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Visuospatial Function is a Significant Contributor to Functional Status in Patients With Alzheimer's Disease

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Background: Contribution of visuospatial abilities to the functional status in patients with Alzheimer's disease (AD) has been controversial. *Aim:* To address whether visuospatial abilities have independent association with functional measures in patients with AD. *Methods:* We regressed performances on a global cognitive (the revised Hasegawa Dementia Scale: HDSR), executive/visuoconstruction (Clock drawing), visuoperception (Clock reading: CRT), simple visuoconstruction (figure copying), and frontal behavioral tasks on measures of basic and instrumental activities of daily living (BADL and IADL) in 57 patients (78.0 ± 6.1 years) with AD of various severity (mean HDSR score: 16.0 ± 5.9). We sought independent contributions of these visuospatial measures to functional status. *Results:* Performance on the CRT contributed significantly to BADL and IADL and the results of HDSR contributed to IADL. Results of figure copying related significantly to BADL especially in mild AD. *Conclusion:* Visuospatial ability is one of the important contributors to functional status.

Keywords: Alzheimer's disease; visuospatial function; executive function; Clock drawing test; Clock reading test; figure copying

Introduction

Functional status is composed of basic and instrumental activities of daily life (BADL and IADL). One widely used questionnaire to assess functional levels is the Physical Self-Maintenance Scale (PSMS) and Instrumental Activities of Daily Living Scale (IADL).[1] The PSMS is a measure of BADL and Lawton's IADL is a measure of higher-level functional status, which is also referred to as "IADL." As pointed out by Lawton and Brody, it should be underlined that the description of functional status provided by these scales is an integration of current cognitive-motor abilities and thus results from PSMS and IADL measures require fitting with evaluation of cognitive functions.[1]

Significant association of executive function to functional competency has been well established. Cahn-Weiner et al investigated contributions of episodic memory, executive function, and brain volumes to baseline IADL and rate of IADL change in elderly persons with cognitive function falling between normal and moderate dementia.[2] They found that memory and executive function were associated with baseline IADL scores, but only executive function was independently associated with rate of change in IADL. When both cognitive and neuroimaging predictors were considered, only executive function independently predicted rate of decline in IADL scores.[2] A study using community-dwelling women correlated executive function (the Trail Making Test: TMT) and global cognitive function (the Mini-Mental State Examination: MMSE) with the levels of BADL and IADL at baseline and at 6-year follow-up.[3] At baseline, impairment on the TMT only or both TMT and MMSE was associated with the highest proportion of dependence in both BADL and IADL. At the 6-year follow-up, participants with only TMT impairment were more likely to have declined with regard to dependence.[3] Among executive function elements (working memory, generation, inhibition, planning,

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and sequencing), inhibitory control was the most relevant to maintenance of IADL.[4] Thus, it may be a general understanding that executive function plays a more important role than global cognitive function or memory in the maintenance of both BADL and IADL and can be used to monitor future deterioration in functional levels.

Because AD is characterized specifically by early impairment of memory and visuospatial cognition, there remains an important issue of whether deficits in visuospatial abilities affect functional status of patients with AD. Some studies consider visuospatial function[5,6] as a significant determinant of functional status in patients with AD[5] as well as nonspecified dementia.[6] In contrast, in 1 study that focused on value of various cognitive abilities in predicting functional competence, the authors did not find visuoperceptive and constructive tasks useful but they found scores for orientation, abstract thinking, and psychomotor speed helpful for the prediction.[7]

These inconsistent findings prompted us to investigate the contribution of visuospatial as well as executive and other cognitive functions to functional status in an AD population. We used the clock tasks in assessing executive/visuoconstruction (the Clock drawing test: CDT) and visuoperception (the Clock reading test: CRT) to look at the usefulness of these simple tools in correlating with functional levels of patients with AD.

Patients

We included 64 consecutive outpatients with probable AD who did not have apparent psychiatric symptoms. A certified neurologist (T.F.) conducted neurological and screening cognitive examinations in all the patients at presentation, making the diagnosis of AD according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria with a reference to brain magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT) findings. These patients were clinically stable under long-term treatment with donepezil hydrochloride. We tested them on their regular quarterly visits to the Memory & Cognitive Clinic during May to November 2007. Seven patients were excluded because of aphasia (3), recalcitrance (2), or advanced dementia (2) that prevented testing. The demographics, cognitive data, and the results of the PSMS and IADL scales in the remaining 57 patients (17 men and 40 women) are shown in Table 1. Twelve patients had mild AD (scores on the revised Hasegawa Dementia Scale: HDSR $\geq$ 21, median 22.5), 32 moderate AD (20$\geq$ HDSR $\geq$ 11, median 16.5), and 13 severe AD (10$\geq$ HDSR, median 9). They were capable of walking unassisted and had no serious medical complications other than well-controlled arterial hypertension, diabetes mellitus, or hypercholesterolemia. None were taking psychoactive medication other than donepezil at the time of testing, indicating no active psychiatric problems in this group that would necessitate treatment.

A written informed consent was obtained from patients and caregivers prior to administration of the tests. This study was approved by the Ethics Committee of the Showa University Northern Yokohama Hospital.

Methods

Evaluation of Cognitive Functions and Frontal Behaviors

A psychometrist (EL) blind to the patients' clinical backgrounds except for the diagnosis administered a set of cognitive tests. Every patient was examined using the HDSR, CDT, CRT, figure copying (Figcopy), and Frontal Assessment Battery (FAB). Caregivers stayed in the testing room and seated silently out of sight of the patient.

The HDSR is a composite global cognitive test and its purpose is similar to that of the MMSE. Correlation of HDSR with the MMSE and Wechsler Adult Intelligence Scale-Revised established validation.[8] The full score is 30 and the subscales are described in Table 2. Given that scores for the HDSR correlates highly with those of the MMSE ($r = .87$),[8] the upper tertile of HDSR scores (HDSR $\geq$ 21) correspond to normal cognition or mild dementia, the middle tertile (20 $\geq$ HDSR $\geq$ 11) moderate dementia, and lower tertile (10$\geq$ HDSR) severe dementia. We used HDSR because we had used this measure instead of MMSE in our previous series of studies. The HDSR consists of 9 subscales; HDSR 1: recalling one's age, 2: orientation to time, 3: orientation to place, 4: immediate recall of 3 unassociated words, 5: serial subtraction of 7 from 100 (till 86), 6: backward digit span, 7: delayed recall of words presented for HDSR 4, 8: immediate recall of 5 visually presented objects, and 9: semantic fluency of vegetables (Table 2). For the HDSR 9, we used the

Table 1. Patient Demography and Results of Cognitive and ADL Scales. Mean, Standard Deviation (SD), Median, Maximum, and Minimum Values for Each Item Are Shown

	Mean	SD	Median	Max	Min
Age	78.0	6.1	80	88	62
Duration (years)	3.4	2.0	3	8	0.5
Education (years)	11.2	3.0	12	18	6
PSMS	27.2	3.5	28	30	17
IADL-R[a]	0.65	0.23	0.68	1	0.26
HDSR	16.0	5.9	16	28	3
CDT	11.3	3.9	12.5	15	0
CRT	6.9	4.1	8	12	0
Fig-copy	4.1	1.1	4.5	5	0
FAB	9.7	3.1	10	16	3

Abbreviations: CDT, Clock Drawing Test; CRT, Clock Reading Test; HDSR, the revised Hasegawa Dementia Scale; IADL, Instrumental Activities of Daily Living Scale; FAB, the Frontal Assessment Battery; Fig-copy, figure copying; PSMS, the Physical Self-Maintenance Scale.
[a] IADL-R (IADL ratios) is the IADL score divided by its full scores, 31 for women and 19 for men.

Table 2. The Revised Hasegawa Dementia Scale (HDSR)[a]

		Subscores
1	Recalling one's own age	1
2	Orientation to time	
	Month, date, day, year	1 For each
3	Orientation to place	Complete: 2
		Partial: 1
4	Immediate recall of 3 words	
	Cherry tree, cat, train	1 For each
5	Subtraction	
	100 − 7 =	1
	93 − 7 =	1
6	Repeat backwards	
	268, 3529	1 For each
7	Delayed recall of 3 words presented for HDSR 4	6
		Unprompted: 2 for each
		Prompted: 1 for each
8	Immediate recall of 5 visually presented objects: clock, coin, tobacco, pen, match	1 For each
9	Vegetable word fluency/minute	≤5 Words: 0
		6 Words: 1
		7 Words: 2
		8 Words: 3
		9 Words: 4
		>10 Words: 5
	Total	30

[a] Subscales and scoring rules are shown. For HDSR 7, 2 points are given to a correct unprompted response to each of the 3 words presented for HDSR 4. In case of failure, semantic hints such as tree (for cherry tree), animal (for cat), or vehicle (for train) are given. One point is given to a correct prompted answer. The original scoring for HDSR 9 is a 6-level scale. The total score is 30.

total numbers of words produced instead of the original 6-level scoring to avoid ceiling or floor effect in statistical procedures.

The CDT is considered primarily an executive task that also taps visuoconstruction, semantic, and numerical abilities.[9,10] We placed a blank sheet of paper (without a predrawn circle) and instructed patients to "Draw a big-enough round clock face with all the numbers in it. Make it read 10 past 10." Instructions could be repeated to ensure they were fully understood but the examiner did not comment once the patient began the task. There was no time limit and patients finished when they decided they had completed the task. We scored 15 items regarding the circle, numbers, hands, and center using Freedman's 15-point method.[11] We selected this scoring method postulating a finer grading system to be more sensitive in detecting subtle cognitive differences. For this specific purpose, the CLOX 15-point scoring[9] was an alternative choice, but we preferred Freedman's method mainly because of our long experience with this method. The Freedman's method contrasts with other standard scoring methods with fewer scoring levels, eg, Sunderland's[12] and Wolf-Klein's[13] methods with 10 levels or Shulman's[14] with 5. We scored 0 for total or near total failure, 0.5 for partially correct but incomplete responses, and 1 for perfect or near perfect performance for each of 15 items.

The CRT is another type of clock task that is strongly focused on visuoperception abilities and requires little executive processing.[15] We adopted a 12-item CRT that allows a finely-graded assessment of clock-reading ability[15]: the task clocks represent various hand positions (2:15, 10:30, 4:25, 8:55, 7:35, 12:55, 1:42, 8:22, 1:47, 4:43, 1:05, and 7:45). A clock face does not have numbers but only small marks on the circle indicating locations of numbers. Patients were reminded that the top of clocks corresponded to the top of a task sheet and asked to read each clock carefully. We followed the original rules with regard to a time limit (1 minute) and scoring.[15]: 1 point was given for a correct reading (tolerance: 3 minutes); one-half point was given for readings which are 4 to 5 minutes, or exactly 1 hour off the correct time; all other readings were scored 0.

We developed the figure-copying task (Fig-copy) to assess relatively pure visuoconstructive abilities. Fig-copy may differ from either the CDT or CRT in that it requires little executive, language, semantic

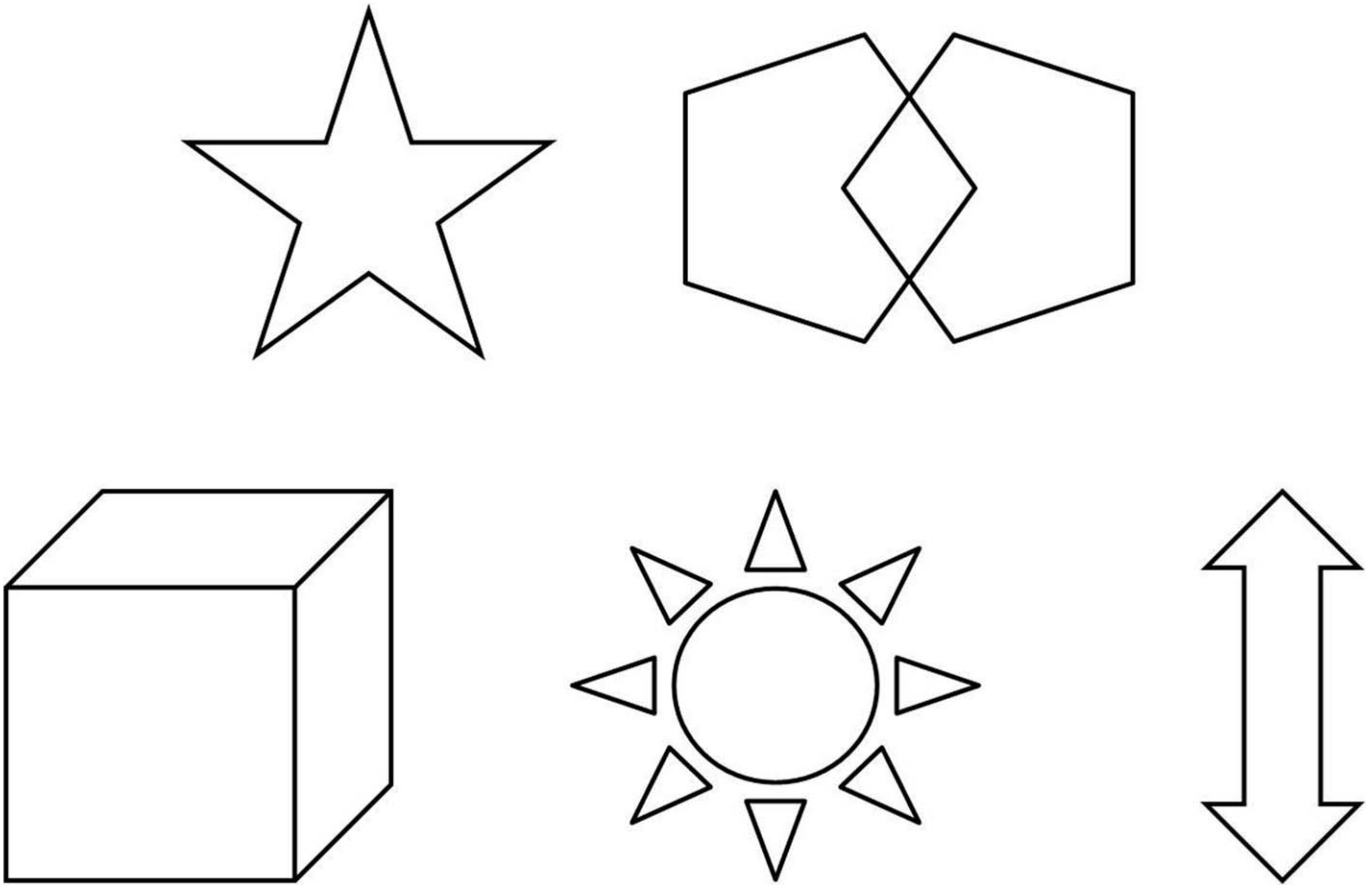

Figure 1. Tasks for the figure copying (Fig-copy).

memory, or numerical knowledge for its performance. Fig-copy task consisted of 5 figures including a 5-point star, interlocking pentagons, a solid cube in perspective, an iconic shining sun, and a bi-directional arrow (Figure 1). We selected these figures de novo taking into account different levels of complexities, symmetry/asymmetry, and a wide range of basic shapes (circles, triangles, squares, and pentagons), lines (vertical, horizontal and slanted), and angles. The scoring rules were the same as those described above for the CDT: a point of 0 (total or near total failure), 0.5 (partially correct but incomplete), or 1 (perfect or near perfect) was given to each figure. The basic concept of our scoring system for the Fig-copy is similar to Shulman's CDT scoring[14] in terms of its pure qualitative nature. Performances ranging from perfection to failing were stratified into 6 levels in Shulman's CDT and 3 levels in the Fig-copy.

To assess frontal behavioral symptoms, we used a standardized Japanese version[16] of the Frontal Assessment Battery (FAB),[17] which we modified taking into account the unfamiliarity among elderly Japanese population of orange (changed to mandarin) and daisy (changed to dandelion) for the conceptualization task (FAB 1). Back translation of the Japanese version is exactly the same as the original English version except for the alternations described above. For FAB 2 (phonemic word fluency), we used the total numbers of words produced instead of the original 4-level scoring for the same reason described for the semantic fluency task.

We confirmed that patients had sufficient visual and acoustic acuity for these tasks.

Evaluation of ADL

Prior to cognitive evaluations, the physician (T.F.) evaluated BADL and IADL by use of the Lawton's PSMS and IADL[1] on the basis of caregivers' observations and the physician's direct observations. In an attempt to reflect subtle differences in impairments of functional status, we used raw scores instead of the original 0 or 1 grading. All 6 items in the PSMS were scored using a 5-level scale with 1 representing the lowest and 5 representing the highest level of independence. The sum score of 6 items was used for statistical procedures. Similarly, the IADL were scored by a 3-level (for laundry, medication, and finances), 4-level (telephone, shopping and food preparation), or 5-level scale (housekeeping and transportation) with the full marks representing complete independence. We respected the original gender differences in IADL: all the 8 items were considered in women while 3 items (food preparation, housekeeping, and laundry) were not applied to men, resulting in the full scores for the IADL of 31 for women and 19 for men. For the statistical comparisons, we used the IADL ratio (IADL-R): the total IADL score divided by 31 for women or 19 for men. Higher scores for the PSMS and IADL-R represented higher levels of independence in BADL and IADL, respectively.

Statistical Methods (SPSS Version 11.5J)

Correlations among cognitive, frontal behavioral, and ADL measures. We correlated scores of the HDSR, CDT, CRT, Fig-copy and FAB, and 2 ADL scales (PSMS and IADL-R) by Spearman correlation with Bonferroni correction for multiple comparisons. The level of statistical significance was set at a $P = .0024$ (0.05/21) for 21 ($\{7 \times 7 - 7\}/2$) comparisons.

Linear regression analyses. We conducted a stepwise linear regression analysis to seek independent contributions of each cognitive domain (global cognition [HDSR], executive/visuoconstructive [CDT], visuoperceptive [CRT], and visuoconstructive [Fig-copy]) and frontal behaviors (FAB) to ADL measures (PSMS and IADL). We assigned the PSMS or IADL-R scores to dependent variables. The first set of independent variables included scores of HDSR (total), CDT, CRT, Fig-copy, and FAB (total), and demographic factors (age, education years, and duration of illness). We considered first the entire cohort and then 3 patient groups classified according to the severity of dementia. In the second set of independent variables, we substituted the total scores of HDSR and FAB with their subscale scores to investigate what cognitive and frontal elements associated with functional status. The level of statistical significance was set at a $P = .05$.

Intrarater and interrater reliability of the Fig-copy task (*reliability analysis*). Results of Fig-copy from 20 patients were selected randomly and blindly by a third party for reliability analysis. One of the authors (EL) scored these samples twice, more than 3 months apart between the evaluations, to address intrarater reliability. The other author (TF) scored the same samples blindly to address the interrater reliability.

Results

Patient Backgrounds

The HDSR scores for the entire cohort ranged widely from 3 to 28, and the mean score corresponded with the median score of 16. The medians for patients with mild, moderate, and severe AD were 22.5, 16.5, and 9, respectively, and 45 patients out of 57 scored in the midrange of 22.5 and 9 on the HDSR. Thus, the majority of patients corresponded to the moderate range when judged by the HDSR.[8] The average scores for the PSMS and IADL-R were 27.2 ± 3.5 (out of 30) and 0.65 ± 0.23 (out of 1.0), respectively, indicating that patients were physically capable while more impaired in more sophisticated activities (Table 1).

Correlations Studies

Statistically significant ($P < .0024$) correlation coefficients are selectively shown in Table 3. In spite of a rather stringent *P* value inherent to large numbers of comparisons corrected by Bonferroni method, we found moderate to strong correlations among cognitive, frontal behavioral, and ADL measures. Thus, for the purpose of finding independent contribution of each cognitive or behavioral measure to functional status, linear regression analyses should be used.

Linear Regression Analyses

Among the HDSR, CDT, CRT, Fig-copy, FAB, and demographic factors, CRT ($\beta = .61$, $P < .001$), patients' age ($\beta = -.34$, $P < .01$), and education ($\beta = -.23$, $P < .05$) contributed to the PSMS score ($F_{3,53} = 22.4$, $P < .001$) and these 3 factors accounted for 60% of PSMS variance. The contribution of CRT was independent of performances on the HDSR, CDT, Fig-copy, or FAB, none of which emerged as significant contributors to this measure. Alternatively, the CRT ($\beta = .40$, $P < .01$) and HDSR ($\beta = .28$, $P < .05$) were the significant contributors to IADL-R together with patients' age ($\beta = -.41$, $P < .001$; $F_{3,53} = 20.6$, $P < .001$). These 3 factors accounted for 58% of the variance.

We found essentially similar but somewhat different factors contributing to BADL and IADL at different clinical stages. Significant contributors to the

Table 3. Correlation Coefficients Among Cognitive Tests, FAB, PSMS, and IADL-R (Spearman Correlation)[a]

	PSMS	IADL-R	HDSR	CDT	CRT	Fig-copy	FAB
PSMS		0.86	0.61	0.46	0.61	0.50	
IADL-R			0.59	0.48	0.65	0.53	0.42
HDSR					0.64		0.45
CDT					0.69	0.70	0.53
CRT						0.65	0.56
Fig-copy							
FAB							

Abbreviations: CDT, Clock Drawing Test; CRT, Clock Reading Test; HDSR, the revised Hasegawa Dementia Scale; IADL, Instrumental Activities of Daily Living Scale; IADL-R, IADL ratios; FAB, the Frontal Assessment Battery; Fig-copy, figure copying; PSMS, the Physical Self-Maintenance Scale.

[a] Significant correlation coefficients are selectively shown. We adopted Bonferroni correction for 21 ({7 × 7 − 7}/2) comparisons and the level of statistical significance was thus set at a $P = .05/21 = 0.0024$.

PSMS scores included Fig-copy ($\beta = .77$, $P < .01$) in mild AD ($F_{1,10} = 14.7$, $P < .01$; $R^2 = .60$); CRT ($\beta = .63$, $P < .001$) and patients' age ($\beta = -.65$, $P < 0.001$) in moderate AD ($F_{2,29} = 28.3$, $P < .001$; $R^2 = .69$); and CDT ($\beta = 1.28$, $P < .001$) and patients' age ($\beta = .51$, $P < 0.01$) in severe AD ($F_{2,10} = 55.0$, $P < .001$; $R^2 = .92$). Factors that emerged as significant contributors to IADL-R were education ($\beta = .70$, $P < .05$) in mild AD ($F_{1,10} = 9.6$, $P < .05$; $R^2 = .49$); CRT ($\beta = .56$, $P < .01$) and patients' age ($\beta = -.56$, $P < .01$) in moderate AD ($F_{2,29} = 13.8$, $P < .001$; $R^2 = .55$); and CDT ($\beta = .89$, $P < .01$) in severe AD ($F_{1,\ 11} = 28.8$, $P < .01$; $R^2 = .78$).

Among subscales of the HDSR and FAB, HDSR 1 (orientation to one's age; $\beta = .42$, $P < .001$), HDSR 3 (orientation to place; $\beta = .32$, $P < 0.001$), and FAB 5 (Go-No go task; $\beta = .17$, $P < .05$) emerged as significant contributors to PSMS score together with Fig-copy ($\beta = .25$, $P < 0.01$), age ($\beta = -.25$, $P < .05$), and education ($\beta = -.32$, $P < 0.001$; F (6, 50) = 77.3, $P < .001$; $R^2 = .75$). Significant contributors to IADL-R included HDSR 3 (orientation to place; $\beta = .22$, $P < .05$) and HDSR 6 (backward digit span; $\beta = .20$, $P < .05$) together with CRT ($\beta = .42$, $P < .001$) and patients' age ($\beta = -.41$, $P < .001$; F (4, 52) = 18.1, $P < .001$; $R^2 = .59$).

Reliability Analysis

The reliability coefficients were 0.99 for double scorings by a single rater and 0.96 for parallel scorings by 2 raters, suggesting a high intrarater and interrater reliability in the Fig-copy scoring system.

Discussion

The findings from this study suggest that the cognitive domains essential for the CRT are closely associated with both BADL and IADL in patients with AD at various clinical stages. Although the results of CRT positively correlated with those of global cognitive (HDSR), executive/visuoconstructive (CDT), and visuoconstructive (Fig-copy) tasks, contribution of the CRT to functional status was independent of these relevant factors.

In addition, factors associated with functional status may vary according to the severity of dementia. In mild AD, simple visuoconstructive abilities (Fig-copy) and educational levels associated positively with BADL and IADL, respectively. In moderate AD, complex visuoperception abilities (CRT) and the age of patients contributed to both BADL and IADL. In advanced AD, executive/visuoconstruction function (CDT) appeared to play an important role in functional status.

Among subscales of the HDSR and FAB, orientation (to place and age) and inhibitory control (Go-No go) contributed significantly to BADL. Contributors to IADL-R included orientation to place and working memory (backward digit span). Given inhibitory control and working memory be classified as executive function, these results reinforce previous findings that executive function is essential for the maintenance of functional status.[2-4,18-21]

Compared to well-recognized importance of executive function, the contribution of visuospatial cognition to functional status has not drawn enough attention. The importance of visuospatial ability has been noticed in the area of stroke rehabilitation. Visuoconstruction impairment, together with advanced age and general cognitive decline, has been suggested as one of the negative factors for functional status in post-stroke population.[22] Visuospatial ability related strongly to self-care as well as outdoor and social activities of chronic stroke patients.[23]

In dementia population, 1 study suggested that functional status in early AD population correlated strongly with visuospatial function and semantic memory while episodic memory had no association with functional status.[5] Among variables within demographic, psychometric, and memory domains, visuoperceptive impairment measured by the Poppelreuter's figures and severity of dementia were significant determinants of the levels of BADL and IADL in patients with nonspecified dementia.[6]

The present study underlined vital contribution of visuoperception abilities, represented by the CRT, to functional status especially in moderate AD. Significant association between simple visuoconstructive function (Fig-copy) and BADL may also accentuate importance of visuospatial function for functional status.

Performance on the 12-item CRT was a major determinant of BADL and IADL; this method was proposed as a visuoperception test that requires minimal executive function involvement.[15] The CRT requires for successful performance visual apperception and interpretation of various hand positions in relation to the numberless circle. Keeping in mind correspondence of the top of a clock face and the position of "12," patients have to transform the locations of the long and short hands into the frame of time concept according to abstract numerical knowledge specific to a clock. Divided attention may also be required to read the hour and minute separately based on their different numerical rules. Additionally, reading a series of different clocks requires sustained attention as well as the ability to change mental sets from task to task. Construction ability is not required. Conversely, Fig-copy is a much simpler visuoperception/construction task than the clock tasks in that little executive function, semantic memory, or numerical knowledge is required.

Orientation to place may represent 1 aspect of broadly defined visuospatial function. Orientation to place, time, and age may predict functions both in BADL and IADL.[7] Disorientation has been suggested as one of the factors aggravating caregivers' burden[24] or quality of life of patients with dementia.[25,26] Similarly, we found that orientation to place was a significant contributor to both BADL and IADL.

Although results of the CRT significantly contribute both to BADL and IADL, the CDT did not emerge as an independent contributor to functional status when the entire cohort was assessed. However, we found that performance on the CDT was closely associated with both BADL and IADL in patients with severe AD.

The CRT and CDT are based on similar but different cognitive domains: the major differences between the CRT and CDT may be the quantity of executive function and types of visuospatial functions that are needed for their performance. Goal-directed planning and organization in the processes of constructing various components into a well-formed clock face is essential for the CDT but not for CRT. The CDT requires executive function-based visuoconstruction abilities while the CRT may necessitate semantic and numerical knowledge-based visuoperception abilities. The CDT has long been advocated as a reliable measure of levels of IADL.[6,20,21] The association between the CDT performance and functional status in patients with severe AD in the present study suggests that functional status becomes more dependent on executive function as the severity of dementia advances.

Results from the present study do not necessarily undervalue the already known association of global cognitive levels (HDSR) with functional levels. We also showed that the total scores of HDSR, a gauge of global cognitive levels, was an independent contributor to IADL while HDSR subscales related to episodic memory did not emerge as independent contributors to functional status. These findings are in line with a general agreement that global cognitive level is a significant determinant of functional status[3,6,23-25] while memory per se may be of less importance.[2,3,5,19]

In sum, the present study supplements previous investigations by showing that visuoperception, visuoconstruction, executive functions as well as global cognition may in combination associate with functional status in AD population and that their contributions may vary according to the severity of AD. Results from the present study also expanded the value of the clock tasks in the evaluation of functional status in AD population.

The FAB assesses frontal behavioral abnormalities by tapping integrity of conceptualization, mental flexibility, programming, behavioral self-regulation, inhibitory control, and suppression of environmental dependency.[17] We did not find any independent association of the total FAB scores with results of functional measures. Among subscales of the FAB, inhibitory control (a Go-No go task) was a significant contributor to the PSMS score. Our results may be partially comparable to the findings that inhibitory control was the most relevant to IADL among executive function elements.[4] Conversely, we were unable to address to possible influences of impaired motivation, initiation, or moods on functional status[27] because we did not include any measures that assess psychiatric symptoms of dementia.

Advanced age is generally a common cause of impaired functions[20,22] as shown in the present study. Accordingly, a positive contribution of patients' age to the PSMS scores in severe AD may be circumstantial assumedly because of a small sample size; we need a larger population to conclude on this issue. Educational levels may[6] or may not[28] have protective effects on functional status. We could not confirm benefits of education to BADL or IADL except for its positive contribution to IADL in mild AD.

Finally, there are some limitations to this study. The number of participants is rather small for a definite conclusion and the results should be considered preliminary. Nonetheless, we found a relatively robust contribution of CRT to both BADL and IADL and possible contribution of simple figure copying abilities to functional status. We also confirmed some of the previous theories regarding the association between functional status and global/executive functions. Using a larger population, we may be able to strengthen the power of contributing factors specific to different levels of dementia severity. Moreover, cognitive tests were restricted to easily performed bedside cognitive tests and thus cognitive domains that we assessed were not comprehensive. Specifically, we did not address neuropsychiatric problems. Also there might be a bias at the level of patient selection because we excluded patients with apparent amotivation, distraction, hostility, or a lack of cooperation. Detrimental effects of behavior and psychological symptoms of dementia to functional status should be addressed separately.

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