

Object Perception Impairments Predict Instrumental Activities of Daily Living Dependence in Alzheimer's Disease

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This study examined the contribution of object perception and spatial localization to functional dependence among Alzheimer's disease (AD) patients. Forty patients with probable AD completed measures assessing verbal recognition memory, working memory, object perception, spatial localization, semantic knowledge, and global cognition. Primary caregivers completed a measure of activities of daily living (ADLs) that included instrumental and basic self-care subscales (i.e., IADLs and BADLs, respectively). Stepwise multiple regressions revealed that global cognition accounted for significant portions of variance among the ADL total, IADL, and BADL scores. However, when global cognition was removed from the model, object perception was the only significant cognitive predictor of the ADL total and IADL subscale scores, accounting for 18.5% and 19.3% of the variance, respectively. When considering multiple cognitive components simultaneously, object perception and the integrity of the inferotemporal cortex is important in the completion of functional abilities in general and IADLs in particular among AD patients.

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Introduction

Cognitive impairment is the hallmark feature of Alzheimer's disease (AD (McKhann et al., 1984)) and is associated with numerous cognitive changes. Multiple diagnostic criteria (e.g., DSM-IV, ICD-10, NINCDS-ADRDA) require that these cognitive changes contribute to significant functional decline for the diagnosis of AD. Though dementia severity has been shown to be a robust predictor of functional decline among patients with AD, its inclusion in the examination of the association between specific cognitive components and functional impairment obscures the identification of individual cognitive determinants. It is important to understand specific cognitive components that underlie functional decline in patients with dementia because these associations remain unclear. Identifying correlates, and ideally, predictors, of functional decline will allow clinicians to make determinations regarding patients' personal independence and safety. Such information would be extremely useful in clinical cases where patients lack direct care providers.

Executive function (Boyle et al., 2003a) and memory (Teri, Borson, Kiyak, & Yamagishi, 1989) have been shown to have specific relationships to ADLs in AD. However, some previous studies are limited to small sample sizes and correlational data that do not account for possible relationships with other cognitive domains (Mahurin, DeBettignies, & Pirozzolo, 1991). Additional investigation of other relevant cognitive components is warranted, and one cognitive component that has been implicated in AD, but not well investigated with respect to functional dependence, is visuo-perceptual functioning.

Histological evidence has documented high densities of neuropathology associated with AD in the inferotemporal and occipito-parietal cortices. These areas correspond to the ventral visual stream involved in shape perception and the dorsal visual stream involved in spatial localization, respectively (Arnold, Hyman, Flory, Damasio, & Van Hoesen, 1991; Brun & Englund, 1981; Corkin et al., 1991; Hof, Bouras, Constantinidis, & Morrison, 1989; Hof & Morrison, 1990; Lewis, Campbell, Terry, & Morrison, 1987; Pearson, Esiri, Hiorns, Wilcock, & Powell, 1985). The density of neurofibrillary tangles is twenty times greater in the visual association cortex (i.e., Brodmann area 18) as compared to primary visual cortex (i.e., Brodmann area 17) and doubles in higher-level visual association cortex (i.e., Brodmann area 20, inferotemporal cortex; (Lewis et al., 1987)).

Consistent with the neuropathological distribution, behavioral data have shown higher-level visual processing impairments among patients with AD (Kurylo, Corkin, Rizzo, & Growdon, 1996; Mendez, Mendez, Martin, Smyth, & Whitehouse, 1990). In particular, impairments have been reported in object recognition (also referred to as *object perception*), mediated by the inferotemporal cortex or the ventral visual stream (Binetti et al., 1998; Binetti, Cappa, Magni, Bianchetti, & Trabucchi, 1996; Kurylo et al., 1996; Mendez et al., 1990) and spatial localization, mediated by the occipito-parietal cortex or dorsal visual stream (Binetti et al., 1998; Binetti et al., 1996; Butter, Trobe, Foster, & Berent, 1996; Hof, Bouras, Constantinidis, & Morrison, 1990; Kurylo et al., 1996; Levine, Lee, & Fisher, 1993; Mendez et al., 1990). When assessed concurrently, behavioral evidence implicates greater impairment of object recognition and form discrimination than spatial processing (Kurylo et al., 1996), even in the mild disease stage (Binetti et al., 1998).

Based on these histopathological and corresponding behavioral data, it is not surprising that such visual deficits contribute to visually-mediated cognitive functions. Such a link has been reported by Glosser and colleagues (2001) who found that difficulty

processing the visual characteristics of letters and objects was associated with reading impairments in AD. In contrast, performance on lexical-semantic measures (e.g., naming, rapid word generation) was not associated with reading impairments. Thus, impaired higher-level visual processing may contribute to cognitive difficulties found in patients with AD.

In light of neuropathological changes in the higher-level visual streams, the well-established perceptual deficits, and the association between higher-level visual processes and other cognitive performances, visuo-perceptual deficits may also contribute to functional impairments in AD. Indeed, functional status among patients with AD has been assessed simultaneously with abilities mediated by the higher-level visual streams. Mahurin et al. (1991) reported that an Instrumental Activities of Daily Living measure significantly correlated with the Visual Discrimination Test (Wepman, Morency, & Seidi, 1975), suggesting some association between higher-level visual processes and instrumental everyday activities. Willis and colleagues (1998) assessed a group of patients with AD and found that the Block Design subtest from the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981) was significantly correlated with a performance-based functional measure, suggesting that visuospatial constructional abilities are associated with everyday functioning among patients with AD.

These studies preliminarily suggest that there is an association between functional status and visuospatial performances among AD samples (Mahurin et al., 1991; Willis et al., 1998); however, conclusions are limited by correlational design, which does not account for the impact of other important cognitive domains (e.g., executive function). Conclusions are similarly limited by the utilization of measures confounded by executive demands, as previous research has found that some visuospatial measures, such as those used by Willis and colleagues (1998), are strongly associated with executive functioning (Libon et al., 1994). Therefore, studies assessing visual-spatial and perceptual functions that utilize measures loaded with 'executive' control demands may actually reflect associations with executive versus perceptual dysfunction.

The purpose of the present study was two-fold:

1. To demonstrate that global cognition is a robust predictor of functional decline among patients with AD, yet its inclusion in the examination of the association between specific cognitive components and functional impairment may obscure the identification of individual cognitive determinants
2. To assess the relative contribution of higher-level perceptual processes to ADL functions in a sample of patients with AD. Object perception and spatial localization were assessed simultaneously with those cognitive domains that have strong associations with functional status (i.e., declarative memory, executive function, semantic knowledge).

Methods

Participants

Participants consisted of 40 individuals diagnosed with probable AD according to NINCDS-ADRDA criteria (McKhann et al., 1984) by experienced neurologists at both the University of Pennsylvania Medical Center in Philadelphia, Pennsylvania and the Miriam

Hospital, a Brown Medical School affiliated teaching hospital in Providence, Rhode Island. All patients underwent extensive medical and neurodiagnostic evaluations to ensure that their symptoms were not attributable to any cause other than a diagnosis of probable AD. Additional inclusion criteria required that all participants be native English speakers with at least an 8th grade level of education and have normal corrected hearing and vision at the time of assessment. Individuals with pre-existing learning problems or major psychiatric histories (e.g., schizophrenia) were excluded from participation. At the time of testing, participants were screened for symptoms of depression using the Geriatric Depression Scale (GDS), a validated 30-item, self-report inventory developed specifically for use with older adults (Olin, Schneider, Eaton, Zemansky, & Pollock, 1992; Yesavage et al., 1983). All participants scored in the normal range (i.e., <11).

To be included in the present study, each patient had to have a reliable informant capable of answering questions about the patient's functional activities. A reliable informant was operationally defined as a knowledgeable individual who spends a minimum of 3 days per week with the patient. The informant was not required to be a native English speaker, but was required to have an 8th grade level of education to ensure reading abilities were sufficient to understand the informant questionnaires.

The AD Sample had a mean age of 75.68 years ($SD = 7.89$) and a mean education of 13.85 years ($SD = 2.97$). The range of dementia severity was robust, with Mini-Mental State Examination (MMSE (Folstein, Folstein, & McHugh, 1975)) scores between 8 and 30. The mean MMSE score was 20.85 ($SD = 5.04$).

Functional Measures

Activities of Daily Living Questionnaire. The Instrumental Activities of Daily Living & Physical Self-Maintenance Scale (IADL-PSMS (Lawton & Brody, 1969)) was administered to primary caregivers who judged participants' performance of basic self-care activities (i.e., BADLs, including feeding, dressing, grooming, bathing, toileting, ambulating) and more complex instrumental activities that facilitate independence (i.e., IADLs, including traveling, management of finances, telephone use, meal preparation, housekeeping, laundry, shopping, and medication maintenance). The original IADL-PSMS permitted only dichotomous choices for everyday functions (i.e., intact vs. impaired). However, the modified version used in the present study allows for gradations in performance ranging from total dependence to complete independence. Summary scores can be calculated based on basic self care functions (i.e., BADLs, 5 items, scores range 0–20), instrumental activities (i.e., IADLs, 8 items, scores range 0–24), or a combination of both reflecting global functional status (ADL total scores range 0–44). Higher scores denote more intact functional competencies. In those cases where a particular item did not apply to a participant, a pro-rated score was calculated to exclude impertinent items, while preserving the overall estimate of functional status.

Cognitive Measures

The cognitive protocol was developed to include measures sensitive to specific cognitive components with previously demonstrated relationships to functional abilities. Cognitive measures assessing verbal expression (e.g., naming, verbal fluency) were not included because of insufficient research to justify their inclusion (Giovannetti, Libon, Buxbaum, & Schwartz, 2002; Glosser et al., 2002). The specific cognitive measures were selected based on their anatomic specificity (Baddeley, Della Sala, Gray, Papagno, & Spinnler, 1997;

D'Esposito et al., 1995; Koehler, Kapur, & Winocur, 1995; Stark & Squire, 2000), and efforts were made to minimize verbal, perceptual, and executive demands when possible.

MMSE (Folstein et al., 1975). The MMSE is a valid measure of dementia severity. It provides a brief screen of orientation, registration, attention, working memory, recall, language, and construction. Total scores on this measure range from 0–30, with lower scores reflecting more compromised cognitive functioning.

Warrington's Recognition Memory Test (RMT (Warrington, 1984)). Verbal recognition memory was assessed with the word subtest of the RMT. Participants were shown a series of target words on stimulus cards consisting of 50 one-syllable, high-frequency words (e.g., sink) at a rate of one item every three seconds. Immediately following completion of the presentation of all 50 stimuli, a forced-choice recognition task was used in which 50 pairs of words (i.e., a target and a foil) were presented. The participant was asked to identify the target word from the original list. The number of correctly identified words (i.e., 0 to 50) served as the total score with lower scores reflecting greater impairment.

Pencil-and-Paper Version of the Dual-Task (Baddeley et al., 1997; Greene, Hodges, & Baddeley, 1995). Executive control functions were assessed via a dual task measure of the central executive of Baddeley's working memory model (1986). The dual task consists of a paper-and-pencil measure that combines the task of crossing out a chain of boxes with the task of repeating digit spans provided by the experimenter during a two-minute trial. Consistent with other decrement-based dual task paradigms, the following formula yields a total score sensitive to any decrement in either task while performing the two tasks concurrently:

$$mu = [1 - (pm + pt)/2 \times 100]$$

where *pm* is the proportional decrement in span under the dual-task condition and *pt* is the proportional loss in tracking score.

Birmingham Object Recognition Battery (BORB (Riddoch & Humphreys, 1997)). Object perception was assessed via two subtests from the Birmingham Object Recognition Battery (BORB (Riddoch & Humphreys, 1997)). Each of the BORB subtests consists of 25 trials of a matching-to-sample task in which the participant was shown three line drawings. The drawing at the top of the page represents the target object with two drawings located below the target. One of these drawings is a different view of the target object, while the third drawing is a foil object that is visually similar to the target. The participant was asked to point to the drawing that showed the target object in a different view. The first set of 25 items constituted the 'Minimal Features' subtest in which the differing view reflects the target object rotated within plane, which reduces the saliency of the primary distinctive features (Humphreys & Riddoch, 1984). The second set of 25 items consisted of the 'Foreshortened View' subtest in which the target object is rotated in depth so that the principal axis was foreshortened (Humphreys & Riddoch, 1984). The score for this measure equaled the sum of correct responses achieved across both subtests (i.e., 'Foreshortened View' and 'Minimal-Features'; range 0–50), with higher scores denoting better performance.

Spatial Dot Location Test (SDLT (Warrington & James, 1988)). Spatial localization was assessed via a modification (Glosser et al., 2001; Glosser et al., 2002) of Warrington and James' (1988) dot position task. The SDLT involves the presentation of a 4 × 6 inch rectangle with a small black target dot located inside. This stimulus remains in view while the participant is asked to reproduce the target dot in the exact same location within a similar 4 × 6 inch rectangle that is blank. The distance between the target dot and the participant's response dot was measured in millimeters and averaged across all 25 trials. Higher scores indicate worse performance.

Pyramids & Palm Trees (PPT (Howard & Patterson, 1992)). Previous research has utilized the PPT (Howard & Patterson, 1992) as a means of assessing semantic knowledge (Hodges & Patterson, 1995; Kremin, Beauchamp, & Perrier, 1994; Mummery et al., 1999; Van der Hurk & Hodges, 1995). The PPT consists of two subtests (i.e., pictures and words) that are methodologically identical in administration. For the picture subtest there are 52 trials in which participants are shown a target line drawing at the top and asked to select one of two line drawings at the bottom that best matches the target. The word version is identical in format, but words are substituted for pictures. The total score for this measure ranges from 0–104, with lower scores denoting more impaired semantic knowledge.

Procedures

The appropriate Institutional Review Boards approved the proposed protocol. After providing informed consent, participants were administered the cognitive protocol during a single session lasting approximately one to two hours. At this time, informants also completed the ADL measure.

The protocol began with collection of basic demographic data, followed by the GDS and the MMSE. The remainder of the cognitive protocol, including the Dual Task, PPT, BORB, SDLT, and RMT, was administered in a counterbalanced fashion to avoid confound secondary to order-effects. Similarly, for the PPT, the picture and word subtests were counterbalanced across administration to avoid order effects.

All but two participants completed the testing session without incident. One participant was unable to tolerate the entire research protocol in one testing session, so two sessions were utilized to reduce the impact of fatigue on test performance. A second participant was able to participate well in most tasks but expressed frustration during memory testing, and the task was discontinued. Thus, for analyses involving the RMT, 39 participants were included.

Results

Descriptive Statistics

Descriptive statistics, including means and standard deviations, were calculated for all participant demographic variables (e.g., age, education level, disease duration; Table 1) and cognitive and functional performances (Table 2). A one-way analysis of variance revealed no significant differences between participants enrolled through the Rhode Island or Pennsylvania recruitment sites with respect to age, education level, or disease duration.

Table 1
Participant demographic statistics

Demographic variable	Patient participants M (SD)	Caregiver participants M (SD)
Age (years)	75.68 (7.89) range = 57–89	n/a
Education level (years)	13.85 (2.97) range = 8–19	15.14 (2.48) range = 8–11
Gender (% female)	45.0	65.0
GDS Total	2.53 (2.37) range = 0–9	n/a
Positive family history of dementia	72.2%	n/a
Disease duration (years)	5.17 (2.34) range = 2–13	n/a
MMSE total	20.85 (5.04) range = 8–30	n/a

M = mean; SD = standard deviation; MMSE = Mini-Mental State Examination (Folstein et al., 1975); GDS = Geriatric Depression Scale (Olin et al., 1992; Yesavage et al., 1983); n/a = not applicable; Please note that disease duration reflects amount of time elapsed since patient's initial diagnosis of dementia.

Table 2
Means and standard deviations for cognitive and functional measures

Measure (range)	M (SD)
Cognitive measures	
MMSE (0–30)	20.85 (5.04)
RMT (0–50)	28.31 (5.32)
PPT (0–104)	88.38 (11.98)
Dual Task (0–100)	75.77 (20.44)
BORB (0–50)	44.20 (6.16)
SDLT (0–150)	9.94 (7.15)
Functional measures	
ADL Total	30.90 (8.10)
IADL Subscale	13.00 (6.13)
BADL Subscale	17.90 (2.76)

M = mean; SD = standard deviation; MMSE = Mini-Mental State Examination (Folstein et al., 1975); RMT = Recognition Memory Test (Warrington, 1984); PPT = Pyramid & Palm Trees (Howard & Patterson, 1992); Dual Task = Paper-and-Pencil Version of the Dual Task (Baddeley et al., 1997; Greene et al., 1995); BORB = Birmingham Object Recognition Battery (Riddoch & Humphreys, 1997); SDLT = Spatial Dot Location Test (Warrington & James, 1988); ADL = Activities of Daily Living Questionnaire (Lawton & Brody, 1969).

Hypothesis Testing Analyses for Global Cognitive Functioning

A series of stepwise multiple regression analyses were conducted to assess the relative contribution of several predictor variables (i.e., dementia severity as assessed by the MMSE, memory as assessed by the RMT, executive function as assessed by the Dual Task, semantic knowledge as assessed by the PPT, object perception as assessed by the BORB, and spatial localization as assessed by the SDLT) to a criterion variable (i.e., global functional status as assessed by the ADL total and ADL subscales (i.e., IADL and BADL)).

Global Functional Status. For the ADL total score, the regression model was significant ($F(1, 37) = 20.38, p = .0001$), accounting for 35.5% (Adjusted $R^2 = .34$) of the total variance of the ADL measure. Examination of the unique contribution of the predictor variables revealed that only the MMSE accounted for a significant portion of variance in the ADL measure ($t(39) = 4.51, p = .0001$).

Instrumental Activities of Daily Living (IADLs). For the IADL subscale, the regression model was significant ($F(1, 37) = 20.21, p = .0001$), accounting for 35.3% (Adjusted $R^2 = 0.34$) of the total variance of the IADL subscale. Examination of the predictor variables revealed that only the MMSE accounted for a significant portion of the variance ($t(39) = 20.21, p = .0001$).

Basic Self-Care Activities of Daily Living (BADLs). For the BADL subscale, the regression model was significant ($F(1, 37) = 7.36, p = .01$), accounting for 16.6% (Adjusted $R^2 = 0.14$) of the total variance of the IADL subscale. Examination of the predictor variables revealed that only the MMSE accounted for a significant portion of the variance ($t(39) = 2.71, p = .01$).

Hypothesis Testing for Visuoperceptual Abilities

A series of stepwise multiple regression analyses were conducted to assess the relative contribution of several predictor variables (i.e., memory as assessed by the RMT, executive function as assessed by the Dual Task, semantic knowledge as assessed by the PPT, object perception as assessed by the BORB, and spatial localization as assessed by the SDLT) to a criterion variable (i.e., global functional status as assessed by the ADL total, ADL subscales (i.e., IADL and BADL)). The MMSE measure was not entered as a predictor variable for this analysis.

Global Functional Status. For the ADL total score, the regression model was significant ($F(1, 37) = 8.39, p = .006$), accounting for 18.5% (Adjusted $R^2 = .16$) of the total variance of the ADL total score. Examination of the unique contribution of the predictor variables revealed that only the object perception measure (i.e., the BORB) accounted for a significant portion of the variance in the ADL measure ($t(39) = 2.90, p = .006$).

IADLs. For the IADL subscale, the regression model was significant ($F(1, 37) = 8.84, p = .005$), accounting for 19.3% (Adjusted $R^2 = .17$) of the total variance of the IADL measure. Examination of the unique contribution of the predictor variables revealed

that only the object perception measure (i.e., the BORB) accounted statistically for a significant portion of the variance in the IADL subscale ($t(39) = 2.97, p = .005$).

BADLs. For the BADL subscale, the model did not reach statistical significance.

Discussion

The purpose of the present study was to first demonstrate that dementia severity (as measured by the MMSE) is the most robust predictor of functional decline among patients with AD and to secondly, and most importantly, assess the relative contribution of higher-level visual processes to functional dependence in a sample of patients with AD independent of global cognitive functioning (i.e., MMSE score). Findings suggest that a measure of dementia severity is the only significant statistical predictor of both IADL and BADL dependence; however, when removed from the regression model, object recognition emerges as a significant predictor of IADL dependence.

Previous research has shown that dementia severity correlates with functional decline (Teri et al., 1989) as well as naturalistic action (Giovannetti et al., 2002). Naturalistic action (NA) is defined as movement in the service of practical goals, such as food preparation and consumption (Schwartz & Buxbaum, 1997). NA encompasses all activities that require the use of multiple objects and a sequence of steps to achieve an end goal. Examples include gift wrapping (Giovannetti et al., 2002), making tea (Rusted & Sheppard, 2002), as well as traditional ADL tasks that facilitate independent living, such as food shopping and dressing. NAs such as making tea or preparing food demand cognitive resources, and a depletion of resources secondary to neurological or neurodegenerative illness results in NA errors and difficulties. The resource theory of NA states that the more limited one's cognitive resources, the less resources available to employ in task completion resulting in impairment. Giovannetti and others (2002) examined NA (e.g., gift wrapping, toast preparation) in a heterogeneous dementia sample and found that global cognitive functioning was the best predictor of errors over measures of executive functioning and semantic knowledge. Studies of patients with closed head injury, right-hemisphere stroke, and left-hemisphere stroke (Buxbaum, Schwartz, & Montgomery, 1998; Schwartz et al., 1998) have yielded similar findings. Thus, dementia severity is a robust predictor of functional decline.

However, when global cognition is removed from the regression model, results from the present study reveal that object perception is a significant statistical contributor to global functional abilities and, more specifically, instrumental functional abilities such as food preparation, driving, and medication management. Interestingly, a task of spatial localization, sensitive to dorsal visual stream function, was not significantly associated with functional dependence. Though patients with AD were impaired on measures of executive function, memory, and semantic knowledge, these deficits were not significantly related to performance of functional abilities among our sample.

The specificity of the observed relationship between object perception and IADLs suggest that particular brain systems may be necessary for the performance of IADLs. Object perception reflects the capacity to achieve and manipulate structural descriptions of previously encountered objects. Research assessing object vision and recognition has shown that these functions are dependent on the ventrolateral and ventromesial occipito-temporal cortex (Cabeza & Nyberg, 2000; Grady et al., 1988; Mishkin, Ungerleider, & Macko, 1983). Functional imaging data have illustrated that object recognition processing is dependent on the integrity of the infero-temporal or occipitotemporal cortex (Grill-Spector et al., 1998;

Koehler et al., 1995; McIntosh et al., 1994). Recently, van Rhijn and colleagues (2004) showed associations between informant-ratings of IADLs and regional cerebral activity in the bilateral occipito-temporal and middle inferotemporal regions. Taken together with data from the present study, this evidence suggests that there is some specificity between the integrity of the ventral visual pathway and the performance of IADLs such as medication and financial management in individuals with AD. The findings from the current study highlight the need to consider perceptual processes when making inferences about functional abilities, as properly achieving the structural description of objects is uniquely related to instrumental functional abilities.

The current results extend previous AD-related work by Mahurin and others (1991) and more recent work by Glosser and colleagues (2001) by demonstrating that object perception is a significant predictor of instrumental functional dependence as compared to memory, executive function, and semantic knowledge abilities. The present findings also compliment the more general dementia literature. Among a heterogeneous dementia sample, Glosser et al. (2002) found that object form discrimination abilities were significantly associated with visually-based ADL errors such as “misjudging distances when reaching for things” and “does not recognize faces of familiar people.” However, non-visually based ADLs, such as “forgets and leaves the stove turned on” or “cannot concentrate on one thing,” were not significantly associated with visual perceptual functions. The present data extend these findings by simultaneously assessing other cognitive components (i.e., memory, executive function skills, and semantic knowledge) that have previously demonstrated relationships with functional abilities. Furthermore, the present study emphasizes *dependence* in instrumental activities that facilitate independent living, as compared to ADL errors as assessed by Glosser et al. (2002).

We found that a dual-task paradigm assessing the central executive system was not a significant statistical predictor of functional abilities. The dual task paradigm reflects working memory capacity as compared to traditional clinical use of heterogeneous executive function tasks such as the Trail Making Test Part B. Though this study did not directly compare the contribution of such clinical executive tasks versus measures of specific executive elements (e.g., working memory, planning, sequencing) to functional abilities, the null findings for the dual task suggest that specific elements of executive function (i.e., working memory) may not be critical to ADL dependence among AD patients as previously reported (Boyle et al., 2003a). The validity of our account must be empirically tested with future research parceling out elements of executive function to assess their individual contribution to ADL integrity.

Our conclusions must be tempered by a couple of caveats. First, the present findings may not generalize to other dementia groups, as the literature has suggested different ADL abilities and cognitive correlates across dementia groups (Boyle, Cohen, Paul, Moser, & Gordon, 2002; Boyle et al., 2003b). Furthermore, preliminary data suggest dementia groups differ in their degree of functional impairment. Tomaszewski, Mackin, Mungas, Reed, and Jagust (2002) reported that while patients with AD and frontotemporal dementia have similar levels of IADL impairment, patients with VaD have significantly better IADL integrity than those with AD. Future studies are needed to elucidate these relationships. Identification of particular IADLs abilities that are more susceptible to decline in various dementia groups may provide useful diagnostic information for clinicians. Future research should also examine patients with mild cognitive impairment to identify functional changes that are associated with conversion to dementia. Comparison of patients with mild and moderate dementia

severity may elucidate whether cognitive components contribute to functional status differentially across the disease course.

A second limitation of the present study was the utilization of only one measure per cognitive domain of interest (e.g., dual task paradigm for executive function). The methodology was intentionally designed to identify very specific cognitive components while minimizing additional cognitive (e.g., verbal or executive) demands that may confound performance, resulting in the predominant use of experimental measures rather than widely-used clinical measures. Findings may have differed with inclusion of multiple measures tapping each domain of interest or with inclusion of clinical measures that tap cognition more heterogeneously. Future studies may prefer to include several measures tapping a single construct.

With these caveats in mind, the findings of the current study highlight the important contribution of detailed cognitive analysis to the prediction of everyday functional abilities among patients with dementia, as object perception is a significant predictor of instrumental functional abilities in patients with AD. However, this association is obscured by the inclusion of a measure of global cognition in the regression model. The present results underscore the importance of visual perceptual functioning in the evaluation of AD patients, and information gathered from such assessments may be useful in the prediction of instrumental abilities, such as managing prescriptions, preparing food, and organizing finances.

References

- Arnold, S.E., Hyman, B.T., Flory, J., Damasio, A.R., & Van Hoesen, G.W. (1991). The topographical and neuroanatomical distribution of neurofibrillary tangles and neuritic plaques in the cerebral cortex in patients with Alzheimer's disease. *Cerebral Cortex*, *1*, 103–116.
- Baddeley, A.D. (1986). *Working Memory*. Oxford, England: Oxford University Press.
- Baddeley, A., Della Sala, S., Gray, C., Papagno, C., & Spinnler, H. (1997). Testing central executive functioning with a pencil-and-paper test. In P. Rabbit (Ed.), *Methodology of frontal and executive functions*. Hove, UK: Psychology Press.
- Binetti, G., Cappa, S.F., Magni, E.A.P., Bianchetti, A., & Trabucchi, M. (1996). Disorders of visual and spatial perception in the early stage of Alzheimer's disease. In R. J. Wurtman, S. Corkin, J.H. Growdon & R.M. Nitsch (Eds.), *Annals of New York Academy of Sciences: Vol. 777. The neurobiology of Alzheimer's disease* (pp. 221–225). New York: New York Academy of Sciences.
- Binetti, G., Cappa, S.F., Magni, E., Padovani, A., Bianchetti, A., & Trabucchi, M. (1998). Visual and spatial perception in the early phase of Alzheimer's disease. *Neuropsychology*, *12*(1), 29–33.
- Boyle, P.A., Cohen, R.A., Paul, R.H., Moser, D.J., & Gordon, N. (2002). Cognitive and motor impairments predict functional declines in patients with vascular dementia. *International Journal of Geriatric Psychiatry*, *17*(2), 164–169.
- Boyle, P.A., Malloy, P.F., Salloway, S., Cahn-Weiner, D.A., Cohen, R.A., & Cummings, J.L. (2003a). Executive cognitive dysfunction and apathy predict functional impairment in Alzheimer's disease. *American Journal of Geriatric Psychiatry*, *11*(2), 214–221.
- Boyle, P.A., Paul, R.H., Moser, D.J., Zawacki, T., Gordon, N., & Cohen, R.A. (2003b). Cognitive and neurologic predictors of functional impairment in vascular dementia. *American Journal of Geriatric Psychiatry*, *11*(1), 103–106.
- Brun, A., & Englund, E. (1981). Regional pattern of degeneration in Alzheimer's disease: Neuronal loss and histopathological grading. *Histopathology*, *5*, 549–564.
- Butter, C.M., Trobe, J.D., Foster, N.L., & Berent, S. (1996). Visual-spatial deficits explain visual symptoms in Alzheimer's disease. *American Journal of Ophthalmology*, *22*(97–105).
- Buxbaum, L.J., Schwartz, M.F., & Montgomery, M.W. (1998). Ideational apraxia and naturalistic action. *Cognitive Neuropsychology*, *15*, 617–643.

- Cabeza, R., & Nyberg, L. (2000). Imaging cognition II. An empirical review of 275 PET and fMRI studies. *Journal of Cognitive Neuroscience*, *12*, 1–47.
- Corkin, S., Kurylo, D.D., Dolan, R., Hyman, B.T., Arriagada, P.V., McKee, A., et al. (1991). Brain-behavior correlations for audition and vision in a very mild case of Alzheimer's disease (AD). *Society of Neuroscience Abstracts*, *17*, 352.
- D'Esposito, M., Detre, J.A., Alsop, D.C., Shin, R.K., Atlas, S., & Grossman, M. (1995). The neural basis of the central executive system of working memory. *Nature*, *378*(16), 279–281.
- Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*, 189–198.
- Giovannetti, T., Libon, D.J., Buxbaum, L., & Schwartz, M.F. (2002). Naturalistic action impairments in dementia. *Neuropsychologia*, *40*(8), 1220–1232.
- Glosser, G., Baker, K.M., deVries, J.J., Alavi, A., Grossman, M., & Clark, C.M. (2001). Disturbed visual processing contributes to impaired reading in Alzheimer's disease. *Neuropsychologia*, *40*, 902–909.
- Glosser, G., Gallo, J., Duda, N., de Vries, J.J., Clark, C.M., & Grossman, M. (2002). Visual perceptual functions predict instrumental activities of daily living in patients with dementia. *Neuropsychiatry, Neuropsychology, & Behavioral Neurology*, *15*(3), 198–206.
- Grady, C.L., Haxby, J.V., Horwitz, B., Sundaram, M., Berg, G., Schapiro, M., et al. (1988). Longitudinal study of the early neuropsychological and cerebral metabolic changes in dementia of the Alzheimer type. *Journal of Clinical & Experimental Neuropsychology*, *10*, 576–596.
- Greene, J.D.W., Hodges, J.R., & Baddeley, A.D. (1995). Autobiographical memory and executive function in early dementia of Alzheimer type. *Neuropsychologia*, *33*, 1647–1670.
- Grill-Spector, K., Kushnir, T., Hendler, T., Edelman, S., Itzchak, Y., & Malach, R. (1998). A sequence of object-processing stages revealed by fMRI in the human occipital lobe. *Human Brain Mapping*, *6*(4), 316–328.
- Hodges, J.R., & Patterson, K. (1995). Is semantic memory consistently impaired early in the course of Alzheimer's disease? Neuroanatomical and diagnostic implications. *Neuropsychologia*, *33*(4), 441–459.
- Hof, P.R., Bouras, C., Constantinidis, J., & Morrison, J.H. (1989). Balint's syndrome in Alzheimer's disease: Specific disruption of the occipito-parietal visual pathway. *Brain Research*, *493*, 368–375.
- Hof, P.R., Bouras, C., Constantinidis, J., & Morrison, J.H. (1990). Selective disconnection of specific visual association pathways in cases of Alzheimer's disease presenting with Balint's syndrome. *Journal of Neuropathology and Experimental Neurology*, *49*(2), 168–184.
- Hof, P.R., & Morrison, J.H. (1990). Quantitative analysis of a vulnerable subset of pyramidal neurons in Alzheimer's disease: II. Primary and secondary visual cortex. *Journal of Comparative Neurology*, *301*, 55–64.
- Howard, D., & Patterson, K. (1992). *The Pyramids and Palm Trees Test: A test of semantic access from words and pictures*. Bury St. Edmunds: Thames Valley Test Company.
- Humphreys, G.W., & Riddoch, M.J. (1984). Routes to object constancy: Implications from neurological impairments of object constancy. *The Quarterly Journal of Experimental Psychology*, *36A*, 385–415.
- Koehler, S., Kapur, S.M., M., & Winocur, G. (1995). Dissociation of pathways for object and spatial vision: A PET study in humans. *Neuroreport: an International Journal for the Rapid Communication of Research in Neuroscience*, *6*(14), 1865–1868.
- Kremin, H., Beauchamp, D., & Perrier, D. (1994). Naming without picture comprehension? Apropos the oral naming and semantic comprehension of pictures by patients with Alzheimer's disease. *Aphasiology*, *8*(3), 291–294.
- Kurylo, D.D., Corkin, S., Rizzo III, J.F., & Growdon, J.H. (1996). Greater relative impairment of object recognition than of visuospatial abilities in Alzheimer's disease. *Neuropsychology*, *10*(1), 74–81.
- Lawton, M.P., & Brody, E. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. *Gerontologist*, *9*, 179–186.

- Levine, D.N., Lee, J.M., & Fisher, C.M. (1993). The visual variant of Alzheimer's disease: A clinicopathologic case study. *Neurology*, *43*, 305–313.
- Lewis, D.A., Campbell, M.J., Terry, R.D., & Morrison, J.H. (1987). Laminar and regional distributions of neurofibrillary tangles and neuritic plaques in Alzheimer's disease: A quantitative study of visual and auditory cortices. *Journal of Neuroscience*, *7*, 1799–1808.
- Libon, D.J., Glosser, G., Malamut, B.L., Kaplan, E., Goldberg, E., Swenson, R., et al. (1994). Age, executive functions, and visuospatial functioning in healthy older adults. *Neuropsychology*, *8*(1), 38–43.
- Mahurin, R.K., DeBettignies, B.H., & Pirozzolo, F.J. (1991). Structured assessment of independent living skills: Preliminary report of a performance measure of functional abilities in dementia. *Journal of Gerontology*, *46*, 58–66.
- McIntosh, A.R., Grady, C.L., Ungerleider, L.G., Haxby, J.V., Rapoport, S.I., & Horowitz, B. (1994). Network analysis of cortical visual pathways mapped with PET. *Journal of Neuroscience*, *14*(2), 655–666.
- McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E.M. (1984). Clinical diagnosis of Alzheimer's disease: Report on the NINCDS-ADRDA work group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology*, *34*, 939–944.
- Mendez, M.F., Mendez, M.A., Martin, R., Smyth, K.A., & Whitehouse, P.J. (1990). Complex visual disturbances in Alzheimer's disease. *Neurology*, *40*, 439–443.
- Mishkin, M., Ungerleider, L.G., & Macko, K.A. (1983). Object vision and spatial vision: Two cortical pathways. *Trends in Neuroscience*, *6*, 414–417.
- Mummery, C.J., Patterson, K., Wise, R.J.S., Vandenberg, R., Price, C.J., & Hodges, J.R. (1999). Disrupted temporal lobe connections in semantic dementia. *Brain*, *122*(1), 61–73.
- Olin, J.T., Schneider, L.S., Eaton, E.E., Zemansky, M.F., & Pollock, V.E. (1992). The Geriatric Depression Scale and the Beck Depression Inventory as screening instruments in an older adult outpatient population. *Psychological Assessment*, *4*, 190–192.
- Pearson, R.C.A., Esiri, M.M., Hiorns, R.W., Wilcock, G.K., & Powell, T.P. (1985). Anatomical correlates of the distribution of the pathological changes in the neocortex in Alzheimer disease. *Proceedings of the National Academy of Science*, *82*, 4531–4534.
- Riddoch, M.J., & Humphreys, G.W. (1997). *Birmingham Object Recognition Battery*. London: Psychology Press.
- Rusted, J., & Sheppard, L. (2002). Action-based memory in Alzheimer's disease: A longitudinal look at tea making. *Neurocase*, *8*, 111–126.
- Schwartz, M.F., & Buxbaum, L.J. (1997). Naturalistic action. In L.J.G. Rothi & K.M. Heilman (Eds.), *Apraxia: The Neuropsychology of Action*. Location unknown: Psychology Press.
- Schwartz, M.F., Montgomery, M.W., Buxbaum, L.J., Lee, S.S., Carew, T.G., Coslett, H.B., et al. (1998). Naturalistic action impairment in closed head injury. *Neuropsychology*, *12*, 13–28.
- Stark, C.E.L., & Squire, L.R. (2000). Functional magnetic resonance imaging (fMRI) activity in the hippocampal region during recognition memory. *The Journal of Neuroscience*, *20*(20), 7776–7781.
- Teri, L., Borson, S., Kiyak, A., & Yamagishi, M. (1989). Behavioral disturbance, cognitive dysfunction, and functional skill: Prevalence and relationship in Alzheimer's disease. *Journal of the American Geriatrics Society*, *37*, 109–116.
- Tomaszewski, S.S., Mackin, S., Mungas, D., Reed, B., & Jagust, W. (2002). Differences in degree of impaired daily functioning in Alzheimer's disease, ischemic vascular dementia, and frontotemporal dementia. *Archives of Clinical Neuropsychology*, *17*(8), 735.
- Van der Hurk, P.R., & Hodges, J.R. (1995). Episodic and semantic memory in Alzheimer's disease and progressive supranuclear palsy: A comparative study. *Journal of Clinical & Experimental Neuropsychology*, *17*(3), 459–471.
- van Rhijn, S.J., Glosser, G., de Vries, J.J., Clark, C.M., Newberg, A.B., & Alavi, A. (2004). Visual processing impairments and decrements in regional brain activity in Alzheimer's disease. *Journal of Clinical & Experimental Neuropsychology*, *26*(1), 11–23.

- Warrington, E.K. (1984). *Recognition Memory Test*. Windsor, UK: NFER-Nelson.
- Warrington, E.K., & James, M. (1988). Visual apperceptive agnosia: A clinico-anatomic study of three cases. *Cortex*, *24*, 13–32.
- Wechsler, D. (1981). *Wechsler Adult Intelligence Scale – revised manual*. New York: Psychological Cooperation.
- Wepman, J.M., Morency, A., & Seidi, M. (1975). *Visual Discrimination Test*. Los Angeles: Western Psychological Services.
- Willis, S.L., Allen-Burge, R., Dolan, M.M., Bertrand, R.M., Yesavage, J., & Taylor, J.L. (1998). Everyday problem solving among individuals with Alzheimer’s disease. *The Gerontologist*, *38*(5), 569–577.
- Yesavage, J.A., Brink, T.L., Rose, T.L., Lum, O., Huang, V., Adey, M., et al. (1983). Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of Psychiatric Research*, *17*, 37–49.