Sensitivity and specificity of the Mini-Mental State Exam in the diagnosis of dementia

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The Mini-Mental State Exam (MMSE) is a brief cognitive test that assesses several cognitive domains, such as orientation, attention, concentration, memory, language, and constructional abilities. While the MMSE was found to be valid and reliable in the diagnosis of moderate dementia, its sensitivity and specificity for the diagnosis of mild dementia has been rarely examined. We assessed the specificity and sensitivity of the MMSE in a consecutive series of 44 patients with mild dementia, and a group of age-comparable normal controls. While the specificity of the MMSE for the diagnosis of mild dementia was very high (100%), the sensitivity was only 55% [20 of the 44 patients with mild dementia had an MMSE score in the normal range (≥ 26 points)]. On the other hand, the assessment with both the Buschke Selective Reminding and the Boston Naming tests discriminated mild Alzheimer's disease patients with normal MMSE scores from controls with a sensitivity and specificity of 64%. In conclusion, the assessment with verbal memory and naming tasks provided a significantly more sensitive measure of early dementia than the MMSE.

Keywords: Alzheimer's disease – Dementia – Mini-Mental State Exam

INTRODUCTION

Dementia is a highly prevalent disease among elderly individuals. While the mental status evaluation is a critical part of the diagnosis of dementia, most neuropsychological batteries, such as the Wechsler Adult Intelligence Scale (Wechsler, 1955), usually take several hours to complete. Folstein *et al.* (1975) developed the Mini-Mental State Exam (MMSE) as an easily administered test that can be completed in 10-15 min, and samples important cognitive domains, such as orientation, attention-concentration, recall, language, and constructional praxis.

While the MMSE has been found to be a valid and reliable instrument for the diagnosis of moderate dementia (Folstein *et al.*, 1975), several studies suggest it may not be useful in the diagnosis of mild dementia (Knopman and Ryberg, 1989; Galasko *et al.*, 1990; Welsh *et al.*, 1991). The aim of the present study was to examine the sensitivity and specificity of the MMSE in the diagnosis of mild dementia, and to determine whether a brief neuropsychological battery that included tests of verbal naming, verbal memory, verbal comprehension, verbal fluency, and non-verbal abstract reasoning had a better sensitivity and specificity.

METHODS

Patients

We examined a consecutive series of 44 patients attending the Neurology Outpatient Unit of our Institute, who met the NINCDS-ADRDA (McKhann *et al.*, 1984) criteria for probable Alzheimer's disease (AD) and the DSM-III-R (APA, 1987) criteria for mild dementia. Every patient underwent a clinical and laboratory evaluation to rule out other causes of dementia. Additional inclusion criteria were: (1) no focal cerebral lesions on the CT scan; (2) a Hachinski Ischemic score ≤ 4 (Hachinski *et al.*, 1975); and (3) no history of closed head injuries with loss of consciousness, strokes, or other neurologic disorders with central nervous system involvement. A series of 14 controls, who were mostly spouses of AD patients, were also examined. None of them had neurological or psychiatric disorders, and all of them had a normal CT scan.

Neurological examination

After informed consent, patients had a comprehensive neurological evaluation, which included a standardized questionnaire that assessed the onset and duration of illness, the presence of impairments in activities of daily

living, and limitations in work and social activities. The same interviewer assessed patients and controls with the Mini-Mental State Exam (MMSE).

Neuropsychological examination

Blind to group membership, demographic data, and MMSE scores, both patients and controls had a neuropsychological evaluation that consisted of the following tasks.

Buschke Selective Reminding Test (Buschke and Fuld, 1974): this test measures verbal learning and memory during a multiple-trial list learning task. The outcome measure was the long-term retrieval (LTR) score.

Token Test (De Renzi and Faglioni, 1978): this test measures verbal comprehension of commands of increasing complexity.

Boston Naming Test (Kaplan *et al.*, 1983): this test measures the ability to name pictured objects.

Controlled Oral Word Association Test (Benton, 1968): this test examines the spontaneous production of words beginning with the letters F, A, and S.

Raven's Progressive Matrices (Raven *et al.*, 1986): this test measures reasoning in the visual modality.

Statistical analysis

Statistical analysis was carried out using means and S.D., two-way analysis of variance (ANOVA) with repeated measures, and *post-hoc t*-tests. Sensitivity and specificity of cognitive tests were examined with a discriminant function analysis. All *p* values are two-tailed.

TABLE I. Demographic findings

	Mild dementia with MMSE < 26	Mild dementia with MMSE ≥ 26	Control group
Number of patients	24	20	14
Age (mean years)	74.1 (6.9)	70.7 (6.5)	68.3 (8.8)
Sex (% females)	67	75	57
Education (mean years)	8.6 (5.0)	12.7 (4.0)	12.5 (4.0)
Duration of illness (mean years)	3.4 (1.9)	3.9 (2.3)	—

S.D.s are in parentheses.

TABLE II. Neuropsychological findings

	Mild dementia with MMSE < 26	Mild dementia with MMSE ≥ 26	Control group
MMSE scores (mean) ¹	20.5 (3.9)	27.3 (1.3)	28.0 (1.2)
Buschke Selective RT ^{1,2}	1.8 (1.9)	4.1 (2.6)	6.5 (3.0)
Boston Naming Test ^{1,2}	12.7 (5.4)	16.3 (3.1)	19.2 (0.7)
Raven's Progressive Matrices ^{1,2}	38.7 (27.0)	50.2 (36.1)	73.3 (23.7)
Word-controlled Test ¹	27.2 (6.8)	34.1 (11.5)	39.8 (10.3)
Token Test ¹	17.9 (6.4)	21.6 (4.6)	24.3 (1.3)

S.D.s are shown in parentheses.

¹Dementia with MMSE < 26 vs controls, *p* < 0.01.

²Dementia with MMSE ≥ 26 vs controls, *p* < 0.05.

RESULTS

Demographic findings (Table I)

Based on MMSE scores, AD patients were divided into those with normal (≥ 26 points) and abnormal (< 26 points) MMSE scores. We used a cut-off score on the MMSE of 26 points instead of the usual of 25 points so as to select a group of AD patients where the use of the MMSE would clearly be unhelpful.

No significant differences were found in age, sex, and years of education between AD patients and controls.

Neuropsychological findings (Table II)

Using a cut-off score of 26 points on the MMSE, all the controls had a normal MMSE score, compared with 20 of the 44 patients (45%) with mild dementia. While the specificity of the MMSE for the diagnosis of dementia was 100%, the sensitivity was only 55%. Due to this low sensitivity of the MMSE, we examined whether other cognitive tasks had a higher sensitivity. Thus, we compared the 20 patients with mild dementia and MMSE score ≥ 26 with 14 age- and MMSE-comparable normal controls (Tables I and II). A two-way ANOVA with repeated measures [Factor 1: group (AD vs controls), repeated measure: neuropsychological tasks] showed a significant group effect [$F(1,32) = 10.9, p = 0.002$] (AD patients showed an overall worse performance on the neuropsychological battery than the normal controls), and a significant group × task interaction [$F(4,112) = 3.90, p = 0.005$] (Table II). A *post-hoc* analysis showed that the group with mild

dementia and normal MMSE scores had significantly worse performances on the Buschke long-term retrieval ($p = 0.002$), Boston Naming Test ($p < 0.05$), and Raven's Progressive Matrices ($p < 0.05$) than the control group. In order to examine which of these tasks better separated AD patients from normal controls, a discriminant function analysis was carried out. Both the Boston Naming Test and the Buschke Selective Reminding Test, had a significant discriminant power (Wilks' = 0.75, $p = 0.009$, and Wilks' = 0.69, $p < 0.05$, respectively), showing both a sensitivity and specificity of 64% for the diagnosis of mild dementia among patients with an MMSE score ≥ 26 .

DISCUSSION

The present study showed two important findings. First, the MMSE had a high specificity (100%) but a low sensitivity (55%) for the diagnosis of mild dementia. Second, when patients with mild dementia and normal MMSE scores were compared on a brief neuropsychological battery with age-comparable normal controls with similar MMSE scores, patients with mild dementia showed significant deficits on anterograde verbal memory and naming tasks.

The MMSE is a cognitive evaluation that taps different cognitive domains, has a high reliability, and needs a brief time for completion. While this instrument is used by clinicians for research and clinical assessments, recent studies suggest the MMSE may not be sensitive for the diagnosis of mild dementia. Galasko *et al.* (1990) found that 24 of 74 patients with mild AD had MMSE scores > 23 (i.e. a sensitivity of 68%). Similarly, our study demonstrated a high specificity among patients with mild dementia, but a low sensitivity since 20 of 44 patients (45%) had an MMSE score ≥ 26 .

Other neuropsychological tasks may be more effective for the diagnosis of mild dementia, and this possibility was explored in several recent studies. Storandt *et al.* (1984) assessed 42 patients with a large neuropsychological battery and found that the Logical Memory subtest of the Wechsler Memory Scale (WMS) (Wechsler, 1945), the Trail Making Test (a test of visual scanning and graphomotor speed) (Reitan, 1958), the Controlled Oral Word-Association Test (a test of verbal fluency), and the Mental Control subtest of the WMS (which involves sequenced cognition with a verbal response) adequately classified all patients with mild AD and normal controls. However, MMSE scores in patients with mild AD were not reported.

Knopman and Ryberg (1989) assessed the MMSE and a short neuropsychological battery that included the Symbol-Digit Modalities Test (Smith, 1973), the Raven's Progressive Matrices, and a delayed word recall task in a group of 28 patients with mild AD. They found that all three neuropsychological tasks classified patients and

normal controls with a sensitivity of 100% and a specificity of 93%. This high rate of correct classification may be related to the fact that the AD group included patients with MMSE scores > 18 , while we assessed our cognitive battery in AD patients with MMSE scores ≥ 26 . In a recent study, Robinson-Whelen and Storandt (1992) demonstrated the importance of verbal delayed recall in the diagnosis of early dementia. They compared 51 patients with very mild dementia and 64 controls using the Logical Memory subtest of the WMS, and found that patients with very mild dementia recalled significantly less information in both the immediate and delayed conditions than the controls. Flicker *et al.* (1991) have also examined neuropsychological differences between patients with mild dementia and normal controls and found that patients with mild dementia had significantly more impairments on tests of recent and remote memory, language function, concept formation, and visuospatial tasks. However, neither Robinson-Whelen and Storandt nor Flicker *et al.* restricted their cognitive assessment to patients with mild dementia and normal MMSE scores. Welsh *et al.* (1991) examined a series of 49 patients with mild dementia and MMSE score ≥ 24 with a brief neuropsychological battery that included tests of language, constructional praxis, and verbal memory. They found that delayed memory proved to be the most effective task to distinguish mild dementia from normal controls, and naming was useful in confirming the presence of dementia and staging the disease. When our 20 patients with mild dementia were compared with 14 age- and MMSE-comparable normal controls, patients with mild dementia and normal MMSE scores showed a significantly worse performance on a brief neuropsychological battery that included tests of verbal memory, naming, verbal comprehension, verbal fluency, and non-verbal (abstract) reasoning. A discriminant function analysis demonstrated that the Buschke Verbal Reminding Test (a measure of anterograde verbal memory) and the Boston Naming Test significantly discriminated patients with mild dementia and normal MMSE scores from normal controls. Patients with mild dementia and a normal MMSE score also showed significantly lower scores on the Raven's Progressive Matrices (which assesses abstract reasoning) than the control group. However, the inclusion of this test in the discriminant function analysis did not improve the discriminant power. Finally, there were no significant differences between patients with mild dementia and normal controls in either the Token Test or the verbal fluency task.

In conclusion, the present findings suggest that a brief neuropsychological assessment that includes the MMSE, the Buschke Verbal Reminding Test, and the Boston Naming Test provides the highest sensitivity and specificity for the diagnosis of mild dementia in patients with probable AD.

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