

# Problem Solving Ability in Patients With Mild Cognitive Impairment

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**Background and Objective:** It is important to determine which patients with mild cognitive impairment (MCI) are at risk for progression to dementia. The presence of mild impairments not restricted to the domain of memory may suggest such progression. Our goal is to determine how well a visuospatial problem solving task assessing the cumulative burden of frontal and posterior damage differentiates MCI patients from matched controls.

**Methods:** Twenty-six patients with MCI [Clinical Dementia Rating (CDR) score of 0.5] and mini-mental state examination (MMSE) scores of at least 24/30, were compared with 20 age and education level matched controls without cognitive impairment. All patients were given the MMSE, Hopkins Verbal Learning Test (HVLT), Boston Naming Test (BNT), Rey Complex Figures copying (RCF), anagrams, and visuospatial problem solving battery (VPS). The VPS is a complex problem solving task, which we predicted would better discriminate patient groups than the relatively simpler tasks.

**Results:** Differences existed between groups on most tasks, but logistic regression revealed that the VPS discriminated the 2 groups better than the other nonmemory cognitive tests.

**Conclusions:** The VPS, a problem solving task assessing the cumulative burden of frontal and posterior damage is more

sensitive for detecting nonmemory impairments in MCI than other tasks. Future research will be needed to determine if impairment in the VPS is a sensitive predictor of progression to dementia or treatment response.

**Key Words:** mild cognitive impairment, problem solving, dementia, visuospatial, memory, language, executive function, Alzheimer disease

(*Cog Behav Neurol* 2007;20:44–47)

Mild cognitive impairment (MCI) is a condition characterized by impaired memory and preserved activities of daily living.<sup>1,2</sup> Patients with MCI are at significantly increased risk for developing dementia.<sup>3–5</sup> Some researchers propose MCI as the mildest end point on the spectrum of Alzheimer disease.<sup>4</sup> With the recent advances in the treatment options for Alzheimer disease, much attention has been directed at early recognition of Alzheimer disease for implementation of treatment. Therefore, one would wish to identify affected patients before the disease becomes fully manifested using a test that has minimal cost. The potential role of neuropsychologic testing has been demonstrated in identifying preclinical Alzheimer disease in community-based epidemiologic studies.<sup>6</sup>

Most common methods of testing for cognitive impairment suggestive of Alzheimer disease rely upon tests, which are commonly described as focusing on a few cognitive domains (language, memory, visuospatial function, etc) or batteries of combinations of such tests. However, all such tasks, regardless of how they are categorized, will use multiple cognitive domains.

Functional ability may be supported by compensatory mechanisms if individual cognitive domains are mildly impaired. Patients with Alzheimer disease have deficits in multiple domains and are therefore less able to compensate. Some researchers have suggested that tests assessing cognitive flexibility are more sensitive than other cognitive tests for detecting the early impairment in Alzheimer disease.<sup>7</sup> Cognitive flexibility is predominantly considered an integrated function of the frontal lobes,<sup>8–11</sup> and frontal lobe related findings are common in most forms of dementia, including Alzheimer disease.<sup>7,12</sup> It is proposed that the frontal lobe findings may be further

Received for publication November 7, 2006; accepted November 7, 2006.

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Funded by a "Seed Grant" from The Ohio State University Research Foundation. Dr Nagaraja is supported by an NIH grant (M01-RR-00034) awarded to The Ohio State University. Dr Scharre has grants from Janssen, Forest, Pfizer, Eisai, Ono, Fujisawa, Mitsubishi Pharma, and Sanofi-Synthelabo; he is a consultant for Forest, Janssen, and Pfizer; he is on the speaker's bureau for Janssen, Pfizer, Eisai, Abbott, and Astra-Zeneca. Dr Beversdorf has received grants from Pfizer and Eisai and Repligen; he is a consultant for Pfizer; he is on the speaker's bureau for Forest, Pfizer, and Eisai. Dr Beversdorf is also supported by NIH grants (NS045222 and DA15734).

Portions of this research were presented at the American Academy of Neurology, 2001.

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enhanced by disordered interactions between the frontal lobes and the impaired posterior cortical regions,<sup>7</sup> thus further diminishing the patient's ability to compensate.

As a result, we used a problem solving task, which includes cognitive flexibility and a visuospatial task with a multistep command. We will use this task to determine which patients with MCI are beginning to develop nonmemory impairments. This task has demonstrated impairments in patients with frontal lobe lesions, due to impaired strategy shifting (cognitive flexibility), and in patients with parietal lobe lesions, due to difficulty manipulating visual material,<sup>13</sup> which would seem optimal for examining the interaction of frontal and posterior cortical regions in this setting. Such a task may therefore result in a more sensitive assessment of the cumulative effect of the nonmemory cognitive impairments and thus help discriminate patients with stable isolated memory impairments from those at greatest risk for progression to dementia. Our hypothesis is that the visuospatial problem solving task (VPS) will be more sensitive for detecting nonmemory impairments in MCI than other tests of nonmemory impairment.

**METHOD**

**Participants**

Participants were considered for this study if they were referred to one of the authors (D.Q.B.) at the Ohio State University Memory Disorders Clinic for a chief complaint of memory loss and if family members reported no impairment of activities of daily living. MCI participants were 26 consecutive patients referred in this manner with a Clinical Dementia Rating (CDR)<sup>14,15</sup> score of 0.5, and a Folstein Mini-Mental Status Examination (MMSE)<sup>16</sup> score of at least 24. Controls were 20 age and education level matched individuals without cognitive impairment as initially judged independently by both the clinician and a reliable friend or family member. Fourteen participants with mild-to-moderate dementia (CDR = 1 to 2, MMSE = 17-23, mean = 20.4, standard deviation = 2.2) were also tested. Table 1 shows the subject demographic variables. All participants were consented before participation in accordance with the Institutional Review Board of The Ohio State University.

**Procedure**

All patients were given the MMSE to assess global function across several domains including memory, and the Hopkins Verbal Learning Test (HVLT)<sup>17</sup> to assess

verbal memory, and also nonmemory tasks including the Boston Naming Test (BNT)<sup>18</sup> [primarily considered as assessing language (naming)], Rey Complex Figure copying (Rey CFT)<sup>19-21</sup> (primarily considered as assessing visuospatial ability), a series of anagrams (primarily considered as assessing verbal and divergent cognitive flexibility)<sup>22</sup> (Rearrange these letters to form an English word: OGRF, RDWO, FALC, LANI, MHBTU, HTRSI, DSLEI, TMLAE), and the visuospatial problem solving battery (VPS) adapted from the "matchstick" problems<sup>13,23</sup> (Fig. 1). Patients were given sample problems for the VPS and anagrams before testing, and were subsequently allowed to see examples of solutions for these samples, so that they understood the tasks (Fig. 1). As with our previous work with these types of tasks,<sup>22</sup> solution latencies were recorded as the measure of performance for both VPS and the anagrams test, and a maximum time of 4 minutes was allowed for each VPS problem, and 2 minutes for each anagram. All measures were administered in 1 hour testing sessions.

**RESULTS**

Fourteen mild-to-moderate dementia patients were largely unable to complete the VPS task. Eleven of the patients failed to solve any problems, and an average of less than 1 VPS problem (0.79) was solved by the mild-to-moderately impaired group. In contrast, all of the control subjects solved at least 3 of the 6 problems (mean = 5.05, SD = 1.00) with 8 of these subjects solving all 6 correctly. The mild-to-moderate dementia patients were thus excluded from further analysis.

Performance of MCI patients on these tasks was compared with control subjects using independent samples *t* tests (Table 2). MCI patients demonstrated significantly worse performance on all tasks aside from anagrams, which demonstrated a trend towards a worse performance in MCI patients.

Nonmemory tasks showing significant differences were used in logistic regression models with single and multiple predictors to determine the discriminatory power of these tasks. As a single predictor, each of the BNT (*P* = 0.029), Rey CFT (*P* = 0.012), and VPS (*P* = 0.002) are significant, with increasing ability to predict in that order (*R*<sup>2</sup> for VPS = 0.24 and 0.13 for the other 2). In 2 predictor models with VPS as a predictor it was always significant (*P* < 0.015) whereas the other factor (BNT, *P* = 0.353 or Rey CFT, *P* = 0.300) was not. The associated *R*<sup>2</sup> values in both models were 0.26. Sum of

**TABLE 1.** Patient Demographics

	MCI	Controls	Dementia	Sig. (MCI vs. Controls)
N	26	20	14	
Sex	12 male, 14 female	6 male, 14 female	3 male, 9 female	
Age (y)	67.5 (SD 8.9)	68.0 (SD = 8.3)	72.4 (SD = 7.1)	t(44) = 0.194, <i>P</i> = ns
Education level (y)	14.4 (SD = 2.8)	14.4 (SD = 2.8)	13.8 (SD = 3.4)	t(44) = 0.028, <i>P</i> = ns

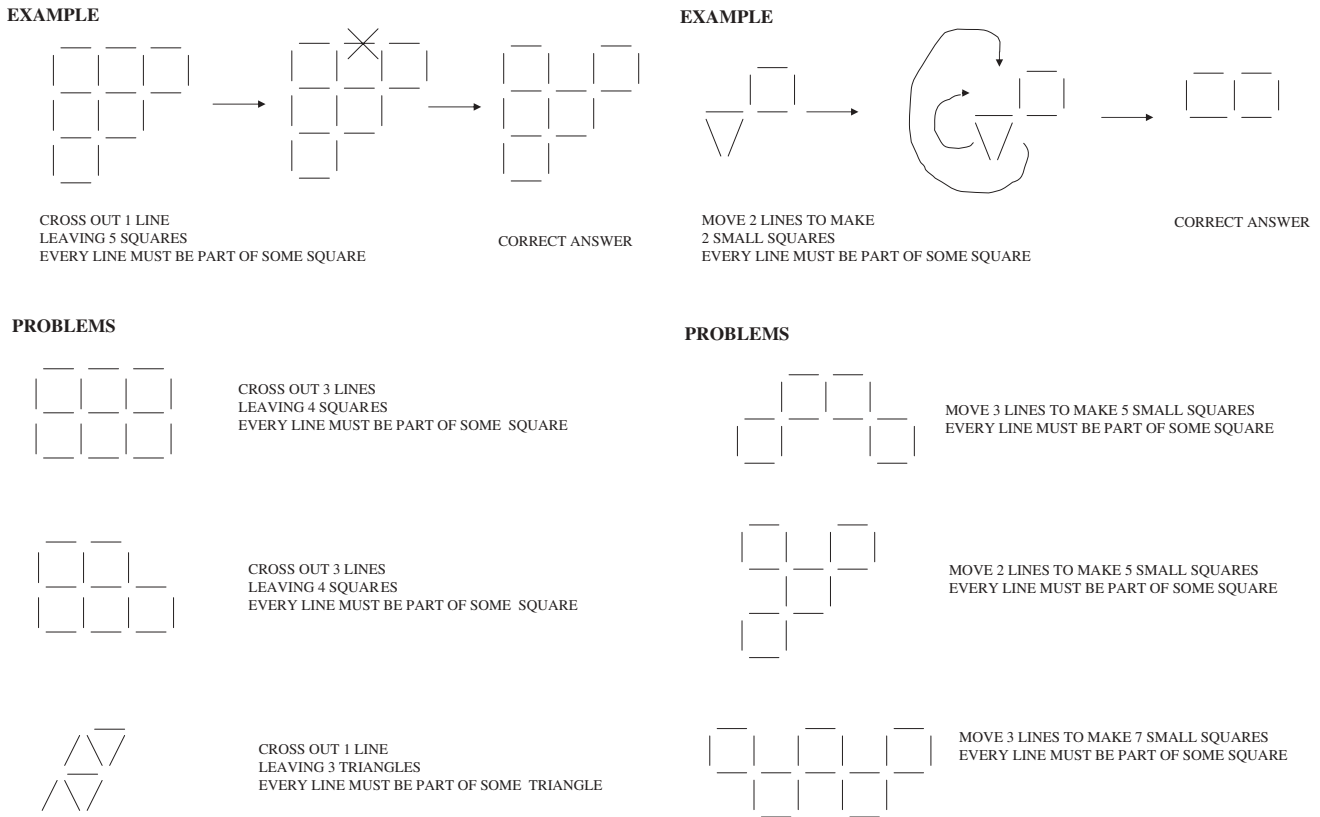


FIGURE 1. Visuospatial problem solving task and sample tasks.

the standardized VPS (inverted), Rey CFT, and BNT was a significant predictor ( $P = 0.0013$ ) with a model  $R^2 = 0.28$ , improving upon each of the individual predictors. When combined with education, the model  $R^2$  increased to 0.33, with the sum of scores being a highly significant predictor ( $P = 0.0007$ ) and education level showed a trend ( $P = 0.09$ ). SAS JMP (Version 5.1; SAS Institute, Cary, NC) was used for these analyses. A stepwise discriminant function analysis was also performed including VPS, Rey CFT, and BNT to determine the relative strength in discriminating between the groups. At the first step, the VPS was entered into the equation, which significantly discriminated between the groups ( $\chi^2 = 17.1, P < 0.0005$ ). Neither of the other variables met required tolerance limits, and thus failed to provide any additional discriminatory power.

**DISCUSSION**

Since participants were referred for memory loss and met our criteria for MCI, we expected that the HVLТ (verbal memory task) and MMSE (which includes a significant memory component—both orientation and verbal memory) would yield significant impairment in our MCI patients. However, we wished to detect which MCI patients are developing impairments beyond the domain of memory, to potentially detect greatest risk for the development of dementia. Among those nonmemory tasks that demonstrated a significant difference between groups, logistic regression showed that the VPS provided additional discriminatory power beyond the other tasks. Furthermore, with stepwise discriminant function analysis, after entering the VPS, which significantly discriminated between groups, neither of the other tasks provided

**TABLE 2.** Comparison Between Groups on Each Task

	MCI	Controls	Sig.
MMSE	26.1 (SD 1.7)	28.8 (SD 1.4)	t(44) = 5.643, $P < 0.0005$
HVLТ	14.8 (SD 5.9)	25.0 (SD 5.7)	t(44) = 5.905, $P < 0.0005$
Rey CFT	18.8 (SD 6.6)	24.0 (SD 5.1)	t(44) = 2.882, $P < 0.006$
BNT	48.1 (SD 10.0)	54.4 (SD 5.0)	t(44) = 2.547, $P < 0.009$
VPS	881.0 (SD 360.7)	493.7 (SD 241.5)	t(44) = 4.137, $P < 0.0005$
Anagrams	471.7 (SD 192.9)	389.5 (SD 120.1)	t(44) = 1.669, $P < 0.084$

any additional discriminatory power. Therefore, the VPS seems to be more sensitive for nonmemory impairments than the other tests. Furthermore, the VPS task is sufficiently sensitive that patients with mild-to-moderate dementia (MMSE 17-23) were largely unable to perform the task. We cannot exclude the possibility that the timed nature of the VPS may have contributed to our findings. However, the anagrams were also timed and were not as sensitive for discriminating the 2 groups as the VPS. Furthermore, the limited nature of the neuropsychologic battery used also serves as a limitation in this pilot study.

Functional ability may be maintained by using compensatory mechanisms when individual cognitive domains are mildly affected, but patients with Alzheimer disease have significant deficits in multiple domains and are therefore less able to compensate. While cognitive flexibility is often considered a frontal lobe function,<sup>8-11</sup> tests assessing cognitive flexibility have been proposed as sensitive for detecting early impairment in Alzheimer disease.<sup>7</sup> Frontal lobe findings remain common in Alzheimer disease,<sup>7,12</sup> likely due to frontal lobe impairments being augmented by disordered interaction between the frontal lobes and posterior cortical regions.<sup>7</sup> The VPS was designed as a task assessing the cumulative burden of frontal and posterior damage, including cognitive flexibility (ability to shift strategy), within one task,<sup>13</sup> thus, we propose, enabling a more sensitive assessment of the cumulative effect of the nonmemory cognitive impairments. Therefore, the VPS may provide a sensitive and inexpensive test for the presence of nonmemory impairments in MCI. Future work will be needed to examine whether the VPS, or other tasks designed in a similar manner (tasks assessing the cumulative burden of frontal and posterior damage), are sensitive predictors of progression to dementia in MCI patients. Future work will also be needed to determine whether the VPS is a more sensitive measure of response to Alzheimer drugs such as cholinesterase inhibitors in MCI.

## REFERENCES

- Petersen RC, Doody R, Kurz A, et al. Current concepts in mild cognitive impairment. *Arch Neurol.* 2001;58:1985-1992.
- Petersen RC, Smith GE, Waring SC, et al. Mild cognitive impairment: clinical characterization and outcome. *Arch Neurol.* 1999;56:303-308.
- Bennett DA, Wilson RS, Schneider JA, et al. Natural history of mild cognitive impairment in older persons. *Neurology.* 2002;59:198-205.
- Morris JC, Storandt M, Miller JP, et al. Mild cognitive impairment represents early-stage Alzheimer disease. *Arch Neurol.* 2001;58:397-405.
- Storandt M, Grant EA, Miller JP, et al. Rates of progression in mild cognitive impairment and early Alzheimer's disease. *Neurology.* 2002;59:1034-1041.
- Jacobs DM, Sano M, Dooneief G, et al. Neuropsychological detection and characterization of preclinical Alzheimer's disease. *Neurology.* 1995;45:957-962.
- Albert MS. Cognitive and neurobiological markers of early Alzheimer's disease. *Proc Natl Acad Sci.* 1996;93:12547-12551.
- Vilki J. Cognitive flexibility and mental programming after closed head injuries and anterior and posterior cerebral excisions. *Neuropsychologia.* 1992;30:807-814.
- Karnath HO, Wallech CW. Inflexibility of mental planning: a characteristic disorder with prefrontal lobe lesions. *Neuropsychologia.* 1992;30:1011-1016.
- Eslinger PJ, Grattan LM. Frontal lobe and frontal-striatal substrates for different forms of human cognitive flexibility. *Neuropsychologia.* 1993;31:17-28.
- Duncan J, Burgess P, Emslie H. Fluid intelligence after frontal lobe lesions. *Neuropsychologia.* 1995;33:261-268.
- Beverdort DQ, Heilman KM. Facilitory paratonia and frontal lobe functioning. *Neurology.* 1998;51:968-971.
- Miller LA, Tippett LJ. Effects of focal brain lesions on visual problem-solving. *Neuropsychologia.* 1996;34:387-398.
- Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology.* 1993;43:2412-2414.
- Berg L. Clinical Dementia Rating (CDR). *Psychopharmacol Bull.* 1988;24:637-639.
- Folstein ME, Folstein SE, McHugh PR. Mini-mental state. *J Psychiatr Res.* 1975;12:189-198.
- Brandt J. The Hopkins Verbal Learning Test: development of a new verbal memory test with six equivalent forms. *Clin Neuropsychol.* 1991;5:125-142.
- Kaplan EF, Goodglass H, Weintraub S. *The Boston Naming Test.* 2nd ed. Philadelphia: Lea & Febiger; 1983.
- Rey A. L'examen Psychologique dans les cas d'encéphalopathie traumatique. *Arch Psychol.* 1944;28:286-340.
- Osterieth PA. Le test de copie d'une figure complexe. *Arch Psychol.* 1944;30:206-356.
- Corwin J, Bylsma FW. Translations of excerpts from André Rey's Psychological examination of traumatic encephalopathy and P.A. Osterieth's The Complex Figure Copy Test. *Clin Neuropsychol.* 1993;7:3-15.
- Beverdort DQ, Hughes JK, Steinberg BA, et al. Noradrenergic modulation of cognitive flexibility in problem solving. *NeuroReport.* 1999;10:2763-2767.
- Guilford LP. *The Nature of Human Intelligence.* New York: McGraw-Hill; 1967.