Giovannetti, Schwartz, & Buxbaum, 2007) and AD populations (Giovannetti, Bettcher, & Libon, 2007), but never assessed directly. Complex tasks require more focused, sustained, divided, and selective attention skills than habitual, routine functional tasks. Many aspects of attention are highly vulnerable in AD (Baddeley, Baddeley, Bucks, & Wilcock, 2001; Greenwood & Parasuraman, 1997; Perry & Hodges, 2003). As functional tasks demand more attentional resources (N. S. Foldi, Schaefer, L. A., White, R. E., Johnson, R., Jr., Berger, J. T., Carney, M. T., Macina, L. O., 2005; Levinoff, Saumier, & Chertow, 2005) the decline in attention may have either a direct influence on the variability of ADL performance in patients with AD or an indirect influence that affects global cognition and neuropsychiatric behavior, which in turn affects ADL performance.

The current study examined the influences of attentional decline on the variability in ADL performance in patients with AD. In this study, three aspects of attention were hypothesized to have an influence on ADL: 1) vigilance for stimuli detection, as measured by a simple detection task (SDT) (N. S. Foldi, White, R. E., Redfield, J. , Vedrody, S., Kaplan, L., Lombardi, K. I., Ly, J., 2006); 2) selective attention as measured by the Trail Making Test (TMT) conditions of the Delis Kaplan Executive Function System (Delis, Kaplan, & Kramer, 2001), and 3) orienting, as measured by covert orienting (M. I. Posner, 1980). The three attention tasks and tests of global cognition were administered to patients with AD. Their daily living skills and behaviors were measured from caregiver reports. Attention, global cognition, and neuropsychiatric status were explored as to their influence on the variability of IADL and BADL performance in patients newly diagnosed with AD.

Pathology of Alzheimer's Disease

Alzheimer's disease (AD) is a neurodegenerative disorder (McKhann et al., 1984) that affects cognition and function of everyday activities. The DSM-IV-TR (American Psychiatric, 1994) criteria require the presence of both a memory disorder and impairment in at least one additional cognitive domain (aphasia, apraxia, agnosia, or disturbance in executive function) that interferes with social function or ADL.

Importantly, the definition of AD includes the deterioration of ADL tasks as an essential component of the diagnosis and clinically is often seen as one of the markers of disease progression. The clinical diagnosis remains current, although recent changes in understanding of the biology of the disease may eventually include one or more biomarkers such as altered structural neuroimaging (MRI), molecular neuroimaging (PET), and/or evidence of abnormal cerebral spinal fluid (CSF) having amyloid or tau proteins (Dubois et al., 2007). The following sections will discuss the structural, metabolic and neurochemical changes that occur in AD and their relationships to attention and ADL.

Structural and neural changes in AD: Impact on cognition.

AD is characterized by cortical atrophy, loss of neurons (particularly in the parietal and frontal lobes), and ventricular enlargement (Silverberg, Mayo, Saul, Rubenstein, & McGuire, 2003). The neuropathological changes in AD include abundant neurofibrillary tangles (Bamburg & Bloom, 2009; Braak & Braak, 1995) and amyloid plaques (Selkoe, 1991). Neurofibrillary tangles, twisted helical paired filaments, are similar to intracellular microtubules but are composed of tau protein in an abnormally phosphorylated state (Goedert, 1993). Phosphorylated tau is unable to bind to microtubules and is believed to then self-assemble into paired twisted helical filaments tangles. In a healthy cell, microfilaments transport intracellular elements, a process that is disrupted when neurofibrillary tangles become present. These tangles are resistant to chemical or enzymatic breakdown and persist in brain tissue long after the neuron in which they arose has died, thus there is a correlation between tau pathology and loss of synapses (Brickman, Small, & Fleisher, 2009; Mandelkow & Mandelkow, 1998). In AD, increased numbers of neurofibrillary tangles found in association cortex of the frontal, parietal, temporal and occipital lobes, as well as the entorhinal cortex, hippocampus, and amygdala has been associated with cognitive decline (Nelson, Braak, & Markesbery, 2009) and disease severity in humans (Killiany et al., 2002; Marshall, Fairbanks, Tekin, Vinters, & Cummings, 2007) as well as dysfunction in animal models (Eriksen & Janus, 2007).

Extracellular amyloid proteins are also found in abnormal amounts in AD (Selkoe, 1991). The amyloid plaques, usually surrounded by neurons that contain neurofibrillary tangles, are thought to cause vascular damage and cell death (Banich, 2004). The distribution of structural changes (Karas et al., 2003), neuronal loss, and the accumulation of plaques and tangles is evident in cortical and subcortical regions inclusive of the structures of the hippocampus, amygdala, and olfactory systems. These pathological changes are relatively spared in primary motor and sensory cortices (Kemppainen et al., 2006).

Pathology in AD, as measured by functional neuroimaging, appears to first effect entorhinal and the posterior association cortex, and later the disease process "spreads" to involve the frontal cortex. This pattern was seen in the reduction of regional blood flow in the parietal, frontal, and temporal cortices of AD patients as well as in patterns of metabolism of blood glucose (Montaldi et al., 1990). Using SPECT imagining, Brown et al. (1996) measured the change of cognitive performance and the pattern of deficit in cerebral blood flow over time in a group of patients with AD. When tested as mildly affected, the declines in the posterior association cortex exerted the greatest effect on cognitive deficit, however with disease progression to moderate or severe status, changes in the frontal cortex exerted the greatest effect on cognitive decline, suggesting that the disease spreads from posterior to anterior regions as it progresses. In contrast, others (K. A. Johnson & Albert, 2000) report that early changes of reduced blood flow occurred anteriorly, in the frontal and cingulate cortices, when individuals were first exhibiting cognitive problems. Early frontal changes are supported by investigations examining patterns of blood perfusion in individuals with mild cognitive impairment (MCI) who then convert to AD (El Fakhri et al., 2003; K. A. Johnson & Albert, 2000). Results found reduced blood perfusion occurring in frontal cortex. Recent baseline SPECT data (K. A. Johnson et al., 2007) found decreases in blood perfusion specifically in the cingulate cortex in converters (to AD from MCI), compared with the healthy elderly, stable, and rapidly progressing groups of patients with AD. Importantly, the anterior cingulate has been shown to amplify activity in a single perceptual system by either interacting directly with parietal cortex or enlisting the prefrontal cortex, suggesting roles in selection, orienting attention, and the inhibition of cortex that reduces distractibility from events at irrelevant locations (Michael I. Posner & Dehaene, 1994; M. I. Posner & Raichle, 1998). These early frontal changes support the early declines in attentional processes (Small et al., 2003).

PET studies have shown that early stages of AD are also characterized by glucose hypometabolism. Declines in glucose metabolism initially effect the tempoparietal association, cingulate cortex (Alavi et al., 1986) and subsequently the prefrontal association cortex (Millien et al., 2002). Among possible mechanisms for the hypometabolism (Millien, et al., 2002) is the neuronal loss in the perirhinal and entorhinal areas, which have crucial projections to cortical circuitry. The entorhinal cortex is a portion of the parahippocampal gyrus that receives projections from widespread limbic and association areas and gives rise to the perforant pathway, the major cortical excitatory input to the hippocampus (K. A. Johnson & Albert, 2000), playing a role in memory. Perirhinal and entorhinal areas, initially affected by increased neurofibrillary tangles in AD, have been correlated with declines in metabolic rates of glucose in both primates (Millien, et al., 2002) and humans (Minoshima et al., 1997). Significantly, PET glucose metabolism has demonstrated greater diagnostic sensitivity than MRI brain volume in discriminating AD from other dementias (Desanti et al., 2001; Vander et al., 1997), and has correlated with severity of cognitive impairments (Desgranges et al., 1998; Haxby et al., 1990; Kumar, Schapiro, Haxby, Grady, & Friedland, 1990).

Compromised brain function in temporal, cingulate, and frontal cortical regions is further supported by diffusion tensor imaging investigating white matter integrity. Patterns of fractionated anisotropy (a quantitative measure of the integrity of white matter tissue based on the directional flow of water) differed in AD as compared to well elderly and mild cognitively impaired populations. Reductions were noted specifically in the left anterior temporal lobe (Damoiseaux et al., 2009), and in projections between cortex and the thalamus (Rose, Janke, & Chalk, 2007). Mean diffusivity (measure of pathology in neuronal projections where increases result from neuronal loss) was elevated within the hippocampus, amygdala, medial temporal, parietal, and frontal lobe, but most prominently in the cingulate gyrus (Rose, et al., 2007).

Relationship between AD, attention and function

Attentional processes are distributed in the brain (Fan & Posner, 2004). For example, alerting, orienting, and executive attention (selection during high distraction or conflict functions) have been shown to use separate cortical and subcortical networks (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Sarter, Gehring, & Kozak, 2006). In an fMRI study (Fan, et al., 2005) fronto-parietal cortical activation along with thalamic activation were seen during alerting behavior, parietal activation during orienting, and anterior cingulate and frontal cortex activation during executive attention (selection during conflict). The areas affected by the structural and metabolic pathology of AD have been shown to overlap with those brain areas that mediate attention functions, suggesting that communication processes in frontal, anterior cingulate, and parietal areas are vulnerable to the disease. These pathological alterations in brain communication appear to have behavioral consequences as early functional impairments.

Kästner and Ungerleider (2000) tested healthy controls on selective attentional tasks and showed fMRI variations involving the V4/ parietal area, areas typically affected by neuropathic AD changes. Additionally the neuropathology of AD affects cortical pyramidal cells and cells in laminar layers II, III, and IV (Gomez-Isla et al., 1996; Morrison et al., 1986). Cortico-cortical fibers emanate from layers III and IV, forming the anterior-posterior tracts connecting the frontal and parietal cortical association areas. The function of prefrontal-posterior parietal cortical connections was investigated in primates by Selemon and Goldman-Rakic (1988) and was implicated in spatially guiding behavior and directing attention.

Parasuraman et al. (Parasuraman, Greenwood, Haxby, & Grady, 1992) proposed that the distribution of laminar pathology seen in AD disconnects the anterior and posterior attentional networks (M. I. Posner & Petersen, 1990). The disturbed connectivity has been supported by neuroimages of patients with AD. Wang et al. (2007) investigated abnormal functional connectivity throughout the entire brain of early AD patients using resting-state fMRI, and analyzed the global distribution of these abnormalities. Compared with healthy controls, AD patients had decreased positive correlations between the prefrontal and parietal areas. The disconnection between anterior and posterior systems may be part of the underlying mechanism of the attentional deficits seen in AD, and these attentional impairments may be reflected in the pattern of early functional deficits.

Typical to brain disorders, the degree of tissue alteration or loss is associated with behavioral dysfunction, particularly in intellectual, cognitive, and functional domains. Human post mortem findings (Marshall, Fairbanks, Tekin, Vinters, & Cummings, 2006a) showed that increased pathological burden of plaques and tangles in cortical areas correlate with decline in activities of daily living in the middle and later stages of the disease, particularly in the medial temporal, occipital, and orbital frontal regions.

In another study, Marshall et al. (Marshall, Fairbanks, Tekin, Vinters, & Cummings, 2006b) investigated the relationship among pathological changes, chronic apathy and subsequent withdrawal from participation in activities in AD patients. They found that chronic apathy correlated with increased anterior cingulate neurofibrillary tangle count. Further, Marshall et al. (2007) investigated pathological burden in early and late onset of AD symptoms using post mortem neuritic plaque and neurofibrillary tangle count in each group. They found greater overall plaque and tangle burden in the early-onset group. They hypothesized that late-onset AD patients had less cognitive reserve than early-onset patients and required fewer pathologic changes to exhibit cognitive deterioration. Thus, in these two groups (late and early onset AD) cognitive and functional changes interacted with individual experiences in daily life (leading to cognitive reserve). The interplay of life experiences and increased plaque and tangle formulation reflected the onset of symptoms and progression of the disease.

Neurochemical changes in AD: ACh depletion.

The pathology of AD includes neurochemical changes in cortical neuromodulatory transmitter systems, such as acetylcholine (ACh) and monoamines. These transmitter systems send projections that innervate the cortex, either exciting or inhibiting cortical neurons depending on the composition of postsynaptic transmitter receptor subtypes. Reduced levels of ACh have been long associated with deficits in memory (Bartus, Dean, Beer, & Lippa, 1982). Other functions (Gu, 2002) of ACh neurotransmitters are believed to be involved in arousal, attention and motivation and behavior regulation.

The primary neurotransmitter system affected in the early stage of AD is the cholinergic system, subsequent to cell loss in the Nucleus Basalis of Meynert of the basal forebrain, the major source of cholinergic innervation of the cerebral cortex (Davies & Maloney, 1976; S. K. Gill et al., 2007; Whitehouse et al., 1982). Using PET, Shinotoh et al. (2000) showed that the progressive cholinergic loss innervating neo-cortex and thalamus corresponded to progressive cognitive decline in patients with AD. The deficits in ACh in AD affect multiple functional and cognitive areas (Guela, 1998), but the connection between acetylcholine and attention has been notable and well documented (Baddeley, et al., 2001; Furey, Pietrini, Haxby, & Drevets, 2008; Sarter, Hasselmo, Bruno, & Givens, 2005).

ACh and attention.

The effect of depleted ACh on attention has been of great interest in the study of AD. Acetylcholine plays a prominent role in attention operations (Lawrence & Sahakian, 1995; Sarter, et al., 2005). Animal studies have shown that attentional mechanisms are directly subserved by the basal forebrain's cortical cholinergic network (Gu, 2002; Passetti, Dalley, O'Connell, Everitt, & Robbins, 2000; Sarter & Bruno, 1999). In humans, the cholinergic forebrain provides the major cholinergic innervations to the hippocampus, amygdala, and neocortex (Gu, 2002) where these cholinergic systems play a role in cognition, particularly in attentional processes (Sarter, et al., 2005; Shinotoh, et al., 2000).

The cortical cholinergic system generally acts to optimize the processing of signals in attention-demanding contexts. Support for this role of the cholinergic network is seen in performance deficits in animals when tasks make high attentional demands

(Himmelheber, Sarter, & Bruno, 2000; Passetti, et al., 2000). The relationship between ACh and attention is demonstrated not only by poor attentional performance when ACh levels are depleted, but also by the higher ACh release that occurs during demanding attentional tasks (Sarter, et al., 2006).

Attentional impairment of AD patients has been well documented (Baddeley, et al., 2001; Perry & Hodges, 1999). Investigations have linked progressive deterioration of the basal forebrain's cortical cholinergic network with attentional deficits seen in AD patients (N. S. Foldi, White, R. E., Schaefer, L. A., 2005; Greenwood, Lambert, Sunderland, & Parasuraman, 2005; Levy, Parasuraman, Greenwood, Dukoff, & Sunderland, 2000; Mufson, Ginsberg, Ikonomovic, & Dekosky, 2003; Pappas, Bayley, Bui, Hansen, & Thal, 2000). Studies demonstrated compromised functions in selective attention (N. S. Foldi, Horn-Levinson, L., Vedrody, S., Leavitt, V. M., 2004; N. S. Foldi, Schaefer, L. A., White, R. E., Johnson, R., Jr., Berger, J. T., Carney, M. T., Macina, L. O., 2005), focused attention (Levinoff, et al., 2005), and in visual search (Levy, et al., 2000). In patients with AD, selection tasks that require detection of stimuli among distracters (particularly in tasks of increased density and similarity of stimuli) and identification of stimuli presented close together in time, appear vulnerable (Baddeley, et al., 2001; N. S. Foldi, Schaefer, L. A., White, R. E., Johnson, R., Jr., Berger, J. T., Carney, M. T., Macina, L. O., 2005; Greenwood & Parasuraman, 1997; Perry & Hodges, 2003). AD patients have been found to have difficulty ignoring distracting information (N. S. Foldi, Jutagir, R., Davidoff, D., Gould, T., 1992; Foster, Behrmann, & Stuss, 1999) and have difficulty with inhibition of responses. Therefore it is reasonable to posit a direct link between attention and cholinergic availability in AD, thus making AD a clinical model of depleted acetylcholine and poor attentional function.

The relationship between cognition and functional behaviors in AD.

Both global cognitive tests (e.g., Mini-Mental Status Examination) (Folstein, Folstein, & McHugh, 1975), and functional tests (e.g., Clinical Dementia Rating Scale) (Hughes, Berg, Danziger, Coben, & Martin, 1982) can serve to determine disease severity (Atchison, et al., 2007; Farias, Harrell, Neumann, & Houtz, 2003; Matsuda & Saito, 2005; Wlodarczyk, Brodaty, & Hawthorne, 2004). Tests of cognition have been found to be more predictive of IADL performance than BADL in a clinical geriatric population that included patients with varied types of dementia (Richardson, et al., 1995) and AD (Jefferson, Barakat, et al., 2006).

To discern which ADLs were dependent upon which cognitive abilities, the relationship between neuropsychological tests and functional tasks was investigated in patients with AD (Baum, et al., 1996). Results showed no association between specific neuropsychological and functional tasks. The authors concluded that both functional tasks and neuropsychological tests assess the same domains of global deterioration in patients with AD. Routine daily activities (BADL) did not correlate with neuropsychological testing and were thought to represent intact procedural memory in the patient population.

Giovannetti et al. (2002) investigated cognitive influences on daily tasks in natural contexts in patients with AD. Results demonstrated that global cognitive measures were better predictors of performance errors on daily living tasks than specific measures of executive functioning or semantic knowledge. Task demands were found to significantly influence the type and frequency of errors, but differences among tasks were not identified in this study. The authors implied that attentional resources might be the basis of the functional impairment. Thus, while there may be a relationship between global cognitive scores and function, the links between specific cognitive domains (e.g., attention) and type of functional task is unclear.

Most assessments of AD patients include ADL tests as a secondary outcome of the disease process (Doble, Fisk, & Rockwood, 1999; Rockwood, 2007). Many of these functional assessments are criterion referenced (Katz & Akpom, 1976; Lawton & Brody, 1969; Reisberg et al., 2001), examining performance level to provide a descriptive picture of current ability. Fewer ADL tests are norm referenced, that is, producing scores that are comparable to normative populations. The relationship between impaired performance on specific tests of cognition, which are usually norm-referenced, and observable effects on a patient's life, is not clear. A cognitive measure may detect change early in the disease that may indicate weakening cognitive processes, however these subtle declines on testing do not necessarily translate into impairments in independent living (Rockwood, 2007). Thus, while cognitive impairment is a core symptom of AD, it has been found to be only globally and moderately associated with functional performance (Bouwens, et al., 2008; Derouesne, et al., 2002). As neuropsychologists are often asked to predict functional status from cognitive assessment results to give caregivers support or obtain services, weight is given to descriptive findings from ADL tests when helping families. Further, determining an individual's capability in everyday life from an ADL test score is also problematic, as the traditional view of "functional status" often does not include contextually relevant, variable conditions like those involved in adapting to technology (e.g., a new cell phone, digital ovens and laundry machines, microwaves), leisure (e.g., travel), employment (e.g., small business owner), or life roles (e.g., being a grandparent). Thus, an ADL measure of familiar tasks often underestimates the actual loss of function in professional or social/personal contexts (Thomas, Rockwood, & McDowell, 1998).

It remains unclear which aspects of cognitive impairment impact early decline of ADL in AD. Some studies (N. S. Foldi, Ly, J.J., Redfield, J., Honig, L.S., White, R.E.C., Kaplan, L.R., Nikelshpur, O.M., Berger, J.T., Gomolin, I.H., Macina, L.O. , 2008) emphasize nonverbal neuropsychological performance as influential in early functional decline. For example, poor spatial localization (Mortimer, Ebbitt, Jun, & Finch, 1992), poor object perception (Glosser et al., 2002; Liu, McDowd, & Lin, 2004), difficulty with the inhibition of responses, and unsystematic search strategies (Jefferson, Barakat, et al., 2006) all have been associated with impairment in IADL. It is possible that these nonverbal cognitive domains have been linked to IADL tasks because perceptual and visual organizational skills rely on, and are integrated with, underlying attention processes in the context of real life functions.

The relationship of neuropsychiatric behavior, attention and ADL

Neuropsychiatric symptoms in AD such as depression, apathy, and/or psychosis may also contribute to progressive decline in independent function (Cummings & McPherson, 2006). Significant relationships have been found among IADL, neuropsychiatric symptoms, and cognitive impairment, suggesting that neuropsychiatric behavior and function worsen with disease severity (Tekin, et al., 2001). However, as noted above, the role of attentional dysfunction in the development of neuropsychiatric symptoms and the consequent functional decline remains to be investigated.

Effects of attention dysfunction in AD may differ in BADL and IADL tasks.

The distinction between IADL and BADL tasks is presented frequently in the literature (Galasko, Schmitt, Thomas, Jin, & Bennett, 2005; Lawton & Brody, 1969; Thomas, et al., 1998). There is evidence that BADL are resilient in AD while IADL decline earlier (K. P. Liu, et al., 2007). What has not been explored, however, is the relationship between impaired attentional processes in AD and declines in IADL and BADL.

The impact of AD pathology, resulting in faltering attention mechanisms early in the disease, may have functional implications (Marshall, et al., 2006a) particularly for IADL. Specifically, tasks that place high demands on attentional resources should be more compromised. To determine the tasks most likely to be compromised early in AD, it is first important to explore the fundamental differences between tasks that either increase or decrease attentional loads.

Many daily activities at home or in the community vary—such that the same task differs each time it is performed (e.g., shopping) and requires the performer to be adaptive (e.g., shopping in a busy supermarket). This is typical of IADL tasks. To independently and successfully complete a task that varies, it is necessary to anticipate, monitor, and detect changes, which puts high demands on attentive and response processes. Variability creates novelty, which demands attention if one is to complete a task with success. Routine activities (e.g., showering, toileting) within settings that are familiar, immobile, and unchanging (such as in a home bathroom) require only limited monitoring of the environment. These characteristics are typical of BADL tasks and responses can quickly become automatic and habitual. Thus, ADL tasks can be categorized according to the degree to which they vary (or not), with this dimension associated with attentional requirements.

We hypothesize that a fundamental characteristic that differentiates tasks for AD patients is variability; that is, the task is performed within environmental conditions that differ in some meaningful way each time. The variability of a task increases attentional demands to detect, monitor, orient, and select salient features, and thus performing a task under variable conditions is effortful (Hasher & Zacks, 1979; Sarter, et al., 2006). In contrast, tasks with low variability are unchanging and routine, require minimal monitoring, and thus are more automatic. Patients performing tasks with low variability can rely on relatively intact procedural memory (Eslinger & Damasio, 1986; Heindel, Salmon, Shults, Walicke, & Butters, 1989), which does not depend as heavily on frontal processes (Willingham, 1998). Our hypothesis is that in AD, attention is a critical mediator of changes in functional performance. The more variable IADL tasks require more monitoring than BADL tasks, are more likely to be demanding of attentional resources, and are the first to be impacted by faltering attentional resources. The categorization of tasks based upon the variability of conditions constitutes a somewhat different approach to traditional categorizations, which tend to group tasks based on factors such as the environment of the task or performer-based skill required.

Classification of Tasks

Classification of ADL tasks by environment.

ADL tests are comprised of task items that are purposeful, goal directed, and appropriate to a population's developmental life stage. Some ADL tests require direct observation of task completion while others rely on self or informant reports of patients' ability. Most tests of ADL for AD patients, being criterion referenced, are used to assess an individual's capacity for independent living or overall functional disability (Potkin, 2002). Decisions about services are often based on these levels of disability. ADL tasks have been validated by their relationships with cognitive assessments and global measures of disease severity such as the MMSE. Others have been validated with self reports, discharge plans, specific cognitive tests such as tests of visual memory, spatial ability, attention, or other ADL measures.

Environments in which ADL tasks are performed can vary. Tests of daily living skills typically classify functional tasks into two types based on the environment of performance: 1) measures of instrumental activities of daily living (IADL) performed in environments in the broader household (e.g., laundry) or community environments (e.g., shopping, driving); and 2) basic activities of daily living (BADL) such as self care in the bathroom or bedroom (Lawton & Brody, 1969; H. C. Liu et al., 2007; Spector, Katz, Murphy, & Fulton, 1987; Tekin, et al., 2001). Collectively, IADL and BADL tasks assess the activities required for personal independence. Examples of measures using environmental characterization of ADL are the Lawton Brody Self Maintenance and Instrumental Living Scales (Lawton & Brody, 1969) and the Kolman Evaluation of Living Skills (KELS) (Thomson, 1992; Zimnavoda, Weinblatt, & Katz, 2002).

BADL tasks were first proposed (Katz, Ford, Moskowitz, Jackson, & Jaffee, 1963) as a cluster of tasks associated with basic biological functions. These tasks were often disrupted by central nervous system damage and originally seen as useful markers for assessing the efficacy of rehabilitation. BADL tasks take place in limited and stationary home environments and include bathing, dressing, "toileting" (getting to the toilet as well as cleaning and refastening clothes), transferring in and out of beds or chairs, and eating.

IADL tasks trace back to Lawton and Brody (1969) who introduced the phrase "instrumental activities of daily living." IADL tasks, which are more diverse, include activities necessary to live independently in the community (i.e., managing money, shopping, meal planning and preparation, housekeeping, and obtaining transportation) (Branch & Hoenig, 1997). Used extensively for research and clinical assessments, the Lawton-Brody ADL Scales remain separated into IADL and BADL tasks, assessing a subject’s performance in eight daily activities essential to maintaining independence in the community and another eight items dealing with physical self care. Based on self report or caregiver interview, each item is scored with a 1 (independent) or 0 (dependent), and a maximum score of eight on either scale is generated if the subject is competent in all tasks. Modifications of the scales using the same set of tasks have been made, (Giovannetti, et al., 2002) where a 3 point scale (0-2) allows scoring when a performer can accomplish a task with assistance or in a limited capacity.

Patients with mild AD (early in the disease progression) are able to perform most basic self care tasks (BADL), several home based IADL tasks, such as laundry and light housework, but require assistance and supervision in community based IADL

(Lechowski, et al., 2008; K. P. Liu, et al., 2007). This profile suggests that change in the performance of IADL tasks occurs in the initial stages of disease, while most BADL are retained. While this appears to be a pattern in AD, the differences that these task types present to the patient with AD should be explored.

In this traditional classification, IADL and BADL tasks differ not only by environment, but are thought to represent different levels of complexity due to subsequent demands of resources on the performer. BADL are performed in relatively invariant settings (e.g., brushing teeth in the bathroom), whereas IADL can vary on a continuum from contexts where the performer must contend with differing stationary spatial features (e.g., picking up a pile of towels versus picking up underwear for laundry), to combined temporal and spatial environments that add variability due to motion of objects and people (e.g., shopping in a crowded supermarket). IADL tasks have been considered to be 'higher order' and more complex than BADL, as they have been noted to make 'higher cognitive' demands (Fitzgerald, Smith, Martin, Freedman, & Wolinsky, 1993). However, differences in categorizing IADL and BADL as a levels of complexity can be challenged. In a new context, an otherwise 'simple' BADL task can become less automatic. For instance, showering at home may be easily accomplished, but in an unfamiliar hotel or new residence bathroom, this otherwise routine task may be difficult to complete for a patient with AD. The hotel condition requires more demands to detect and adapt, and therefore the patient may be unsuccessful and require assistance. Thus, dichotomizing ADL tasks simply into IADL and BADL as two different levels of complexity can be problematic as all contextual features determining successful task performance for an individual are not captured by this environmental classification.

Classification of ADL by performer-based skills.

IADL task items are grouped as either requiring more ‘motor’ or more ‘cognitive’ resources based on the operational definitions of primary underlying resources needed to perform the task (Granger, Hamilton, Linacre, Heinemann, & Wright, 1993). Although this ADL task classification is not consistently defined in tests, it often follows similar task groupings of the IADL/BADL distinction (Mahurin, DeBettignies, & Pirozzolo, 1991), and is geared toward identifying component problems as applied to levels of disability.

Acknowledging that every functional activity involves a degree of both motor and cognitive resources, the Assessment of Motor and Process Skills (Fisher, 1993; Oakley & Sunderland, 1997) differentiates motor and cognitive skills required for daily activities for persons with developmental, psychosocial, and/or musculoskeletal disorders from age 5 through adulthood. The AMPS operationalizes motor and cognitive (referred to as ‘process’) skills, which the examiner rates concurrently during direct observation of tasks appropriate to the performer’s age, culture, and environment. The AMPS is used clinically to interpret how motor or cognitive impairments influence IADL tasks and to anticipate patient supports. However, the AMPS does not directly account for patient ability to adapt to changing task conditions relative to typical variability. Cognitive (process) scores of the AMPS have been shown to correlate with MMSE scores in community-dwelling elderly with and without AD (Doble, Fisk, MacPherson, Fisher, & Rockwood, 1997) whereas motor scores did not. This suggests an association between the AMPS cognitive score, disease presence, and functional decline. Liu (2007) found support for these findings by showing a positive correlation between the Lawton-Brody IADL scale and AMPS cognitive scores in an AD population.

There are tests of ADL specific to AD populations, e.g., AD Activities of Daily Living International Scale (Reisberg, et al., 2001) and the Alzheimer Disease Cooperative Study ADL Scale (Galasko, et al., 2005), which rank tasks based on what patients with AD can perform independently. On close inspection of both above measures, it appears that tasks performed in the most variable environments are most difficult and performed by individuals mostly at baseline (i.e., mild AD), and rarely at moderate or late disease stages. In contrast, routine self-care items deemed less challenging may still be performed at middle and late AD stages (Galasko, et al., 2005). Therefore, many of these functional task items can be ranked by variability.

In summary, some ADL tasks can be characterized categorically (e.g., IADL or BADL, ‘motor’ or ‘cognitive’), or by hierarchical ranking of independent performance. However, regardless of category or rank, performance would likely be very different when the identical task occurs in a variable or *novel* condition (e.g., new residence bathroom or new stove) and would be considered more *complex*. For the AD patient, compromised performance in the presence of novelty may not necessarily reflect a decline in functional status or a sudden worsening of the disease. Rather, unsuccessful performance might simply reveal the current inability to adapt behavior to variable conditions that increasingly tax attentional search, detection, or the allocation of attentional resources.

Resource–based classification of ADL: Contexts that influence demands on the performer

To measure individual function in patients with AD, ADL classifications should be based on characteristics of the task *and* prevailing conditions, as both alter demands on the performer. Gentile (2000) has addressed these issues. Gentile's taxonomy suggests a different perspective toward ADL tasks, one that considers whether objects are stationary or in motion and whether there is variability each time a task is attempted. A person can move and act within an environment that is stationary, such as walking into his/her familiar kitchen. Here the performer controls when to start or stop and determines the speed and spatial direction of the body. Stationary environments can be invariant (e.g., configuration of furniture) or can vary (e.g., configuration of clothes in a closet). Alternatively, an environmental context can be in motion, where objects move during a task and a person's movement relative to the objects influences successful performance. An example of this type of environment would be walking through a mechanically revolving door or catching a ball, where the performer's movements must respond to the environmental change to be successful (Higgins, 1972; Higgins & Spaeth, 1972). The performer is not free to decide when to start the motion, how fast to move, or in what direction, and must conform by adapting to both spatial and temporal aspects of the task. The motion of the revolving door directs where and when one starts to move and the movement of the ball directs the timing and direction of response to catch it. Tasks in motion usually, but not always, have a great deal of intertrial variability in that some aspect of the task is different each time it is attempted. The performer must respond to these environmental changes to be successful (Gentile & Nacson, 1976; Higgins, 1972).

Intertrial variability can be either absent or present over a series of attempts to perform a task (Gentile, 2000) and is determined by the similarity of the environment/task conditions from trial to trial. If the environmental conditions (i.e., stationary or in motion) are virtually the same every time the task is performed (i.e., toileting) and no other characteristics change, then there is little intertrial variability. However, as characteristics change on each attempt (e.g., using a bathroom at a restaurant), then intertrial variability is present. Variability of stationary items from one trial to the next requires higher monitoring and places stronger detection demands on the performer. Changing aspects of the environment affects the performer's need to monitor and select relevant information in the environment, and adapt movements for successful task outcome (Higgins & Spaeth, 1972; Spaeth, 1972).

The Gentile taxonomy (2000) of tasks offers an operational definition of task complexity. For example, two factors, environmental context (in motion or stationary) and intertrial variability (absence or presence) can be used to describe four conditions of task complexity (see Table 1). Presence of intertrial variability and environmental motion conditions are more complex than no intertrial variability and stationary conditions because constraints on timing increase demands on attention and efficiency of processing information.

The benefit of Gentile's taxonomy (Gentile, 2000) is that it provides variables that operationalize why a task is simple or complex. In her full taxonomy, Gentile expands on environmental contexts (stationary or in motion), variability (present or absent), and body functions (postural and upper extremity requirements), and the 16 intersecting conditions operationalize a continuum of task complexity: simple, intermediate, and highly complex tasks that can be used to obtain an analysis of the impact of interacting task requirements on resources (see Gentile 2000). Caregivers of patients with AD need to anticipate which tasks can be performed independently, under which conditions, and which present safety hazards. This method of defining task complexity, which identifies variables required to function in various contexts, has the potential to demonstrate which task features are problematic for a patient, assist in anticipating activities that can still be performed independently, and direct where support is needed.

Interaction of environment and attention resources in patients with early AD.

An inherent construct of the Gentile system is that unchanging tasks are responded to automatically, while novel tasks require adapting responses to prevailing conditions and are more effortful. That is, task conditions place different demands on the attentional system. The application of the theory of automatic–effortful processing (Hasher & Zacks, 1979; Schiffrin & Schneider, 1977) to changes in ADL performance suggests that for invariant task conditions, low monitoring is required and responses could be automatic. In contrast, variable or novel tasks, which put constraints on timing while performing, increase processing demands; patients with AD, who have to adapt with more effort, are likely to show impairment on such tasks.

The linking of attentional processing to ADL demands has not yet been explored in AD. As a way to understand functional deficits in AD, this study will investigate whether attentional demand is a primary predictor of performance deterioration by examining relationships among attention, global cognition, and neuropsychiatric behavior.

Aims and Hypotheses

Aim 1: To differentiate types of functional tasks in which patients with AD had initial declines. We hypothesized that more variable functional tasks (i.e., IADL tasks) would be more sensitive to disease progression. We expected that:

1a) patients with AD would have more impaired IADL (higher scores) than BADL scores.

1b) IADL tasks would be better indicators than BADL of global cognitive status.

1c) IADL tasks would be better indicators than BADL of neuropsychiatric behaviors

Aim 2: To identify the contribution of attention, global cognition, and neuropsychiatric status to the variability of performance on IADL and BADL tasks.

2a) We hypothesized that higher order attentional resources (attention resources involved in set switch and selecting) would be influential in impaired IADL performance, exceeding that of the combined influence of neuropsychiatric status and global cognitive scores.

2b) We hypothesized that lower order attentional resources (attention resources involved in vigilance/detection and orienting) would have a combined influence on BADL that exceeded the combined influence of neuropsychiatric status and global cognition.

METHOD

Participants

Twenty-seven participants with AD and their caregivers were recruited from the Neuropsychology Service and Geriatric Division of Winthrop-University Hospital in Mineola, NY. Patients were recruited after they were newly diagnosed with AD , based on full medical, neuropsychological, neuroradiological (MRI) assessment, and consensus of the neuropsychologist, geriatrician and/or neurologist and radiologist. The range of disease progression was wide, however mean and frequency of scores indicated most participants in the early stages of the disease (see Table 2 for demographic status). Twenty-five (92.6%) participants had not initiated acetylcholinesterase inhibitor treatment for AD or memory loss. One patient had been treated with 10mg of donepezil (Aricept) for one year and another with 10 mg of donepezil afor 8 months in addition to 20 mg/day of memantine hydrochloride (Nemenda) that had been taken for 2-3 years prior to testing for memory loss. Fifteen (56%) participants were female and 12 (45%) were male. While 40% of participants had at least a high school education, 38% completed college and/or graduate degrees.

Inclusion criteria were: minimum of 40 years of age, MMSE score greater than 15/30 (Folstein, et al., 1975; Monsch et al., 1995), normal or corrected bilateral vision, and English fluency. Pharmacological treatments required for other systemic disease (e.g., hypertension, cardiac disease), depression, anxiety, non-steroidal anti-inflammatory agents, and vitamin supplements were allowed and did not exclude participation.

Exclusion criteria were: primary neurological conditions (e.g., history of significant CVA, other etiologies of dementia, Parkinson’s or Huntington’s disease), Axis

I psychiatric disorders (e.g., schizophrenia or bipolar disease), and vision impairments that interfered with visual attention tasks (e.g., scotoma, macular degeneration).

A caregiver was operationalized as a family member who reported having consistent contact with the participant and who (based on prior interview assessment) oversaw care and decision making. Participants with AD who were married (56%) were accompanied by caregiver spouses, whereas caregivers of participants who were widowed (41%) or divorced (3%) were accompanied by their adult children.

Stimuli and Measures

Three domains were measured: 1) *Global cognition:* Cognitive screening tests staging severity of cognitive dysfunction; 2) *Daily behav*iors: Caregiver ratings of performance of activities of daily living (IADL and BADL) and neuropsychiatric status; and 3) *Attention*: Selective search measuring stimuli detection and sequencing and experimental computerized tests measuring reaction time to detection and spatial orienting.

1) Global cognition: a) The Dementia Rating Scale-2 (DRS: Mattis, 2005). This widely used, standardized, brief assessment is comprised of subdomains of attention, initiation-perseveration, construction, conceptualization, and memory with a total maximum score of 144. The test's total score is used to assess level of cognitive deficit for individuals with dementia, and subscales have been used to describe profiles within patient populations (Vitaliano, Breen, Albert, Russo, & Prinz, 1984). Alpha was set at .05. Test-retest reliability (r = .93) after administration twice within a 12-28 day interval has been reported (Schmidt, Mattis, Adams, & Nestor, 2005). Observed Chronbach Alpha = .66. Regression analyses conducted for each of the five cognitive domains have revealed significant predictive relationships (*p* <.01) between DRS-2 performance and activities of daily living (Nadler, et al., 1993). Further, initiation/perseveration and memory subscales have been shown to be significantly associated with declines in IADL and BADL in patients with vascular dementia (Jefferson et al., 2006).

b) Mini-Mental State Examination (MMSE: Folstein, et al., 1975). This 30-item screening test includes brief assessments of memory, language, praxis, and orientation and has been used extensively in clinical AD research. Reliability was found to be moderate to high among healthy elderly and those with AD ((Tombaugh, 2005), but demonstrated poor sensitivity for disease detection (Monsch, et al., 1995). Observed Chronbach Alpha = .80. Structural neuroimaging correlates to MMSE performance in patients with clinical and preclinical AD were seen in the gray matter integrity of entorhinal, parahippocampal, precuneus, superior parietal, and cingulate/orbitofrontal cortices (Apostolova et al., 2006).

c) The Alzheimer Disease Assessment Scale-Cognitive Section (ADAS-Cog: Rosen, Mohs, & Davis, 1984). This cognitive test was originally designed as a measure of drug efficacy and includes tests of memory, language, praxis, and visuospatial function to generate a maximum score of 70. Notably, there are no measures of attention included in the ADAS-Cog. Coefficients of internal consistency and test-retest reliability were .80 and .96, respectively in a sample of patients with AD (Weyer, Erzigkeit, Kanowski, Ihl, & Hadler, 1997). Observed Chronbach Alpha = .73. In a study of 1,648 participants with AD in two identical 26-week multicenter drug trials (Doraiswamy et al., 1997), the ADAS-Cog significantly correlated with the MMSE ($p < 0.0001$).

2) Measures of patient daily behavior: a) IADL and BADL subscale scores were collected from the structured interview with caregivers using a modified version of the Lawton and Brody (1969) Physical Self Maintenance and the Instrumental Activities of Daily Living Scales (Giovannetti, et al., 2002) [See Appendix]. Sixteen items (8 for IADL and 8 for BADL) are scored on a three-point scale of independence = 0, assistance = 1, or dependence = 2, generating a maximum score of 16 for each subscale. Observed Chronbach Alpha = .80 for the 16 IADL and BADL items. In a study of 86 AD patients (K. P. Liu, et al., 2007), the Lawton-Brody IADL subscale correlated significantly with the Clinical Dementia Rating Scale (CDR: Hughes, et al., 1982) a measure of 6 domains that include memory, orientation, judgment, problem solving, community affairs, home /hobbies and personal care ($p = <.05$). The IADL subscale also correlated with the Bartel Index (BI) (Mahoney & Barthel, 1965) and with the Assessment of Motor and Process Skills (AMPS) (Fisher, 2003), a test that includes measures of self care and IADL ($p = <.01$).

b) The Neuropsychiatric Inventory (Cummings et al., 1994) assesses patient behavior using a structured caregiver interview in 12 domains of psychiatric dysfunction, (e.g., delusions, hallucinations, anxiety) using a structured interview with the caregiver. Each item is rated for behavior frequency (0-3) and severity (0-4), and the test generates a maximum score of 144. Reliability and validity for the NPI have been established (Cummings, 1997b; Cummings, et al., 1994), and the NPI has been used extensively in clinical drug trials for AD (Cummings, 2006; Cummings, McRae, & Zhang, 2006). Observed Chronbach Alpha = .61. The NPI has been shown to have associations with ADL and caregiver burden (Monsch & Giannakopoulos, 2004; Tekin, et al., 2001).

3) Measures of Attention: a) The Trail Making Test (TMT) is a subtest of the Delis-Kaplan Executive Function System (D-KEFS; Delis, et al., 2001) and is a standardized neuropsychological measure of selective search. The TMT is a paper and pencil task with five Conditions: Visual Scanning (cancellation), Number Sequencing, Letter Sequencing, Number-Letter switching, and Motor Speed. The test taps the ability to inhibit surrounding distracters while selecting stimuli in increasingly complex conditions. Completion time (measured in seconds) and number of errors (measured by omission, commission, and time constraints) are recorded. Studies have demonstrated that D-KEFS subtests are sensitive to executive-function deficits in numerous clinical populations and highly correlated with the Wisconsin Card Sort Test. Reliability for executive function in numerous clinical populations has been demonstrated (Delis, et al., 2001) and found to be above .80 (Delis, Kramer, Kaplan, & Holdnack, 2004). Observed Chronbach Alpha for TMT conditions = .83, and .63 for completion times and error rates respectively. The D-KEFS and TMT in particular have been found to be significantly related to declines in ADL in AD patients (J. K. Johnson, Lui, & Yaffe, 2007; Mitchell & Miller, 2008).

b) Computerized measures. Two computerized tests of attention, a serial detection task (SDT) and covert orienting task (CV) were administered.

i) *Serial Detection task (SDT):* The period of time waiting for a cue or stimulus prior to detection is a sensitive marker of attentional vigilance and has been associated to length of response time. Much like waiting for a red stop light to change (Bherer & Belleville, 2004), the expectancy of an event alters the time it takes to respond to the imminently upcoming green light: if the wait is long, readiness improves and RT is faster, or, if a wait is unexpectedly short, RT is slower. Thus, a short interval period (high load) prior to an imminent event yields longer RT, indicative of unpreparedness; in contrast, shorter RTs are evident after longer fore-periods (low load) while an individual readies for an upcoming event.

Older adults are less efficient and less prepared to respond to uncertain events, and show larger fore-period effects than younger adults (Bherer & Belleville, 2004). The underlying neurological mediation of the effect has been linked to the integrity of the right dorso-lateral prefrontal region, as patients with focal damage in this location show disproportionately large fore-period effects and fail to use any directive instruction (Alexander, Stuss, Shallice, Picton, & Gillingham, 2005; Stuss et al., 2005). Thus, frontal change may be one source of an aging effect. Further, RT to short intervals has been demonstrated to be correlated with disease severity in mild AD (N. S. Foldi, Horn-Levinson, L., Vedrody, S., Leavitt, V. M., 2004; N. S. Foldi, Ly, J.J., Redfield, J., Honig, L.S., White, R.E.C., Kaplan, L.R., Nikelshpur, O.M., Berger, J.T., Gomolin, I.H., Macina, L.O. , 2008).

The computerized test used in this study involved detection of a stimulus after waiting an interval of time and a response by pressing a button. A 1.52 cm white asterisk stimulus target subtending 0.75^{o} visual angle was centrally presented on a black background. The participant was instructed to respond as soon as he/she saw the asterisk by pressing the button. To avoid regular timing of presentation, serial stimuli presentation rate was varied by six possible randomly presented intervals (Stimulus Onset Asynchrony, SOA) of 350, 500, 650,800, 1100, or 1400 milliseconds (ms) for 60 trials (see Figure 1). SOA was directly related to the monitor refresh rate. The monitor refresh rate, or time of one frame, was 1000 milliseconds (ms)/ assigned hertz; with hertz (Hz) set to 75 the refresh rate is 13.3 ms. To evaluate sustained attention, the task was presented twice, once at the initial point of the evaluation session (administration 1) and again at the end of the computer testing session (administration 2), approximately 45 minutes later. Response time (RT) to target detection on both administrations was recorded in ms. Observed Chronbach Alpha = .94.

ii) *Covert orienting (CV)*: The difference in RT to valid and invalid visual cues (longer RT to invalid than either valid or neutral cues) is a robust and well-established effect in normal adults (M. I. Posner, 1980; M. I. Posner, Snyder, & Davidson, 1980; M. I. Posner, Walker, Friedrich, & Rafal, 1987). Right frontoparietal regions have been implicated in the neural mechanisms of predicting cues (Vossel, Thiel, & Fink, 2006; Vossel, Weidner, Thiel, & Fink, 2009). With progression of AD, changes in covert orienting (Geffen, Wright, Gotch, Farrington, & Geffen, 1991; Vasquez et al., 2010) have revealed slowed RT with increased asymmetry in orienting as compared to normal older adults (Maruff, Malone, & Currie, 1995). To our knowledge, the relationship between orienting to cues and ADL has not been previously investigated. Observed Chronbach Alpha for RT orienting to valid, neutral and invalid cues = .97.

In this computerized test, a blank black screen presented for 500ms initiated each trial and was followed by central fixation (a red cross subtending 1° wide (.8726cm). Two empty white squares, each subtending 2° wide (1.75 cm), were presented for 1000ms on a black background, and were placed eccentrically from the center of the visual field, subtending 8° degrees from center. An exogenous valid, invalid (single filled white square) or neutral cue (both squares filled) appeared briefly for 100ms, reverting back to the hollow square for 150ms. The target, an ‘X’ within a square, was then presented and participants were required to detect and respond to the target as quickly as possible with a button press (see Figure 2). If no response was elicited after 3000ms, the next trial began.

Both covert and overt trials were presented. The stimulus onset asynchrony time (SOA) of 250ms (100ms for cue and 150ms for background) was chosen to maintain a covert response, and obviate voluntary saccades, which typically occur after 300ms. The SOA of 800ms (100ms cue, 700ms background) was chosen as overt orienting trials to further minimize predictability and anticipatory responses. Five experimental blocks, consisting of 34 trials each, resulted in 170 total trials for the experiment. Fifty-eight % (100 trials) were valid, 12% (20 trials) were invalid, 12% (20 trials) were neutral, and 18% (30 trials) were cued trials in which the SOA was 800 ms. Presentation of trial type was randomized within each block. RT to valid, invalid, and neutral cues were derived into two scores: Benefit to RT of having a valid cue, which constituted a Neutral RT-Valid RT and cost to RT of having an invalid cue, Neutral RT-Invalid RT (see Figure 3).

Procedure

Institutional Review Boards of Winthrop University Hospital and Queens College of the City University of New York (CUNY) approved the study. Prior to participation, each participant and each caregiver gave written consent and each received nominal monetary compensation at the end of the session. The testing session occurred following medical, neuropsychological assessment, and diagnosis of AD, but prior to the initiation of medication. All participants with AD completed the tests of disease severity, computerized measures of attention, and neuropsychological battery in the same order. An examiner evaluated each patient in one room and a different examiner obtained ratings of BADL, IADL, and neuropsychiatric behavior from the caregiver in a separate room.

For computerized testing, participants sat 50 cm from the screen. Stimuli were presented on a Dell PC with Windows XP operating system on a black background of a 17” monitor, at a 1280 by 1024 pixel resolution. An Ergodex keyboard was used as the button press and responses were made by the dominant index finger tapping the single button on the board.

Data management

For both computerized tests of attention (SDT and CV), RT was measured in milliseconds (ms), and median response time was used in analyses to correct for any non-normative distributions. In the SDT data, the first trial in every block was deleted because the stimulus did not have a preceding event. For both computerized attention tests, trials with no response, multiple responses, or an anticipatory response (RT < 100 ms) were removed. RT responses were converted to z-score distributions for each subject across task, administration, and SOA. Outlier trials, $-3.0 >$ or $z < +3.0$, were eliminated prior to analysis.

For the CV task, ‘costs’ in RT of having to disengage, move, and re-engage attention due to an invalid cue were calculated by subtracting the median RT of the neutral condition from the median RT of the invalid condition. ‘Benefits’ in RT to having a valid cue presented were calculated by subtracting the RT of the valid condition from the RT of the neutral condition.

All statistical analyses were performed using SPSS version 11.5 software.

Design

This study used correlational analyses (Spearman's non-parametric coefficient and linear regression) to examine relationships among, and the relative contribution of, predictor variables (attention, psychiatric behaviors, disease severity) to the dependent variables of activities of daily living (IADL and BADL).

Data Analysis

First, Spearman's correlation coefficient was used to investigate the redundancy of conditions within domains of attention (SDT: detection, D-KEFS TMT: selection and CV: orienting) and global cognition. Conditions that were not significantly related were determined to be testing separate constructs of the domain and used in further analyses.

Next, a regression analysis comprised of two phases was performed. The first phase investigated conditions of each predictor (identified previously) and its influence on function (IADL and BADL). Thus, separate linear regressions of conditions within each of 5 predictors (3 measures of attention, neuropsychiatric behavior, and global cognition), were used to assess for a unique contribution to the variability of IADL or BADL (as the dependent measure). The condition identified by the regression equation that had a unique contribution to IADL within that measure was kept for the second stage analysis. This procedure was repeated for BADL as the dependent measure.

The second phase regression analysis was used to identify the relative influence of the combined predictors (attention, neuropsychiatric status, and global cognition) with a unique contribution in stage one) on the variability of the function (IADL or BADL).

RESULTS

IADL and BADL Measures

The first study aim was to determine which functional tasks initially decline in patients with AD. Of the 27 participants, 93% (25 participants) were reported to have impaired IADL by their caregivers. This was indicated by reporting the individual needing assistance or being dependent (score > 0 for the item). In contrast 51% (14 participants) were reported as having deficits in BADL, and only 2 participants were reported as having *only* BADL deficits. Participants demonstrated significantly higher mean scores on IADL than BADL tasks (see Table 2), revealing that performance of IADL was more impaired than BADL ($t_{1, 26} = 6.31$, $p \leq .001$). This dissociation suggests that AD patients may have impaired IADL but not BADL skills (48%) early on, at the point of diagnosis. The reverse, however, (impaired BADL and intact IADL) was rare (7%). Thus, regardless of BADL status, IADL was initially more vulnerable to the disease process.

Of the eight IADL tasks, the highest percentage of patients endorsed difficulties handling finances (59%) and shopping (56 %). These are tasks with high demands for mental operations, monitoring change, and variability during performance. The next most problematic IADLs were housekeeping, responsibility for medications, and food preparation (endorsed by 52%, 52% and 51% of patients, respectively). These tasks are variable but performed in more stationary and/or less variable environments. Least problematic IADL were transportation, ability to use the phone, and laundry (endorsed by 43%, 41%, and 37% of participants, respectively). For these latter tasks, patients may draw on routines or supports to be successful (e.g., only dialing familiar numbers on their home phone, or arranging for transportation with family members or friends on a regular basis), and thus are seen by caregivers as less impaired.

Descriptive information from global cognitive measures for the total sample is presented in Table 2. Using non-parametric Spearman's correlations, relationships between global cognition and IADL and BADL were investigated. Among MMSE, DRS-2, and ADAS, greater impairment in IADL was associated with poorer performance on the DRS-2, p = .016 and MMSE, p = .03 (see Table 3). Greater impairment on BADL was associated with poorer performance only on the DRS-2, p = .048 (see Table 4).

Spearman's correlations were used to investigate whether increased neuropsychiatric behaviors were associated with more impaired IADL or BADL. However, these findings are tentative as only 7 (26%) of the caregivers reported patients having any neuropsychiatric problems. Adverse psychiatric behaviors correlated with impaired IADL, p = .034, but not with BADL, p = .176 (See Table 3). The behaviors reported with the highest severity and frequencies on the NPI were anxiety and apathy.

The second study goal was to determine the relative contributions of attention, global cognition, and neuropsychiatric behaviors (i.e., predictors) to performance on IADL and BADL tasks (i.e., dependent measures).

Attention Measures

In order to determine which predictors to enter into a regression analysis, multicollinearity or commonalities within each attention task was established. Descriptive information on all attention variables is reported in Table 5.

D-KEFS: The TMT five conditions were designed to hierarchically integrate with one another (Delis, et al., 2001). Spearman's non-parametric correlation coefficients were used and disparate variables were retained for the regression analysis. As seen in Table 6, completion time of Condition 1 (scanning and identification), Condition 2 (sequencing numbers in field of distracters), and Condition 5 (speed of motor completion) were not significantly related to the completion time of Condition 4 (set switch in a field of distracters), p = .191, p =.081 and p = .074, respectively. Mean errors across Conditions 2+3 (sequencing numbers or letters) did not relate significantly to completion time or total errors of Condition 4 (p = .150, p = .098 respectively). Thus, Conditions 1, 2, 4 and 5 completion times, Conditions 2+3 errors, and Condition 4 errors were used in Phase 1 of the regression analysis.

SDT: As the SDT uses the same detection task at different presentation rates, commonalities of RT as a function of SOA presentation were determined, and disparities were retained for the regression analysis. RT median scores were submitted to a repeated measures ANOVA with SOA (6 levels) and Administration (2 levels) as the within independent variables. Results indicated a significant main effect of SOA, $F5_{, 1\ 25}$ = 37.41, p <.001. Tukey HSD post-hoc analyses indicated significant differences between SOA1 and SOA2, SOA2 and SOA3, and SOA1 and SOA3 (p < .001), but no significant differences among SOA3, SOA4, SOA5 or SOA6 (see Figure 4). Neither the main effect of Administration (p = .46), nor the SOA x Administration interaction (p = .73) were significant. Thus, RT of each of the two short SOA intervals (i.e., SOA1 and SOA2), which demand the fastest processing, and RT performance averaged across the remaining SOAs (SOA3 through SOA6) were used as variables for Phase 1 of the regression analysis.

CV: To assess the Costs and Benefits of cues on orienting, a paired t-test revealed that the RT from the benefit of having a valid cue (Neutral RT-Valid RT) was faster (mean RT = 74.66 ms) and significantly different from the cost (Neutral RT– Invalid RT) (mean RT = 68.12 ms) of having an invalid cue, ($t_{27} = 7.69$, $p \leq .001$) (see Figure 4).

To verify that the identified variables (TMT, SDT and CV) were separate constructs of attention, Spearman’s correlations revealed that mean errors of Conditions 2+3, TMT Condition 4 completion time, and Condition 4 total errors were not significantly related to SDT SOA 1, SOA 2, mean SOA 3-6 or CV Costs or CV Benefits, $p = \geq .05$ (see Table 7). Thus all of these variables were used for the Phase 1 regression analysis.

Phase 1: Contribution of Attention, Neuropsychiatric Behavior or Global Cognition

Influences of attention on IADL, N = 27, see Table 8a.

TMT: Six linear regression analyses were performed using the TMT (Conditions 1, 2, 4 and 5 completion time; Conditions 2+3 mean errors; Condition 4 total errors) with IADL as the dependent measure. Of the six tests, only errors of Condition 4 contributed significantly to the variability of IADL, $p = .008$, and thus was included in Phase 2 of the regression analysis.

SDT: Three linear regressions were performed using three presentation rates of SDT (SOA1, SOA 2, and SOA 3-6) using IADL as the dependent measure. Results revealed that, regardless of presentation rate, detection of stimuli did not contribute to the variability of IADL. Thus, SDT was not included in Phase 2 of the regression analysis.

CV: Two linear regressions were performed using the covert orienting task, with Cost and Benefits as independent variables and IADL as the dependent measure. Neither of these measures significantly contributed to the variability of IADL and were thus not included in Phase 2 of the regression analysis.

Influences of attention on BADL, *n* = 14, see Table 8b.

TMT: For participants with BADL deficits, six linear regressions were performed using the TMT (Conditions 1, 2, 4 and 5 completion times; Conditions 2+3 mean errors; Condition 4 total errors) with BADL as the dependent measure. None of the 6 conditions contributed significantly to the variability of BADL.

SDT: Three linear regressions using the three conditions of SDT (SOA1, SOA 2 and the SOA 3-6) as predictors of BADL performance were performed. Results revealed that regardless of presentation rate, detection of stimuli did not contribute to the variability of BADL. Thus, SDT was not included in Phase 2 of the regression analysis for BADL.

CV: Two linear regressions investigating the contribution of Cost and Benefits of cues revealed that the measures of orienting attention were not significantly contributing to the variability of scores for BADL, and thus not included in Phase 2 regression for BADL.

Influences of global cognition on IADL, *N* = 27.

Measures of global cognition were highly correlated, and the least associated measures were entered into the phase 1 regression (see Table 3). To account for multicollinearity, two linear regression analyses were conducted with IADL as the dependent measure. The ADAS-cog, R^2 = .102, did not contribute to the variability of IADL, β =.187, *p*= .105, and was excluded from Phase 2 of the regression. In contrast, the DRS-2 significantly contributed to IADL, accounting for 21% of the variability and thus was included in Phase 2 of the analysis of IADL, β = -.167, R^2 = .213, *p*= .015.

Influences of global cognition on BADL, *n* = 14.

For participants with BADL deficits, ADAS-Cog scores were unrelated to DRS-2 scores, *p* = .158, demonstrating that these global tests of cognition measured separate constructs for this subgroup (see Table 4). Two linear regression analyses were conducted to investigate the influence of global cognition to the variability of BADL with DRS-2 and ADAS-Cog as predictors.

Each test was entered individually into a linear regression analysis with BADL as the dependent variable. None of the regression analyses showed that ADAS- COG or DRS-2 scores individually contributed to the variability of BADL, β =-.028, R^2 = .010, *p*= .732 and β =-.066, R^2 = .201, *p*= .108 respectively. Both predictors were excluded from Phase 2 of the regression for BADL.

Influence of Neuropsychiatric Behavior on IADL, *N* = 27.

Linear regression analysis revealed that the contribution of neuropsychiatric (NPI) behaviors to IADL was significant, β = .44, R^2 = .194, *p* = .021, accounting for 19% of the variability. Thus NPI scores were included in Phase 2 of the regression analysis.

Influence of neuropsychiatric behaviors on BADL, *n* = 14.

To investigate the contribution of neuropsychiatric (NPI) behaviors to BADL, linear regression analysis revealed that NPI scores did not significantly influence the variability of BADL, β = .022, R^2 = .049, *p* = .445. Thus, neuropsychiatric status was not used in Phase 2 of the regression analysis for BADL.

Summary of Phase 1 analysis.

After investigating for multicollinearity, separate regression analyses of the variables within each of the five predictors (three measures of attention, neuropsychiatric behavior, and global cognition) were assessed for their individual contribution to the variability of either IADL or BADL as the dependent measure. Variables identified by the regression equation that had a significant contribution to IADL or BADL were retained for the second analysis phase. For IADL as the dependent measure, errors on Condition 4 of the TMT, DRS-2, and the NPI showed significant contributions to the variability. For BADL as the dependent measure, none of the measures revealed any contribution.

Phase 2 Regression of Predictors: Global Cognition, Attention, and Neuropsychiatric Behavior on Variability of IADL

Hierarchical regression is the practice of building successive linear regression models, each adding more predictors, to see if they contribute to the dependent variable above and beyond the effect of the initial model (Salthouse, 1991). An order of entry was suggested by the degree of contribution of the variables found to be significant in Phase 1 (attention, global cognition, and neuropsychiatric status). Results are shown in Table 9. The regression of the overall model was found to be significant ($R^2 = .373$, $p = .012$), accounting for 37% of IADL variability. As shown in Table 9, executive attention (TMT condition 4 errors, $p = .008$) contributed more significantly to the variability of IADL than global cognition (DRS-2, $p = .011$) or neuropsychiatric status (NPI, $p = .012$) in this sample of AD patients. Neuropsychiatric symptoms were endorsed by relatively few caregivers and findings should be interpreted with caution.

Phase 2: Regressions of predictors Global Cognition, Attention, and Neuropsychiatric behavior on variability of BADL

None of the tests of global cognition (ADAS-Cog, DRS-2), attention (SDT, Covert Orienting, and D-KEFS TMT Trail Making), or neuropsychiatric function (NPI) significantly contributed to BADL, $p > .05$. Thus, a second phase analysis with BADL as the dependent measure was not conducted.

DISCUSSION

The purpose of this study was to determine the cognitive correlates of different types of daily tasks in patients with AD, with specific emphasis on the role of attention. The results of this study first showed that daily tasks of IADL and BADL are clearly differentiated, and that, for the most part, only IADL was correlated with gross measures of cognition. A second finding was that executive attention performance can account for approximately 25% of IADL variability, suggesting that the degree of attentional dysfunction may be a good predictor of IADL ability. In contrast to IADL, none of the attentional measures, global cognitive measures, or neuropsychiatric measures predicted BADL performance. The dissociation between IADL and BADL and the influence of the high-level attention on functional activity are discussed, with the intent that the information would enable clinicians additional insight into measures that would be best predictive of functional task impairments and caregivers the type of tasks most likely to elicit maladaptive responses early on in the disease process.

The first aim addressed the different performance between IADL and BADL and how they related to measures of global cognition and neuropsychiatric status. In this sample, where participants were newly diagnosed with AD and where most had yet to be medicated, IADL deficits were more prevalent than BADL deficits. This widely documented finding (Derouesne, et al., 2002; K. P. Liu, et al., 2007; Tekin, et al., 2001) illustrates that IADL is a marker of change in the patient that is clearly identifiable to the caregiver. Moreover, impairment in IADL may even precede the diagnosis of AD as has been suggested by the impending criteria for mild cognitive impairment (MCI; Alzheimer Association, 2010). The new criteria for MCI, includes recognized cognitive changes by an informant who is familiar with individual and deficiencies in one or more cognitive domains on testing. Functional criteria of MCI are murky, in that there are expected mild problems in complex tasks of daily but maintenance of independent living and no changes in social or occupational function. Of note is that IADL status in patients with MCI (Desai, Grossberg, & Sheth, 2004) appears to be a critical measure. Kim et al. (1992) compared patients with MCI to normal elderly control participants longitudinally, and found that IADL predicted development of AD in those with MCI. Using a direct measure of observed IADL performance, as opposed to a caregiver survey, Binegar et al. (2009) documented that individuals with MCI and healthy older controls significantly differed in IADL performance. Taken together, these findings suggest IADL may be uniquely sensitive to early presentation of AD. In the current study, BADL impairments were rarely found without accompanying IADL deficits. Thus, with this differentiation between IADL and BADL skills, it was important to characterize what measures were associated with or contributed to each of the two types of functional tasks. The importance of differentiating what discriminates IADL from BADL deficits may be a key feature of discriminating among individuals with symptoms or predicting course of disease.

One possible explanation for the differences in types of impaired activities in AD (IADL with and without BADL deficits) is that worsening cognition accompanies both types of functional decline (Atchison, et al., 2007). However, this has not been consistently found. In the present study, correlational data demonstrated that all screening measures of global cognition (i.e., MMSE, DRS-2, and ADAS-Cog) were associated with IADL, but not BADL performance. Similar findings were observed by

Richardson et al. (1995) where cognitive scores accounted for some of the variance of IADL scores but not BADL in a mixed clinical geriatric population. Also, global scores have to be viewed carefully as individuals with lower socioeconomic and educational status can show early deficits in global cognition while functional status remains stable and unimpaired (Quesada et al., 1997). The dissociation between IADL and BADL has also been found in other dementias, such as Parkinson's disease (Bronnick et al., 2006; Cahn et al., 1998) and vascular dementia (Boyle, Paul, Moser, & Cohen, 2004; Jefferson, Cahn-Weiner, et al., 2006), but, again, the degree to which each are mediated by overall cognitive status is unclear.

Another explanation for the differences in types of impaired activities in AD is that a particular cognitive domain, rather than a global cognitive estimate, explains or accounts for the dissociation between IADL and BADL. More targeted measures of visual perception (Foster, et al., 1999; Glosser, et al., 2002; Jefferson, Barakat, et al., 2006; Liu, et al., 2004; Mortimer, et al., 1992; Parasuraman, et al., 1992) have been found to ber related to IADL. Executive function as tested by Trail Making Test Part B (R.M. Reitan, 1958) has also been shown to be sensitive to IADL performance (Bell-McGinty, Podell, Franzen, Baird, & Williams, 2002). Mitchell et al. (2008) investigating the relationship of all subtests of the D-KEFS with IADL found that only the TMT yielded a significant relationship with IADL. While the current study corroborates this last finding it still leaves open the possibility that both visual and executive tasks are associated to IADL because of some common or shared demand for attentional resources.

As BADL is usually associated with later stages of disease, it was necessary to determine why patients in the current study exhibited basic care deficits. Half the current sample had BADL deficits (as reported by caregivers), yet neither global cognitive scores nor attentional measures predicted BADL performance. Clarification of the relationship between specific cognitive domains influencing performance of BADL has remained largely unexplored (Atchison, et al., 2007; Lim et al., 2006). One explanation may be that underlying influences that impaired BADL in AD are not primarily cognitive in nature. Older patients have pain, general deconditioning, or symptoms secondary to physical disorders (e.g., osteoarthritis, cardiac disease, enuresis) that limit stamina, speed or range of movement. This has the effect of increasing the need for assistance in BADL tasks, such as dressing (problems with fasteners), bathing/showering (inability to get in or out of a bathtub), or getting to the toilet in time. Another reason why BADL impairment was seen at the time of diagnosis may be a reflection of the patient's type of environmental situation. For example, individuals with less demanding jobs (e.g., greeter at a department store compared to a physicist) or individuals living in supported environments (e.g., senior housing or with a spouse) may maintain the appearance of function and not seek or receive a diagnosis until a more advanced stage of disease. As these patients can function in their situation, they appear able to sustain a degree of independence where a diagnosis may be missed, the family may be unaware, or it may be easier to maintain a degree denial of progressive impairments and safety issues. The ability of some individuals to maintain a semblance of independent living despite progressing disease speaks to the need to directly analyze conditions of everyday performance in order to better understand task demands on performer resources.

A third explanation for the IADL–BADL distinction in AD may be the influence of neuropsychiatric behaviors as measured by the NPI. The current study found that worse NPI scores were associated with impaired performance on IADL (*R* = .409), but not BADL. Notably, few caregivers (7 of the 27) endorsed neuropsychiatric deficits. This may be due in part to the sample of individuals who were newly diagnosed and who, in fact, had few psychiatric problems at this stage of disease. Alternatively, caregivers may have been reluctant to admit to the emerging abnormal psychiatric behaviors in loved ones, as these behaviors represent some of the harder symptoms to acknowledge and accept (Rockwood, 2007). Neuropsychiatric behaviors, such as apathy, agitation, mood disturbances, disinhibition, or delusions, have been found in patients with prodromal AD (Apostolova & Cummings, 2008; Hwang, Masterman, Ortiz, Fairbanks, & Cummings, 2004), influence the quality of life in patients with AD, and are a source of significant caregiver burden and distress (Cummings, 1997a). Some neuropsychiatric behavior has been directly associated with worsening IADL performance, but this too has not been consistently supported. Both a correlational (Norton, Malloy, & Salloway, 2001) and a longitudinal study (Green et al., 1999) investigated the relationship between disturbed behavior and functional status in AD, and found that neuropsychiatric behaviors did not impact IADL performance beyond the contribution of worsening cognition. Similarly, Mok et al. (2004) did not find a relationship between NPI behavioral symptoms and IADL performance in patients with AD.

While, the dissociation between IADL and BADL is clearly supported in many studies, the contributing roles of measures of global cognition, specific domains of cognition, or neuropsychiatric behaviors do not fully explain the differentiation. Further research is needed, including more direct observation of function (see Giovannetti, Schwartz, et al., 2007).

The second aim of this study addressed the contribution of attention, global cognition, and neuropsychiatric status to the variability of IADL and separately to the variability of BADL. A two-phase regression analysis was applied. The first-phase linear regression parsed out which variables were individually influential to the variability of IADL. It was hypothesized that higher-order attention mechanisms (such as selective attention and set switch) would be influential in IADL performance, exceeding that of neuropsychiatric status and global cognitive scores. This was supported. While the DRS-2 and NPI showed significant contributions (21% and 19%, respectively) to the variability, the executive attention measure, TMT Condition-4 errors, predicted IADL function and accounted for 25% of the variability. The same analysis was performed using BADL as the dependent variable. Here, we hypothesized that lower-order measures of attention (detecting and orienting) would be related to BADL. This hypothesis was not confirmed as none of the predictor variables showed a significant contribution to the variability of BADL performance. It remains to be determined whether lower-level attention would play a role in BADL in a larger sample with individuals with more advanced disease.

The second phase hierarchical regression addressed the relative contributions of TMT Condition-4, DRS-2 and NPI to the variability of IADL performance. The total model was significant, $p = .012$, and after accounting for the TMT Condition-4 errors, the change in R^2 associated with DRS-2 and NPI was minimal (6.8% and 5.1%, respectively). Thus, as predicted, a measure of higher-order attention played an influential role in the IADL performance of patients with early-stage AD. The particular task of TMT Condition-4 task was likely influential for several reasons. First, the error score of TMT Condition-4 was used in the analysis, not the completion time, as most patients could not complete the task within the time restriction of 240 seconds. Failure to generate a meaningful score that accounted for time prevented any investigation of a speed-accuracy trade-off. Nevertheless, the TMT Condition-4 error score did capture task difficulty, and incorporated all error types including errors of sequencing, errors of set loss, and errors of omission due to the time restriction. Second, this task taxed the ability to succeed using multiple skills. The task requires maintaining a newly-learned rule of alternating numbers and letters, keeping the sequence on hold, scanning the full visual field, searching for the next target item situated among distracters, and doing all of this under a time constraint. This is a high cognitive load task, and the error rate reflected the inability to meet these demands. As such, of the three attention measures used in the current study, TMT Condition-4 best predicted IADL requiring similar types of demands (see Bell-McGinty, et al., 2002).

The current study has confirmed an important relationship between executive attention and IADL. Executive attention is mediated by the frontal brain system (Alexander, Stuss, Picton, Shallice, & Gillingham, 2007). Early frontal system deficits herald the decline in attentional processes in AD (Sarter & Bruno, 2004), signaling structural (MRI), connectivity (Rose, et al., 2007) and cholinergic system decline (Furey, et al., 2008; S. K. Gill, et al., 2007; Sarter, et al., 2005). Executive skills are needed to perform not only TMT Condition-4, but also tasks such as Trails-B (R.M. Reitan, 1958; R. M. Reitan & Wolfson, 1995), or modified Stroop tests (Alexander, et al., 2007), which similarly require the ability to search, select, and attend to multiple simultaneous features. Our data showed that of the eight IADL tasks surveyed, managing money (59% of the total endorsements) and shopping (56 %) were most difficult for patients. These tasks similarly demand attention of multiple simultaneous skills in variable contexts, and their vulnerability lies in the likely underlying frontal disintegration in AD (El Fakhri, et al., 2003; K. A. Johnson & Albert, 2000). Measures that use cognitive and functional tasks similar in contextual and cognitive load may make a stronger ecological bridge among cognitive, functional measures and the status of real life ability.

The clinical value of determining early IADL deterioration and associating it with objective measures of attention, is that IADL is sensitive to disease detection (Kim et al., 2009) and predictive of the progression from MCI to AD (Binegar, et al., 2009). Studies that implicate early executive frontal lobe dysfunction in IADL (Boyle, 2004) support the notion that declining attentional resources underlying impaired IADL is an observable harbinger of brain pathology. Nygård (2003) argued that IADL dysfunction should be included in the diagnostic criteria of MCI although no particular criteria for these activities were defined. The MCI consensus report (Winblad et al., 2004) and the impending new guidelines for MCI diagnosis (Alzheimer Association, 2010) both indicate that complex instrumental activities of daily living may be impaired in early stage dementia: a person may remain independent, but show “mild problems” on more complex tasks. At present, guidelines do not make explicit *what* criteria constitute task complexity or mild performance impairment. The current data may serve to refine these guidelines. For instance, specific tasks, such as handling money and shopping, are high-load for most people and could be the best ones to target. There may be increased difficulties for those individuals who never managed their money, paid bills, or did the shopping. Thus, another possibility would be to individualize tasks categorized as complex or IADL. Given the variability of life experiences, education attainment, and environmental contexts, a series of possible daily activity tasks could be ranked as a function of cognitive demand for each individual. If the top ranked tasks represent high-load skills for a particular individual and correlate with specific measures of executive attention, then such tasks could suggest targeted IADLs to follow over time. In this way, neuropsychological assessment could speak more directly to real life behavioral outcomes.

The current study supported the notion that executive attention contributes to the success of many of the IADL tasks. However, the current findings did not clarify whether cognitive impairment or non-cognitive factors underlie BADL deficits. We had posited that levels of attentional demand could help classify tasks as simple or complex, where increased demands characterize complex tasks (IADL) and lower demands characterize 'simple' tasks (BADL). The data only supported the first hypothesis: not only did executive attention predict IADL performance, but importantly, detection and orientation did not.

IADL tasks are typically seen as complex tasks of daily life that support independence. However, the current methodology did not allow for another important element of measuring the complexity of IADL activity, namely, the context in which the task is performed. Future research needs to address this. In line with Gentile (2000), 'complexity' is not just based on the task itself, but the context in which the task is performed, and both can alter the attentional demand. Thus, unfamiliar, distracting, or novel environments place increased demands on attentional resources, while otherwise familiar, routine environments do not. The exact same task can be effortful in the former situation, but automatic in the latter. For example, a patient may become agitated and require assistance to shower in an unfamiliar hotel, but be able to shower independently at home. As greater effort is believed to increase the demand for cholinergic availability (Kozak, Bruno, & Sarter, 2006), patients with AD who are cholinergic depleted, are disadvantaged whether due to the complexity of the task itself or the novel context in which it is performed. Therefore, any future metric or assessment of ‘task-complexity’ has to incorporate or control for both of these elements.

This study showed that some impairment in attentional processes parallel the declines in daily living skills in AD. The clinical value of this finding is that it may offer clinicians and caregivers insight into why an individual patient struggles with certain tasks and not others, or why a patient suddenly has a maladaptive response to an otherwise familiar activity. Clinicians need to integrate measures of executive attention as important predictors of functional decline. As ADL performance is used to make critical decisions such as whether independent living can be maintained, whether supervision is needed, or whether assisted-living becomes indispensible, effective predictors are invaluable. Educating caregivers about the concept of executive attention may inform their responses when coping with dysfunctional behaviors, and promote discussion of activity adaptations or types of supervision that may be necessary.

There were several limitations to this study which deserve mention. This study tested many variables using a limited sample of patients with AD and their caregivers. Thus, non-findings could have due to a limited power. Future research with a larger sample and broader range of disease progression is needed to confirm the associations and dissociations observed in this study. The sample was relatively homogenous in terms of geographical, racial and socio-economic status, and the average educational level was high. These factors limit generalizability and may not reflect the full population of patients with AD. Further, the lack of control group leaves open the question of how the relationship among global cognitive, attention processes and daily tasks differ in AD from those in a normal group of the same age.

While the modified Lawton-Brody scale employed to collect IADL and BADL information (Giovannetti, et al., 2002; Lawton & Brody, 1969) is widely used and measures some degree of qualitative information, it is limited in that its scoring is not sensitive to gender, culturally-based task preferences, or specific performance impairments. Moreover, it does not capture performance under variable conditions (Gentile, 2000), such as using the telephone in one's home versus using a telephone in a public place. Lastly, this information was provided by the caregiver. Although measures such as the NPI allow for and even directly question the degree of caregiver distress about a particular symptom, the acquisition of the ADL information used in this study was always filtered through the caregiver experience, his or her emotional status, and what he or she felt comfortable revealing to the interviewer. While the majority of caregiver surveys in AD research rely on the assumption of valid accounts of patients' performance, the validity of the actual performance has to remain questioned. Future research in understanding the interaction of ADL and attentional influences will therefore need to accommodate these limitations.

Conclusion

The current study supports previous findings that IADL impairments are primary deficits at the time of diagnosis of AD. As hypothesized and substantiated by regression analysis, a measure of executive attention best predicted the variable daily demands of IADL over and above global measures of cognition and neuropsychiatric status. These findings suggest that cognitive load, tapped by those measures of higher executive attention, are more sensitive to IADL and may better inform clinicians and caregivers of potential difficulty with daily tasks faced by patients with early AD.

Appendix

Modified Activities of Daily Living Scales: Instrumental ADL (IADL Items A-H) Physical Self Maintenance scales (PSMS Items L-P)

Scoring and procedure for interview: Orient the interviewee/caregiver with examiner's statement in the box below. For all questions insert the appropriate term for '*the patient'* when you address the caregiver. For instance, Does *the patient* shop, should be asked as "Does your mother shop?" Read the lead question to item A in bold (i.e., Does *the patient*….). If the caregiver answers 'YES", proceed to the lead question in item B. If the caregiver answers 'NO" to item A, continue to response 1, rephrasing to get information about lower levels of function in that task. Circle the score closest to the description being offered by the caregiver

Examiner:

> "This group of question will be asking how much *the patient* is doing for themselves currently in their daily activities. Please answer based on your most recent experiences and observations

I. INSTRUMENTAL ACTIVITIES OF DAILY LIVING SCALE

A. Ability to use the phone

- **0.** **Does *the patient* initiate operating the phone, looking up and dialing numbers?**
- 1. Answers telephone, dial well known numbers only. Does not look up or dial less frequently used numbers without assistance or calling operator/ directory.
- 2. Does not use telephone at all.

B. Shopping

- **0** **Does *the patient* take care of all his/her shopping needs independently? This includes independently going to the store, selecting, paying for items and bringing them home**?
- 1. Shops independently for small purchases.
- 2. Completely unable to shop alone.

C. Food preparation

- **0** **Does *the patient* plan, prepare and serve adequate meals independently? This includes managing the stove without help.**
- 1. Prepares adequate meals if supplied with ingredients; heats, serves and prepares meals but does not maintain an adequate diet.
- 2. Need to have meals prepared and / or served.

D. Housekeeping

- **0** **Does *the patient* maintain the house alone (vacuum, wash floors) or with occasional assistance?**
- 1. Perform light daily tasks, i.e. dishwashing, bed making, but cannot maintain acceptable level of cleanliness.
- 2 Does not participate in housekeeping tasks.

E. Laundry

- **0** **Do they do their personal laundry completely independently?**
- 1. Launders small items by hand, needs help with major laundry.
- 2. All laundry is done by others.

F. Mode of transportation

- **0** **Does *the patient* travel independently on public transportation, taxi, or drive?**
- 1. Need others to make arrangements for place and time of pick-up; relied on others to keep track of his/her destination.
- 2. Travels only when accompanied by another.

G. Responsibility for medications

- **0** **Does *the patient* take medications independently in correct dosages at the correct time?**
- 1 Takes responsibility of medication if it is prepared in advance in separate dosages.
- 2 Is not capable of dispensing own medications.

H. Ability to handle finances

0 **Is *the patient* able to manage financial matters independently? This includes budgeting, writing checks, paying rent, collecting and keeping track of their income, etc.**
1. Manages day-to-day purchases but needs help with banking, major purchases etc.
2. Incapable of handling money.

II Physical Self-Maintenance Scale

I. Toilet

0 **Are they able to care for themselves at the toilet completely? No incontinence?**
1. Needs to be reminded, needs help cleaning self or redressing, or has rare (weekly at most) accidents.
2. Soiling or wetting more than once a week or total incontinence.

J. Feeding

0 **Are they able to eat without any assistance?**
1. Eats with mild to moderate assistance at mealtimes and /or with special preparation of food or help in clean up.
2. Does not feed self at all.

K. Dressing

0 **Do they dress, undress and select appropriate clothes from the closet without help?**
1. Needs minor to moderate assistance in dressing and or in selection of clothes.
2. Unable to dress self.

L. Hair grooming

0 **Do they wash, comb, brush hair independently?**
1. Needs moderate and regular assistance in grooming and does not wash/ comb hair unless told.
2. Caregiver must wash and comb hair.

M. Dental hygiene

0 **Does *the patient* brush their teeth independently without having to be reminded?**
1. Needs moderate and regular supervision or assistance in brushing teeth (needs to be reminded, needs set up or help gathering correct objects etc)
2. Cannot brush teeth without assistance.

N. Nail care

0 **Does *the patient* clean and clip his/ her nails regularly without assistance?**
1. Must be reminded to care for nails or requires some assistance in cutting nails.
2. Relies on others for total nail grooming care.

O. Bathing

0 **Does the *patient* bathe or shower him/ her self without help?**
1. Needs supervision or assistance in bathing.
2. Does not wash self.

P. Physical ambulation

0 **Can *the patient* <u>independently</u> walk about the grounds, city, or residence at least a one-block distance?**
1. Ambulation with the assistance of : (*circle one)*: a) cane b) walker c) wheelchair
   a. Gets in and out chair without help b. Needs help getting in and out of chair.
2. Sits unsupported in wheelchair or chair but cannot propel self, unable to ambulate.

Modified from : Giovannetti, Libon, Buxbaum, & Schwartz, 2002. Naturalistic action impairments in dementia. *Neuropsychologia, 40*, 1220-1232.)

Table 1.
A Representation of Gentile's Taxonomy of Environmental Conditions. Four Skill Conditions Based on Environmental Contexts (Stationary vs. in Motion), and the Absence or Presence of Intertrial Variability

		Intertrial Variability	
		Present	Absent
Environmental Context	In Motion	Environments in motion that vary from trial to trial (e.g., supermarket shopping).	Environments in motion that do not vary from trial to trial (e.g., escalator).
	Stationary	Environment where features are stationary, but fluctuate with each attempt (e.g., change for purchases).	Environment where features are stationary and objects do not change each time performed (e.g., showering at home).

Note. From the chapter: Skill Acquisition by A.M. Gentile in *Movement Science: Foundations for Physical Therapy in Rehabilitation - Second Edition* (p125), by J. Carr and R. Shepherd, 2000, Austin, TX: PRO-ED. Copyright 2000 by PRO-ED. Reprinted [or Adapted] with permission.

Table 2.

Descriptive Characteristics and Performance on Variables of Total Sample and When Split by Presence or Absence of BADL Deficit

	Total Sample (*N* = 27)		Without BADL Deficit (*n* = 13)		With BADL Deficit (*n* = 14)	
	M (*SD)*	Min -Max	*M* (*SD)*	Min -Max	*M* (*SD)*	Min -Max
Age	79.41 (6.97)	58.00 - 88.00	77.23 (8.93)	58.00 - 87.00	81.43 (3.78)	75.00 - 88.00
Years of education	14.11 (3.91)	8.00 - 22.00	14.00 (3.67)	9.00 - 22.00	14.21 (4.25)	8.00 - 22.00
MMSE (Max 30)	24.00 (3.78)	11.00 - 29.00	23.69 (4.37)	11.00 - 29.00	24.29 (3.29)	18.00 - 28.00
DRS-2 (Max 144)	121.85(10.17)	99.00 - 136.00	122.69 (10.21)	99.00 - 136.00	121.07(10.44)	101.00 -134.00
ADAS-Cog (Max 0)*	15.84 (6.28)	7.97 - 31.33	15.15 (7.16)	7.97 - 31.33	16.48 (5.53)	9.00 - 28.34
NPI (Max 144)*	16.59 (12.98)	0.00 - 59.00	12.92 (8.74)	0.00 - 26.00	20.00 (15.50)	3.00 – 59.00
IADL Max = 16	5.26 (3.69)	0.00 -13.00	4.15 (2.47)	1.00 -10.00	6.28 (4.37)	1.00- 13.00
BADL Max = 16	1.41 (1.76)	0.00 - 5.00	0.00	0.00	2.71 (1.54)	1.00- 5.00

Table 3.

Spearman Correlation Coefficients (r_s) Among Measures of Disease Severity, IADL and BADL, N = 27

	Statistic					
Measure	1	2	3	4	5	6
1.MMSE (Max 30)	1.00	.750**	-.629**	-.095	-.417*	-.082
2.DRS-2 (Max 144)		1.00	-.474*	-.318	-.461*	-.244
3.ADAS- Cog (Max 70)			1.00	-.049	.312	.187
4.NPI (Max 144)				1.00	.409*	.268
5.IADL (Max 16)					1.00	.448*
6. BADL (Max 16)						1.00

*Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.001 level (2-tailed).

Table 4.

Spearman Correlation Coefficients (r_s) Among Measures of Disease Severity, IADL and BADL in Those With BADL Deficits, *n* = 14

	Statistic					
Measure	1	2	3	4	5	6
1.MMSE (Max 30)	1.00	.714**	-.536**	-.125	-.539*	-.404
2.DRS-2 (Max 144)		1.00	-.399	-.278	-.692*	-.537*
3.ADAS- Cog (Max 70)			1.00	-.189	.415	.086
4.NPI (Max 144)				1.00	.442	.313
5.IADL (Max 16)					1.00	.503
6. BADL (Max 16)						1.00

*Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.001 level (2-tailed).

Table 5.

Mean, Standard Deviation (SD), Minimum and Maximum Reaction Time of All Attention Measures, N ***= 27***

Measure	*M (SD)*	Min – Max
Trail Making Subtest: D-KEFS		
(RT in seconds)		
Completion time Condition (1): Scan Numbers +Letters (max150 sec)	40.07 (20.40)	18.00 - 118.00
Completion time: Condition (2): Sequence numbers(max150 sec)	77.37 (34.36)	28.00 - 150.00
Completion time: Condition (3): Sequence letters (max150 sec)	97.19 (40.77)	26.00 - 150.00
Completion time: Condition (4): Switch task (max 240 sec)	206.59 (47.25)	88.00 - 240.00
(Errors)		
Total errors averaged on Conditions 2 + 3	0.69 (1.62)	0.00 - 7.00
Total errors Condition 4	0.04 (9.46)	0.00 - 34.00
Serial Detection Test (SDT): (*N* = 26) *(RT in Milliseconds)*		
SOA1 administration 1 & 2	489.50 (149.66)	273.25 - 881.75
SOA2 across administration 1& 2	425.41 (134.59)	238.00 - 754.25
SOA3-6 administration 1 & 2	348.48 (95.41)	227.38 - 566.94
Covert orienting (CV) *(RT in milliseconds)*		
Valid covert condition	426.81 (85.20)	328.00 - 687.50
Neutral covert condition	459.81 (93.00)	327.00 - 712.00
Invalid covert condition	501.48 (117.45)	335.50 - 856.50
Benefit of cue (neutral– valid)	34.04 (36.20)	-33.69 - 140.73
Cost of invalid cue (neutral–invalid)	-34.08 (34.73)	-121.09 - 46.81

Table 6.

Spearman Correlation for Conditions of the TMT, Testing for Multicollinearity, N = 27
Cells in Bold Font Indicate Those Conditions Retained for Regression Analysis

TMT Condition	1	2	3	4	5	6
1.Condition 1 Completion time	1.00	.788**	.765**	**.259**	.435*	.405*
2. Condition 2 Completion time		1.00	.820**	**.342**	.571**	.405
3. Condition 3 Completion time			1.00	.524**	.679**	.679**
4. Condition 4 Completion time				1.00	**.284**	.695**
5. Mean Errors Conditions 2+3					1.00	**.325**
6. Condition 4 All Error Types						1.00

* Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).

Table 7.

Spearman Correlation Coefficient (r_S) Among Conditions of the DKEF, SDT and CV, N = 27 *Cells in Bold Font Indicate Those Conditions Retained for Regression Analysis*

Measure	1	2	3	4	5	RT SDT SOA 1	RT SDT SOA 2	RT SDT SOA 3-6
D-KEFS *(RT in seconds)*								
1. Condition 1 Completion time	1.00	.788	**.259**	.435	.405*	.483*	.560**	.525**
2. Condition 2 Completion time		1.00	**.342**	.571**	.405*	.392*	.410*	.447*
3. Condition 4 Completion time			1.00	**.284**	.695**	**.237**	**.298**	**308**
4. Mean Errors Conditions 2+33				1.00	**.325**	**.343**	**.308**	**.191**
5. Condition 4 All Error Types	.				1.00	**.182**	**.223**	**.115**
(RT in ms)								
RT Valid cues	.440*	.469*	**.320**	**.278**	**.184**	.452*	.461*	.590**
RT Invalid cues	.567**	.606**	**.299**	**.263**	**.258**	.503**	.544**	.666**
RT Neutral cues	.511**	.548**	**.283**	**.340**	**.220**	.512**	.521**	.631**
RT Benefit = neutral - valid	-.412*	-.395*	**-.154**	-.045	**-.191**	**-.167**	**-.256**	**-.343**
RT Cost = neutral - invalid	.429*	.392*	**.097**	**.351**	**.259**	**.354**	**.321**	**.308**

*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01 level (2-tailed)

Table 8a.

Phase I Regression Table for Attention Tasks With IADL as Dependent Variable, N = 27

Measures	β	F	R^2	p
	IADL			
DEKFS				
1 completion time	.018	.245	.010	.625
2 completion time	.005	.052	.002	.821
4 completion time	.021	2.01	.075	.168
5 completion time	.029	1.28	.049	.268
2+3 mean error	.400	.794	.031	.381
4 total error	.194	8.21	.247	.008**
SDT				
SOA 1	.005	.908	.035	.350
SOA 2	.005	.923	.036	.346
SOA 3-6	.001	.012	.000	.916
Covert				
Cost	.019	.991	.038	.329
Benefit	.020	.681	.026	.417

*p <.05. ** p<.01

Table 8b.

Phase I Regression Table for Attention Tasks With BADL as Dependent Variable, n =14

Measures	β	F	R^2	p
	BADL			
TMT Condition:				
1 completion time	.022	.637	.050	.440
2 completion time	.005	.173	.014	.684
4 completion time	.009	.684	.051	.436
5 completion time	.010	.551	.044	.472
2+3 mean error	.371	1.43	.032	.255
4 total error	.075	3.03	.202	.107
SDT				
SOA 1	.004	2.81	.101	.106
SOA 2	.003	.070	1.89	.181
SOA 3-6	.004	.999	.038	.327
Covert				
Cost	.066	.108	.004	.745
Benefit	.007	.354	.014	.557

*p <.05 ** p<.01

Table 9.
Phase Two Hierarchical Regression: IADL as Dependent Variable, $N = 27$

	IADL			
Predictor	R^2	ΔR^2	F	p
Errors TMT Condition 4	.247		8.21	.008
DRS-2	.315	.068	5.5	.011
NPI	.373	.058	4.60	.012

Note. Change in R^2 (ΔR^2) is associated with adding a variable to the regression equation. The F value evaluates the R^2 for the first variable entered or the change in R^2 associated with the addition of the second or third variable. For example, errors on TMT condition 4 was associated with 25% of the variability of IADL, DRS-2 with 32%, and NPI with 37% when added to the model. The ΔR^2 associated with DRS-2 is 6.8%; after accounting for both TMT and DRS-2 the ΔR^2 related to the addition of NPI 5.8% (Salthouse, 1991).

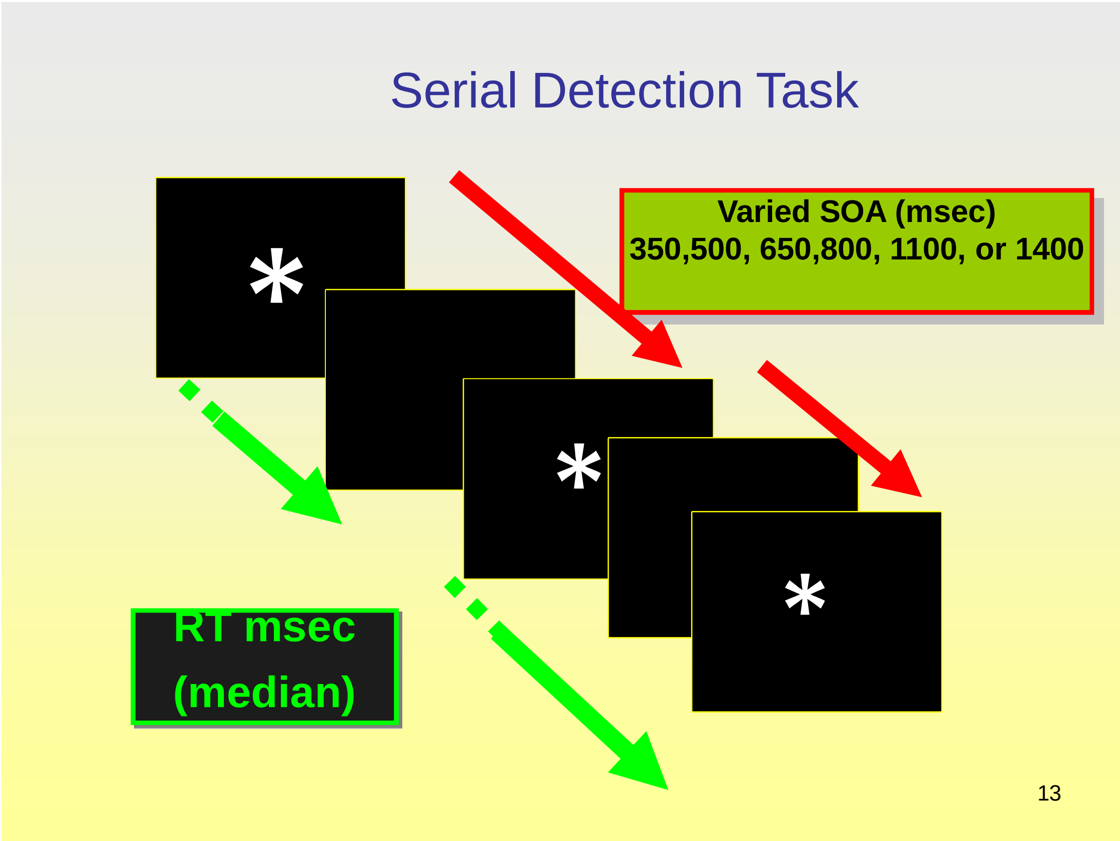

Figure 1.
Diagram of serial detection task showing varied SOA. Participant responds by pushing a button when viewing the asterisk.

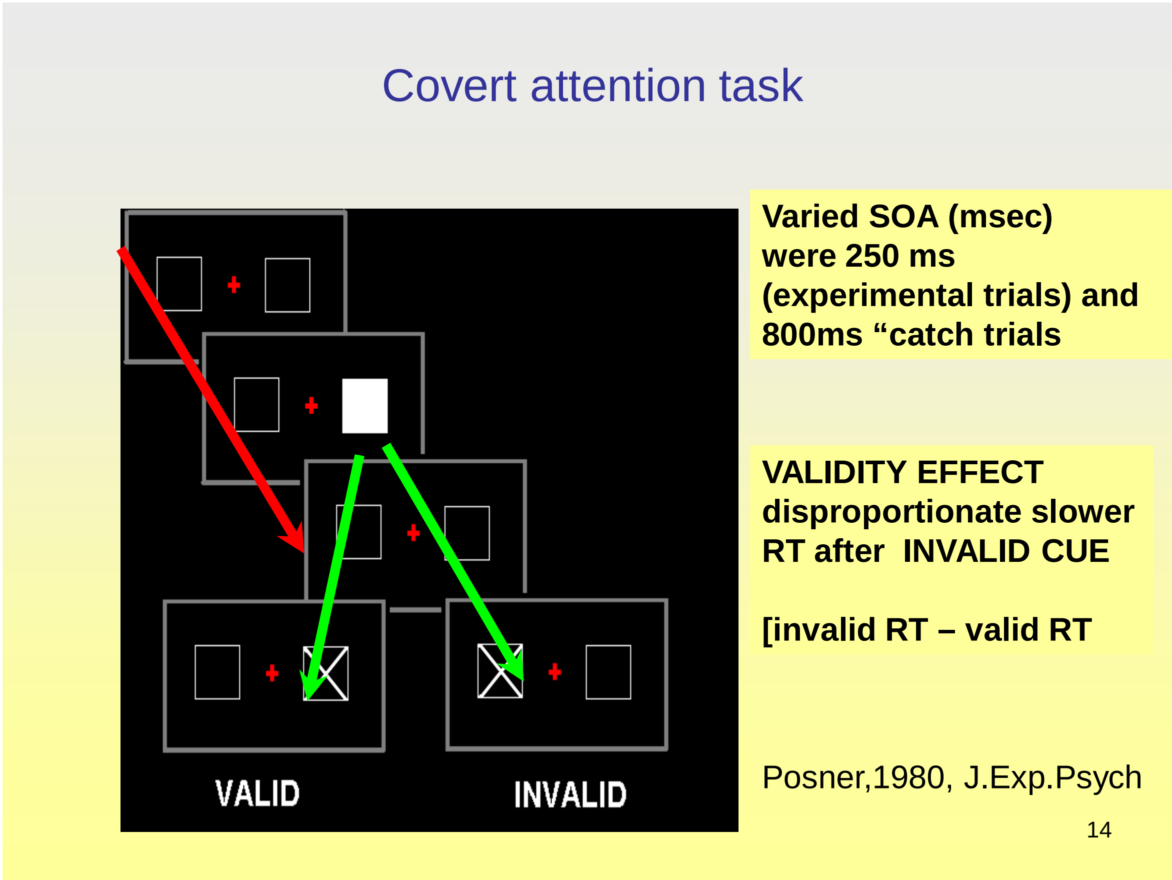

Figure 2.
Diagram of covert attention task showing valid and invalid cue conditions. Participant responds by pushing a button when “X” appears.

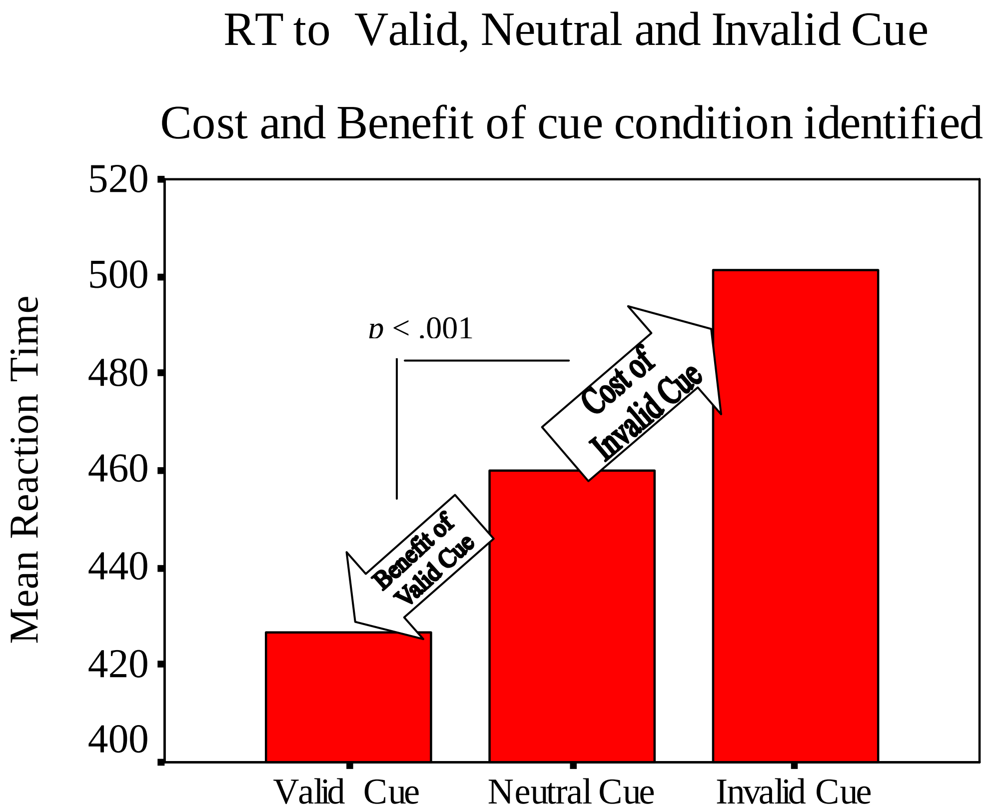

Figure 3.
Representation of cue Costs and Benefits relative RT (ms) to Valid, Neutral and Invalid cue conditions, $N = 27$.

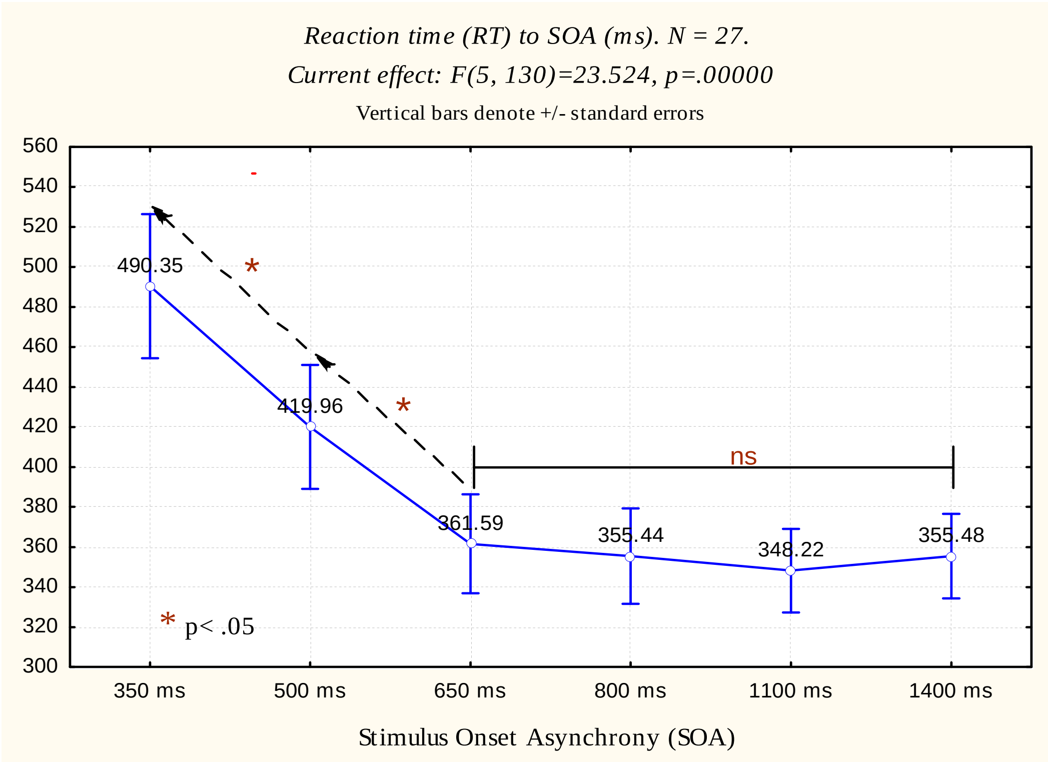

Figure 4.
Graph of median reaction time (ms) for stimulus onset asynchrony (SOA) intervals.

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