Evaluation of visual recognition memory in MCI patients

E. Barbeau, MSc; M. Didic, MD; E. Tramoni, MSc; O. Felician, MD; S. Joubert, PhD; A. Sontheimer, MSc; M. Ceccaldi, MD, PhD; and M. Poncet, MD, PhD

Abstract—*Background:* Neurofibrillary tangles seen early in Alzheimer disease (AD) initially appear in a subregion of the perirhinal cortex. In the monkey, damage to the perirhinal cortex impairs performance on visual recognition memory tasks. The authors evaluated impairment of visual recognition memory as a potential early diagnostic marker of AD. *Methods:* The authors developed a visual delayed matching-to-sample task (DMS48) designed to assess visual recognition memory in humans. Twenty-three patients fulfilling the criteria of amnestic mild cognitive impairment (MCI) (mean Mini-Mental State Examination [MMSE]: 26.6, SD = 1.6) were recruited. All underwent a full neuropsychological evaluation, which included the Free and Cued Selective Reminding (FCSR) test. Their performance was compared with that of 10 patients with mild AD, 20 patients with moderate AD, 20 patients with Parkinson disease (PD), and 40 age-matched controls**.** *Results:* Control subjects and patients with PD performed close to ceiling. Patients with mild AD had very low scores, while patients with moderate AD answered at random. MCI patients obtained scores that were between those of control subjects and patients with mild AD (78%, SD = 16%). MCI patients who failed on the DMS48 had lower scores on free recall ($p < 0.05$) and received less benefit from cueing ($p < 0.01$) on the FCSR than the other MCI, suggesting a profile of genuine memory impairment related to medial temporal lobe lesions. *Conclusion:* The DMS48, a test of visual recognition memory, is impaired early in the course of patients with MCI. Further studies are necessary to determine whether the evaluation of visual recognition memory may contribute to the identification of patients with AD.

NEUROLOGY 2004;62:1317–1322

The major neuropathologic hallmarks of Alzheimer disease (AD) consist of neuritic plaques and neurofibrillary tangles (NFT). Although the neuropathologic criteria that remain in use for the diagnosis of AD are based on the distribution of neuritic plaques,[1,2] clinical symptoms have been shown to correlate with the distribution of NFT.[3,4] NFT initially develop in a subregion of the perirhinal cortex known to correspond to Brodmann area 35, located on the medial wall of the collateral sulcus.[5,6] In a second stage, NFT spread medially to the entorhinal cortex before reaching the hippocampal formation.[4,5] NFT then progress to other regions of the brain while their number in Brodmann area 35 increases. This hierarchical model appears to reflect NFT progression in most cases.[7,8]

Several studies in monkeys have shown that lesions of the perirhinal cortex result in severely impaired performance on visual recognition memory tasks,[9,10] while hippocampal damage does not impair performance at all[11] or only leads to mild deficits.[10] The crucial role of the perirhinal cortex in visual recognition memory is also compatible with data collected in human case studies.[12-14]

The fact that NFT first appear in the perirhinal cortex in AD in conjunction with the role of this structure in visual recognition memory led us to hypothesize that subjects with incipient AD would show impaired performance on visual recognition memory tasks. Testing recognition memory could thus prove to be useful in early detection of AD. In order to test this hypothesis, we studied the performance of three groups of patients on such a task: patients with amnestic mild cognitive impairment (MCI), who are patients at high risk for AD, and patients with mild and moderate probable AD. The performance of these groups was compared with that of patients with Parkinson disease (PD) and age-matched control subjects.

Methods. *Description of the visual recognition memory task (DMS48).* The DMS48 is based on the classic delayed matching-to-sample task used in nonhuman primates, in which monkeys have to choose between a target and a distractor during recognition. In the DMS48, stimuli consist of colored drawings divided into three types of items (figure 1): 1) abstract items—targets and distractors are abstract patterns that cannot be verbalized; 2) paired items—targets and distractors are concrete objects belonging to the same semantic category and with similar shape, color, and name to prevent the use of verbal strategies; and 3) unique items—targets and distractors are dissimilar concrete objects. During the encoding phase, all subjects were asked to consecutively look at 48 pictures and to say whether each contained more or less than three colors. This was followed by a 2-minute verbal fluency interfering task. Then, a recognition task was completed with a first set of 48 distractors (Set 1). Each target was shown simultaneously with a distractor, presented in equal proportion on either the left or the right side of the sheet, and the subject was

From the Laboratoire de Neurophysiologie et Neuropsychologie, Inserm EMI-U 9926, Univ. Mediterranee; and Service de Neurologie et Neuropsychologie, AP-HM Timone, Marseille, France.

Supported by INSERM, AP-HM PHRC 2001/54, and a grant from France Alzheimer (E.B.).

Received May 13, 2003. Accepted in final form December 19, 2003.

Address correspondence and reprint requests to Dr. Emmanuel Barbeau, Laboratoire de Neurophysiologie et de Neuropsychologie, Inserm EMI-U 9926, Faculté de Médecine, 27, boulevard Jean Moulin, 13385 Marseille cedex 05, France; e-mail: emmanuel.barbeau@medecine.univ-mrs.fr

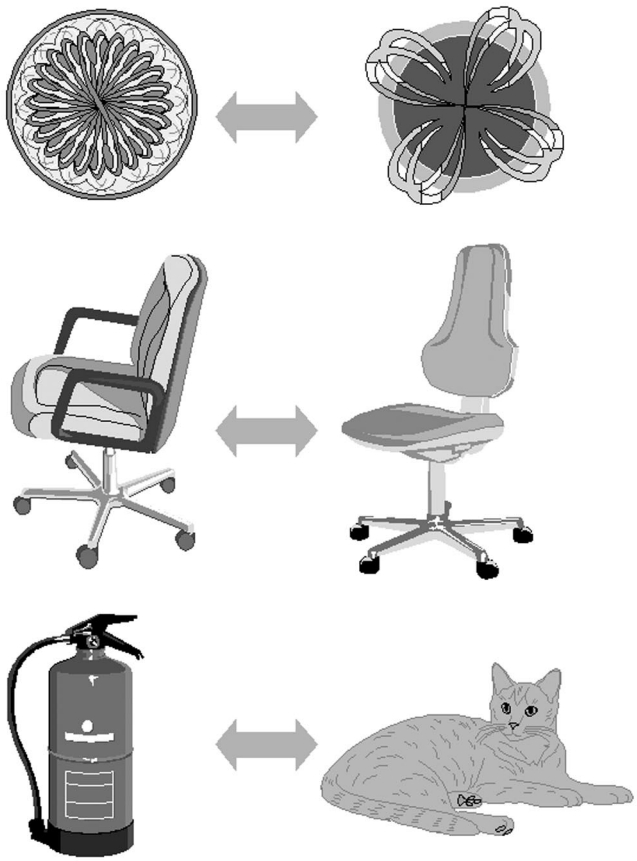

Figure 1. Examples of stimuli used in the DMS48 (in color in the original format).

asked to identify the target, if necessary using forced-choice recognition. Without prior warning, a second recognition task was conducted 1 hour later with a different set of distractors (Set 2). Half of the targets were displaced from the left to the right side of the sheet between Set 1 and 2. In this study, most results are discussed in reference to Set 2, as we were mainly interested in studying delayed recognition.

Each subject's performance was expressed as a percentage of correct answers (level of chance: 50%, recognition of all targets: 100%). Time of completion of the whole test (encoding phase, Set 1 and 2) was also recorded.

Free and Cued Selective Reminding test (FCSR). We used the FCSR as the reference test to evaluate memory. This verbal memory test has been extensively used in the neuropsychological assessment of elderly patients and has been shown to be extremely useful in detecting subjects at high risk to evolve toward dementia.[15-18] In the FCSR, encoding is controlled for by asking the subject to identify each of the words to be remembered by pointing and reading aloud in response to its semantic category (the American FCSR version uses pictures of objects during the initial encoding phase,[15] while the French version[19] is purely verbal). All 16 words have to be retrieved at immediate cued recall before memory assessment begins. Recall is first assessed through free recall, then through cued recall for the missing words. This procedure is repeated three times in order to give the subject the opportunity to improve performance[20] and provides two main scores: free and total (free + cued) recall. The FCSR has been shown to discriminate an apparent memory impairment (subjects impaired on free recall but benefiting from repetition and cueing to normalize their performance) from a genuine memory impairment (subjects incapable of improving their performance although words are repeated and cued).[15] An apparent memory impairment is thought to be due to the use of inefficient strategies or impaired attention and has been related to dysfunction of the frontostriatal loop,[15,17] whereas a genuine memory impairment is considered as a true memory defect and has been related to impaired storage consecutive to medial temporal lobe lesions.[17,20,21] In the present study, we calculated an index of cueing efficiency in order to discriminate between these two types of memory impairment; for example, cueing efficiency is 80% if 8 of 10 words that were not recalled are retrieved after cueing.

Subjects. Forty control subjects, with no neurologic or psychiatric medical history, were included on a voluntary basis and after informed consent. All subjects had Mini-Mental State Examination[22] (MMSE) scores above or equal to 27. Their ages ranged from 60 to 79 years (mean = 69.7 ± 5.6).

We included 23 patients meeting criteria for amnestic MCI.[23] All patients were recruited from a memory clinic and underwent a full examination by a neurologist as well as a neuropsychologist. Activities of daily living were normal, as assessed through the Instrumental Activities of Daily Living (IADL).[24] All patients had a memory impairment of insidious onset and underwent a CT scan or MRI or EEG if necessary, as well as routine biologic screening, thus excluding nondegenerative causes of memory impairment. All patients underwent standard neuropsychological assessment. In order to rule out visual perceptual problems that could interact with DMS48 performance, all patients completed a visual discrimination task,[25] a naming task (line drawings of objects),[26] and a task assessing executive functions using visual stimuli (the matrices subtest of the Wechsler Adult Intelligence Scale–III[27]). Memory was assessed through the FCSR. Patients were included into the MCI group if their FCSR score was at least 1.5 SD below the mean on free delayed recall. This cut-off score, which allows including in the MCI population patients with very mild memory impairment, was chosen as suggested.[28] Patients with a clear deficit in one or more cognitive domains other than memory were excluded. Mean MMSE score of the MCI group was 26.6 ± 1.6. Mean age ($t = -0.7$, $p = 0.46$) and level of education ($t = 0.6$, $p = 0.56$) did not differ from those of control subjects (table 1).

We also included 30 patients meeting National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association[29] criteria for probable AD. Based on the severity of the disease, these patients were divided in two groups. The mild AD group consisted of 10 patients with a mean MMSE score of 21.7 ± 0.5 and the moderate AD group of 20 patients with a mean MMSE score of 17.8 ± 3.4. Twenty patients with PD were also recruited. Their mean age ($t = -0.8$, $p = 0.41$), educational level ($t = -1.0$, $p = 0.30$), and MMSE

Table 1 *Study group characteristics*

Population	n	Age, y	% Male	Education, y	MMSE
Controls	40	69.7 ± 5.6	38	10.6 ± 2.6	28.4 ± 1.0
MCI	23	71.0 ± 8.6	30	10.2 ± 3.3	26.6 ± 1.6
mildAD	10	74.6 ± 5.8	33	8.6 ± 1.8	21.7 ± 0.5
modAD	20	77.1 ± 5.7	45	7.6 ± 1.6	17.8 ± 3.4
PD	20	68.6 ± 10.6	30	9.1 ± 3.1	25.1 ± 2.9

Values are presented as mean ± SD.

MMSE = Mini-Mental State Examination; MCI = mild cognitive impairment; AD = Alzheimer disease; PD = Parkinson disease.

Table 2 *Results on the DMS48*

Population	DMS48 Set 1	DMS48 Set 2
Controls	97 ± 4	98 ± 3
MCI	80 ± 15	78 ± 16
mildAD	65 ± 17	62 ± 14
modAD	53 ± 7	53 ± 4
PD	94 ± 4	96 ± 3

Values are mean % ± SD.

MCI = mild cognitive impairment; AD = Alzheimer disease; PD = Parkinson disease.

score (t = 1.9, $p = 0.07$) did not differ from those of the MCI group.

Statistical analysis. Two-tailed Student *t*-tests were used for between-group comparisons when there were 20 or more subjects under the assumption of normal distribution (Shapiro-Wilks test for the MCI population, $p = 0.28$). Nonparametric Mann-Whitney *U* tests were used to compare the mild AD group (n = 10) with the other groups and for within-group comparisons for the MCI. Level of significance was set to $p = 0.05$. Influence of independent factors was assessed using univariate analysis of variance and linear regression analysis. The dependent variable was performance to Set 2 in most analyses.

Results. Results on the DMS48 for all groups for Set 1 and 2 are shown in table 2. Figure 2 shows the results for Set 2 only. Control subjects performed at ceiling. The MCI group's performance was significantly lower than that of control subjects (t = 7.8, $p < 0.001$). The mild AD group performed worse than the MCI group (U = 47.5, $p < 0.01$), while the moderate AD group performed even lower (U = 54, $p < 0.05$), at the level of chance. Although the PD group obtained lower results than controls (t = 2.8, $p < 0.01$), they performed much better than the patients with MCI (t = 4.9, $p < 0.001$).

Univariate analysis of variance revealed no effect of age, educational level, or interaction between these factors in the control group. A linear regression analysis was used to evaluate the influence of the following independent variables on the DMS48 in the MCI group: FCSR total delayed recall as an index of memory performance, MMSE score as an index of general cognitive level, category fluency score and matrices scaled-score as an index of the executive functions. Only the FCSR was correlated with performance on the DMS48 (t = 4.4, $p < 0.01$; partial correlation coefficient: rho = 0.78).

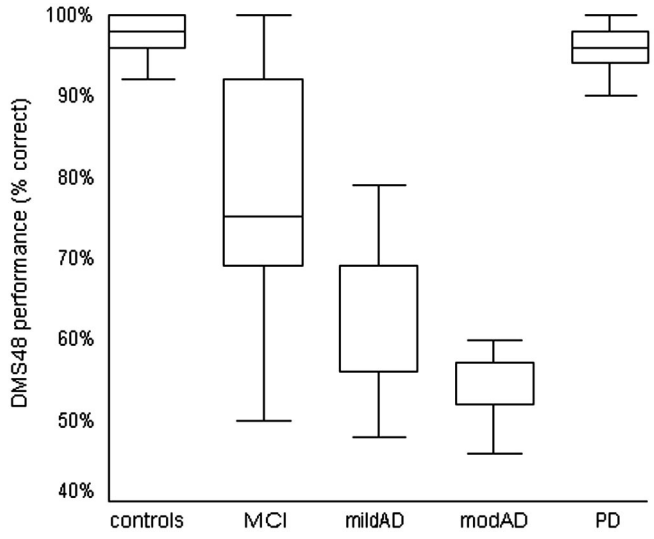

Figure 2. Results on the DMS48 after a 1-hour delay (Set 2). The boxes show the limits of the 25th and 75th percentile; the line in the box shows the median; the bottom and upper horizontal lines show the most extreme performance of each group.

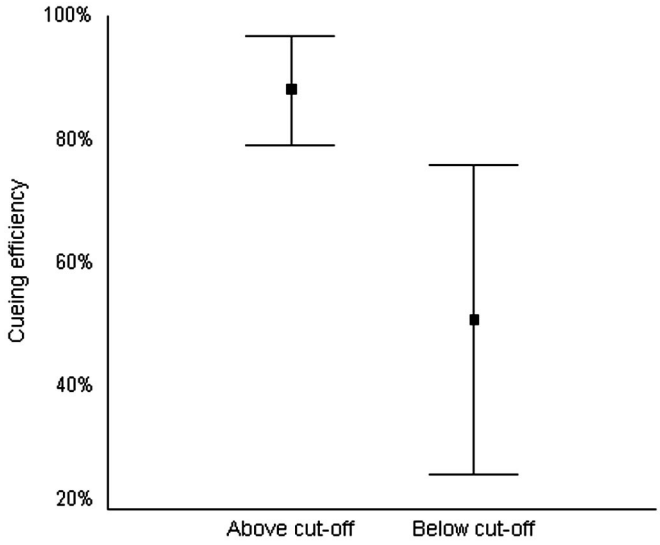

Figure 3. Mean Free and Cued Selective Reminding test cueing efficiency for the MCI patients with normal performance (above cut-off, n = 5) compared with those with impaired performance (below cut-off, n = 18) on the DMS48 ($p < 0.01$*). Vertical lines show standard deviations.*

A wide dispersion of performance was observed in the MCI group. Of the MCI patients, 78% (18/23) had impaired scores (1.5 SD below the mean). Further analysis indicated that 1) MCI patients impaired on the DMS48 had lower delayed free recall scores on the FCSR than the other MCI (U = 12, $p < 0.05$), 2) they also benefited significantly less from cueing on the FSCR (U = 11.5, $p < 0.01$, figure 3), 3) four out of the five MCI patients who succeeded on the DMS48 benefited from cueing to improve their total (free + cued) recall on the FCSR to reach the level of normal control subjects (the remaining MCI patient being 0.71 word below cut-off).

Table 3 shows the number of patients who succeeded and failed on both the DMS48 and total FCSR. Overall, 83% of MCI patients fell into the same category on both tests.

Table 3 *Categorization of MCI patients according to the DMS48 and FCSR total (free + cued) recall*

		DMS48	
		Impaired	Normal
Total FCSR (free + cued)	Impaired	15	1
	Normal	3	4

MCI = mild cognitive impairment; FCSR = Free and Cued Selective Reminding test.

Average time to complete the task. Control subjects completed the task in an average time of 10 minutes 32 seconds (SD = 3 minutes 2 seconds) for the three phases, contrasting with an average 14 minutes 54 seconds (SD = 5 minutes 32 seconds) for the MCI group.

Results by subgroup of stimuli. A within-group analysis showed that all patient groups as well as control subjects recognized the "unique" stimulus type significantly better than the two other types of stimuli. Mean recognition compared to that of control subjects was however impaired for all types of stimuli in the MCI group as well as in the mild AD and moderate AD groups ($p < 0.001$ for all comparisons). Further analyses on mean Z-score for each stimulus type in the MCI group indicated that the severity of impairment for the "unique" stimulus type was equivalent to that of the "abstract" stimulus type ($t = -0.7$, $p = 0.47$).

Discriminant validity. A cut-off score of 1.5 SD below the mean of control subjects for scores on delayed recognition correctly classified 92.5% of the control subjects, 85% of the patients with PD, and 100% of the patients with mild AD and probable AD.

Concurrent validity. As noted above, we found a strong correlation between the DMS48 and the FCSR. In order to evaluate their respective sensibility, we calculated the mean Z-score of each test in the MCI group, but no difference was found (paired-sample *t*-test, $t = -1.3$, $p = 0.19$).

Discussion. In the absence of an early diagnostic marker for AD, the development of neuropsychological tests as possible indicators for patients at risk to develop AD is a focus of intense research. We consequently developed a visual recognition memory task, the DMS48. Normal subjects made an average of only one single error over 48 trials to this task. Patients with amnestic MCI and two groups of patients with probable AD of increasing severity underwent the DMS48. All three groups were impaired when compared with controls. Also, performance significantly worsened from one group to the other. This contrasted with the performance of a group of patients with PD, who performed significantly better than the MCI group (2 errors versus 11 for the MCI), almost as well as control subjects.

All patients with probable AD and 78% of the MCI patients were impaired on the DMS48. Based on studies on visual recognition memory in the monkey, this task was designed to detect medial temporal and perirhinal dysfunction in particular, as it has been shown to be the site of early damage in AD. According to this hypothesis, MCI patients who fail the DMS48 are likely to have medial temporal lobe or perirhinal dysfunction and may thus be at higher risk to develop AD. Additional evidence to support this hypothesis comes from the fact that they obtained significantly lower scores on free recall and received less benefit from cueing on a verbal memory task than MCI patients who succeeded on the DMS48, thus suggesting a profile of genuine memory impairment[15] thought to be related to medial temporal lobe lesions.[17] Interestingly, MCI patients did not benefit from the "easy" condition of the test, which required learning visual targets that could also be verbalized and were different from distractors, suggesting a profound incapacity to store new information. Finally, a recent functional MRI study in mild AD showed that these patients failed to activate medial temporal lobes, and notably the entorhinal cortex, a subhippocampal region medial to the perirhinal cortex, while required to learn geometric shapes.[30]

The DMS48 was compared to the FCSR, which has been proven to be useful in identifying MCI patients who will ultimately evolve toward dementia. Congruence between both tests was 83% of patients classified in the same categories. Furthermore, we found a high correlation between both tests and an evaluation of concurrent validity did not find any difference between them. These results suggest that the DMS48 is as useful as the FCSR, with the major difference being that it enables assessing visual, as opposed to verbal, memory. Results also suggest that MCI patients failing both tests should be considered at very high risk to evolve toward probable AD.

Four MCI patients obtained normal results to the DMS48 and normal result to the total FCSR (these patients were impaired to free delayed recall [inclusion criteria] but normalized their performance with cueing). They can thus be considered as having an apparent memory impairment related to another form of dysfunction than AD. Four patients were not classified the same way by both tests (three were impaired on the DMS48 and were normal on the total FCSR, while one patient showed the reversed pattern). Further analyses indicated that these patients were very mildly impaired on one test and obtained low, albeit normal, score on the other. A plausible hypothesis concerning these patients is that they were assessed very early in the course of the disease (below test sensibility threshold).

The performance on the DMS48 was not related to the general cognitive level of the patient. Although patients with PD had an average MMSE score that was lower than that of the MCI patients, their performance on the DMS48 was much better. This result was confirmed by a linear regression analysis, which showed that performance on the DMS48 was not related to the global cognitive level or to executive functions. The DMS48 thus seems relatively independent from attentional/executive processes.

Our results are consistent with findings of other studies using tasks that assess recognition memory in patients with probable AD. In a study that used a modified matching-to-sample task with intervening stimuli, patients with AD performed consistently lower than patients with PD and it was noted that their "content" recognition abilities were low.[31] The recognition memory subtest of the Rey Auditory Verbal Learning Test was one of the two best neuropsychological predictors out of 10 to distinguish AD from vascular dementia.[32] Using the Doors and People Test[33] in a group of patients with early AD, it was

demonstrated that both recall and recognition processes were equally impaired.[34] Another study evaluated word recall and recognition memory in a group of AD patients 6 years before diagnosis.[35] Performance in both domains was impaired and predicted dementia in a logistic regression analysis, whereas the digit span, for example, did not.

To our knowledge, recognition memory has rarely been studied in patients with MCI. However, in one of the pioneering studies on the concept of MCI,[36] recognition memory was one of the four predictors of decline in subjects with MCI, with a sensitivity of 85.7% and a specificity of 100%. These studies thus suggest that recognition memory is impaired in AD, probably early in the course of the disease. However, recognition memory per se, assessed with an adequate test containing a sufficient number of items as we did in this study, has never been the specific focus of studies in AD. This might explain why these findings on recognition memory have gone relatively unnoticed.

The DMS48 has been extensively used in our memory clinic and has proven to be helpful: it takes little time, is easy to administer, and causes minimal distress for the patient. The patient is always able to provide an answer by choosing one of the pictures, thus avoiding the stress that amnesic patients experience when asked to recall lists of words that they have forgotten. Above all, in conjunction with the FCSR, it provides a decisive evaluation of memory status. The DMS48 provides evidence on the nature of the memory impairment in a routine neuropsychological assessment and assesses visual memory whereas most tests rely on verbal strategies.

In a broader perspective, evaluating visual rather than verbal memory might be useful in cross-cultural studies or in multicultural societies. Furthermore, the DMS48 consists of Set 1, administered 3 minutes after encoding, and Set 2, assessing delayed recognition 1 hour later. There was little quantitative difference between both sets, suggesting that limiting the test to Set 1 for the purpose of clinical trials could shorten the DMS48. A short form of the test could thus be completed in about 10 minutes at the most.

The main limitation of our study is that we were not able to obtain results on the DMS48 in MCI patients who later developed confirmed AD. We also did not use complementary paraclinical data to provide further evidence of probable early AD within the MCI group. Most of our conclusions are thus based upon current knowledge about the neural basis of visual recognition memory and the early pathologic lesions of AD, along with the assessment of visual recognition memory in subjects with potential or probable degenerative processes. Further analysis, using longitudinal follow-up and other complementary paraclinical data, will be necessary to determine the predictive value of the DMS48 in the diagnosis of probable AD at an early stage of the disease process.

Acknowledgment

The authors thank Drs. E. Kaphan and L. Feuillet for referring patients with PD.

References

1. Khachaturian ZS. Diagnosis of Alzheimer's disease. Arch Neurol 1985; 42:1097–1105.
2. Mirra SS, Heyman A, McKeel D, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part II. Standardization of the neuropathologic assessment of Alzheimer's disease. Neurology 1991; 41:479–486.
3. Arriagada PV, Growdon JH, Hedley-Whyte ET, Hyman BT. Neurofibrillary tangles but not senile plaques parallel duration and severity of Alzheimer's disease. Neurology 1992;42:631–639.
4. Delacourte A, David JP, Sergeant N, et al. The biochemical pathway of neurofibrillary degeneration in aging and Alzheimer's disease. Neurology 1999;52:1158–1165.
5. Braak H, Braak E. Neuropathological stageing of Alzheimer-related changes. Acta Neuropathol (Berl) 1991;82:239–259.
6. Van Hoesen GW, Hyman BT, Damasio AR. Entorhinal cortex pathology in Alzheimer's disease. Hippocampus 1991;1:1–8.
7. Gertz HJ, Xuereb J, Huppert F, et al. Examination of the validity of the hierarchical model of neuropathological staging in normal aging and Alzheimer's disease. Acta Neuropathol (Berl) 1998;95:154–158.
8. Galton CJ, Patterson K, Xuereb JH, Hodges JR. Atypical and typical presentations of Alzheimer's disease: a clinical, neuropsychological, neuroimaging and pathological study of 13 cases. Brain 2000;123:484–498.
9. Meunier M, Bachevalier J, Mishkin M, Murray EA. Effects on visual recognition of combined and separate ablations of the entorhinal and perirhinal cortex in rhesus monkeys. J Neurosci 1993;13:5418–5432.
10. Squire LR, Zola SM. Structure and function of declarative and nondeclarative memory systems. Proc Natl Acad Sci USA 1996;93:13515–13522.
11. Murray EA, Mishkin M. Object recognition and location memory in monkeys with excitotoxic lesions of the amygdala and hippocampus. J Neurosci 1998;18:6568–6582.
12. Aggleton JP, Shaw C. Amnesia and recognition memory: a re-analysis of psychometric data. Neuropsychologia 1996;34:51–62.
13. Vargha-Khadem F, Gadian DG, Watkins KE, Connelly A, Van Paesschen W, Mishkin M. Differential effects of early hippocampal pathology on episodic and semantic memory. Science 1997;277:376–380.
14. Mayes AR, Holdstock JS, Isaac CL, Hunkin NM, Roberts N. Relative sparing of item recognition memory in a patient with adult-onset damage limited to the hippocampus. Hippocampus 2002;12:325–340.
15. Grober E, Buschke H, Crystal H, Bang S, Dresner R. Screening for dementia by memory testing. Neurology 1988;38:900–903.
16. Grober E, Lipton RB, Hall C, Crystal H. Memory impairment on free and cued selective reminding predicts dementia. Neurology 2000;54: 827–832.
17. Pillon B, Deweer B, Michon A, Malapani C, Agid Y, Dubois B. Are explicit memory disorders of progressive supranuclear palsy related to damage to striatofrontal circuits? Comparison with Alzheimer's, Parkinson's, and Huntington's diseases. Neurology 1994;44:1264–1270.
18. Boeve B, McCormick J, Smith G, et al. Mild cognitive impairment in the oldest old. Neurology 2003;60:477–480.
19. Ergis A-M, Van der Linden M, Deweer B. Investigation of memory performance with a cued recall test in Alzheimer's disease. Revue Neuropsychol 1994;4:47–68.
20. Petersen RC, Smith GE, Ivnik RJ, Kokmen E, Tangalos EG. Memory function in very early Alzheimer's disease. Neurology 1994;44:867–872.
21. Dubois B. "Prodromal Alzheimer's disease": a more useful concept than mild cognitive impairment? Curr Opin Neurol 2000;13:367–369.
22. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198.
23. Petersen RC, Doody R, Kurz A, et al. Current concepts in mild cognitive impairment. Arch Neurol 2001;58:1985–1992.
24. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179–186.
25. Benton A, Sirvan A, De Hamsher S, Varney N, Spreen O. Facial recognition. New York: Oxford University Press, 1983.
26. Deloche G, Hannequin D. Test de dénomination orale d'images DO80. Paris: Les Editions du Centre de Psychologie Appliquée, 1997.
27. Wechsler D. Echelle d'Intelligence de Wechsler pour Adulte III (WAIS-III). Paris: Les éditions du Centre de Psychologie Appliquée, 2000.
28. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 1999;56:303–308.

29. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984; 34:939–944.
30. Kato T, Knopman D, Liu H. Dissociation of regional activation in mild AD during visual encoding: a functional MRI study. Neurology 2001;57: 812–816.
31. Sagar HJ, Sullivan EV, Gabrieli JD, Corkin S, Growdon JH. Temporal ordering and short-term memory deficits in Parkinson's disease. Brain 1988;111:525–539.
32. Tierney MC, Black SE, Szalai JP, et al. Recognition memory and verbal fluency differentiate probable Alzheimer disease from subcortical ischemic vascular dementia. Arch Neurol 2001;58:1654–1659.
33. Baddeley A, Emslie H, Nimmo-Smith I. Doors and people. A test of visual and verbal recognition. Bury ST Edmunds: Thames Valley Test Company, 1994.
34. Greene JD, Baddeley AD, Hodges JR. Analysis of the episodic memory deficit in early Alzheimer's disease: evidence from the Doors and People Test. Neuropsychologia 1996;34:537–551.
35. Backman L, Small BJ, Fratiglioni L. Stability of the preclinical episodic memory deficit in Alzheimer's disease. Brain 2001;124:96–102.
36. Flicker C, Ferris SH, Reisberg B. Mild cognitive impairment in the elderly: predictors of dementia. Neurology 1991;41:1006–1009.