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The Mini-Mental State Examination: A Comprehensive Review

Tom N. Tombaugh, PhD, CPsych and Nancy J. McIntyre, MA

Objective: The purpose of this paper is to provide a comprehensive review of information accumulated over the past 26 years regarding the psychometric properties and utility of the Mini-Mental State Examination (MMSE).

Participants: The reviewed studies assessed a wide variety of subjects, ranging from cognitively intact community residents to those with severe cognitive impairment associated with various types of dementing illnesses.

Main Outcome Measures: The validity of the MMSE was compared against a variety of gold standards, including DSM-III-R and NINCDS-ADRDA criteria, clinical diagnoses, Activities of Daily Living measures, and other tests that putatively identify and measure cognitive impairment.

Results: Reliability and construct validity were judged to be satisfactory. Measures of criterion validity showed high levels

of sensitivity for moderate-to-severe cognitive impairment and lower levels for mild degrees of impairment. Content analyses revealed the MMSE was highly verbal, and not all items were equally sensitive to cognitive impairment. Items measuring language were judged to be relatively easy and lacked utility for identifying mild language deficits. Overall, MMSE scores were affected by age, education, and cultural background, but not gender.

Conclusions: In general, the MMSE fulfilled its original goal of providing a brief screening test that quantitatively assesses the severity of cognitive impairment and documents cognitive changes occurring over time. The MMSE should not, by itself, be used as a diagnostic tool to identify dementia. Suggestions for the clinical use of the MMSE are made. *J Am Geriatr Soc* 40:922-935, 1992

The use of screening tests to provide brief, objective measures of cognitive functioning has increased dramatically over the last 10 years. Although a substantial number of screening tests exist, the Mini-Mental State Examination (MMSE)¹ is the most widely used. It is a popular clinical measure that is available in many languages.²⁻⁹ The MMSE is also widely used in epidemiological studies and community surveys. It forms part of the Diagnostic Interview Schedule (DIS),¹⁰ a structured interview recently used in a large five-site Epidemiologic Catchment Area (ECA) study sponsored by the National Institute of Mental Health,¹¹ and has been incorporated into several standardized interviews designed to assess cognitive impairment and to help diagnose dementia.^{12,13,14} Moreover, the MMSE serves as one of the tests recommended by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA)¹⁵ to document the clinical diagnosis of probable Alzheimer's disease. The aim of this paper is to review information accumulated over the past 26 years regarding the psychometric properties and utility of the English version of the MMSE.

DESCRIPTION OF THE MMSE

Folstein, Folstein, and McHugh¹ originally created the MMSE to differentiate organic from functional psychiatric patients. They stated explicitly that MMSE scores were "useful in quantitatively estimating the severity of cognitive impairment" and "in serially doc-

umenting cognitive change." The MMSE was not, on its own, intended to provide a diagnosis for any particular nosological entity.

The MMSE consists of a variety of questions (see Appendix), has a maximum score of 30 points, and ordinarily can be administered in 5-10 minutes. The questions typically have been grouped into seven categories, each rationally representing a different cognitive domain or function: Orientation to time (5 points); Orientation to place (5 points); Registration of three words (3 points); Attention and Calculation (5 points); Recall of three words (3 points); Language (8 points) and Visual Construction (1 point). Originally, however, all of the orientation questions were combined into a single orientation category, and the visual construction task was classified as one of the language items.

Variations

Variations in the wording and content of some questions, as well as in the administration and scoring of the MMSE, commonly occur. Some of these variations are described below.

Orientation to Place Since the MMSE was developed to test hospital patients, the orientation questions require the respondent to specify the name and floor of their hospital. However, alternative items frequently are used when the MMSE is administered outside the hospital, particularly in community surveys and epidemiological studies.¹⁶⁻¹⁸

Registration and Recall of Three Words The choice of words used to test a person's ability to learn and retain three words was left originally to the discretion of the examiner. When the MMSE was incorporated into the DIS, the words apple, penny, and table

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were employed, a convention adopted by most subsequent studies. Exceptions to this practice, however, have included words such as shirt, brown, honesty, flag, ball, tree, rose, ring, elephant, and dog.¹⁹⁻²³

Attention and Calculation Folstein et al¹ routinely administered the serial 7s task on every test. However, patients were permitted to spell the word WORLD backward if they could not or would not perform the serial 7s task. While using WORLD as an alternative task has been followed in many studies, several other procedures have been adopted. Some applications, including CERAD,¹³ use only WORLD²³⁻²⁶ while others, including CAMDEX,¹² use only the serial 7s task.^{12, 20, 27, 28} Others routinely include both tasks, which are scored in one of the following ways: (1) the higher of the two scores is used^{2, 16, 19, 21, 29-33}; (2) the two scores are combined^{21, 30, 34, 35} or (3) each task is analyzed separately.^{16, 22, 36, 37} Variations also exist in how WORLD is scored.^{1, 13, 23, 36, 38}

General Scoring Procedures and Cut-off Scores

Ordinarily, the MMSE score is the total number of correct answers. Although, this may not be appropriate when individuals refuse to answer many questions, Fillenbaum et al.³⁹ concluded that, at least in epidemiological surveys, a refusal most likely represents an inability to correctly answer the question.

A score of 23 or less generally has been accepted as indicating the presence of cognitive impairment. This cut-off score evolved from research findings rather than being recommended in the original article. Its high degree of acceptance is illustrated by the fact that several community surveys have employed the cut-off score, even though modified forms of the MMSE were used.^{18, 31, 32, 34} More recently, largely due to the ECA study,⁴⁰ the trend has been to classify the severity of cognitive impairment into three, rather than two, levels: 24-30 = no cognitive impairment; 18-23 = mild cognitive impairment; and 0-17 = severe cognitive impairment. MMSE scores are also frequently used to classify dementia patients as mild, moderate, or severe, a practice supported by evidence from longitudinal studies (reviewed in the current paper) and dementia rating scales.⁴¹⁻⁴³

RELIABILITY

Internal Consistency Four studies that provide data on internal consistency (ie, item homogeneity) are shown in Table 1. The highest alpha level (.96) was obtained with a mixed group of medical patients, while more modest levels (.68 and .77) were reported with community samples. Jorm et al³⁰ reported an association between alpha levels and years of education: the alpha level for a community sample with only a primary education (.65) was higher than for a sample with 8 or more years of education (.54). Holzer et al¹⁶ discuss two factors that may influence alpha levels. First, in community surveys, individuals correctly answered most of the questions, thereby reducing the range of scores and decreasing the likelihood of obtaining high alpha coefficients. Higher alphas should be obtained in clinical populations in which greater vari-

ability exists, a prediction substantiated by the .96 alpha obtained with a mixed sample of hospital patients.⁴⁴ Second, since the MMSE attempted to measure a variety of cognitive processes, item heterogeneity was intentionally created. Thus, in this case, lower alpha levels may be viewed as desirable.

Test-Retest Reliability In order to reduce the influence that illness-induced changes might exert on reliability estimates, reliability coefficients only are reported from studies where the test-retest interval was 2 months or less. The results from these studies (Table 1) show that reliability coefficients for both cognitively intact and impaired subjects generally fell between .80 and .95. These reliability estimates are consistent with those reported by Leshner and Whelihan⁵³ for other brief cognitive screening tests. The unusually low coefficient of .56 for delirium patients⁴⁵ probably reflects the fluctuating course of this illness. The .38 reliability coefficient for the control subjects in the Morris et al.⁵⁰ study probably reflects the truncated distribution of scores (ie, mean MMSE = 28.9) that statistically restricts correlation coefficients.⁵⁴ Several studies reported increased scores on retest, presumably due to practice effects.^{1, 29, 32, 46, 48} Moreover, evidence exists suggesting that some patients "study" for mental status tests by rehearsing answers given on a previous administration of the MMSE.⁵⁵ The site of testing can also influence retest scores.³⁷ For example, two studies reported that patients tested at home achieved significantly higher scores than when they were tested in a clinic.^{56, 57}

The results with short test-retest intervals are compared to those obtained in six studies that used extended test-retest intervals (eg, 1 to 2 years) with subjects judged to be cognitively intact.^{33, 50, 58-61} These results show that the amount of change was relatively small (usually within two points) and not statistically significant. However, in the only two studies reporting reliability estimates,^{33, 60} correlation coefficients were less than .50, a value substantially less than those reported previously for studies using short test-retest intervals. Olin and Zelinski³³ attribute the decreased reliability to several psychometric problems, including regression to the mean, method for assessing attention/concentration, and lack of explicit scoring criteria for the pentagon. The finding reported by O'Connor et al³² that the second lowest kappa value for interrater reliability occurred for the pentagon item further suggests that the lack of scoring criteria may affect the stability scores. Regardless of their cause, the relatively low reliability coefficients that occurred for "normal" subjects have important implications for using the MMSE with longitudinal assessment, suggesting that small changes in scores should be interpreted with caution.

VALIDITY

Sensitivity and Specificity One way to assess the validity of the MMSE is to determine how well it correctly identifies normal and impaired individuals. The sensitivity of the MMSE refers to its ability to correctly identify those individuals who have been classified as cognitively impaired according to some

TABLE 1. INTERNAL RELIABILITY AND TEST-RETEST RELIABILITY OF THE MMSE

Measure	Sample	n	Age*	Test/Retest Interval	Correlations**
Internal Consistency					
Holzer et al ¹⁶	Community survey	4917	18-85+		.77
Kay et al ^{34***}	Community survey	274	70-80+		.68
Foreman ⁴⁴	Medical patients (normal, dementia, & delirium)	66	76		.96
Jorm et al ³⁰	Community survey	269	70+		.65 (grades 0-8) .54 (> grade 8)
Test-Retest					
Folstein et al ¹					
	Medical patients				
	1. Depression	22	41	1 day (same tester)	.89
	2. Depression	19	46	1 day (different tester)	.83
	3. Dementia, depression & schizophrenia	23	74	28 days (unspecified)	.99
Anthony et al ⁴⁵					
	Medical patients				
	1. Cognitively intact	58	20-80+	1 day	.85
	2. Dementia	12			.90
	3. Delirium	7			.56
Pfeffer et al ⁴⁶					
	Mixed sample of dementia/delirium & cognitively intact	23	58-86	4 days median interval	.94
Dick et al ⁴⁷					
	Neurological patients	15	50	1 day (different tester)	.95
		44		1-70 days (same tester) (M = 31)	.92
Thal et al ⁴⁸					
	Probable AD	40	50-90	1 week	.84
				3 weeks	.79
				6 weeks	.80
Bird et al ²					
	Community survey	189	44	same day	.90
Fillenbaum et al ³⁹					
	Probable AD	24	54-75	1 month	.89
O'Connor et al ³²					
	Cognitively intact	285	75+	2 months	.64
	Dementia	196	75+		.83
Kafonek et al ⁴⁹					
	Dementia, delirium, & depression	29	65+	1 week (different tester)	.84
Morris et al ⁵⁰					
	Control	278	68	1 month	.38
	Mild AD	200	72	1 month	.74
	Moderate AD	132	72	1 month	.79
Teng et al ⁵¹					
	Cognitively intact	27		64 days	.79
van Belle et al ⁵²					
	AD	8	60+	1-2 weeks	.94
	AD	30	60+	3-4 weeks	.85
Zaudig et al ¹⁴					
	Cognitively intact	66	77	24-72 hours (M = 26 hours)	.97
Jorm et al ²⁹					
	Mixed sample of dementia, depression & cognitively intact	57	80	1-14 days (M = 2.8 days)	.79

* Single age score represents mean age. Pair of age scores represents range of ages.

** All correlations are significant, $P < 0.05$.

*** The Kay et al⁴ and Jorm et al³ analyses are based on data from the same study.

generally accepted criteria or gold standard (eg, DSM-III, NINCDS-ADRDA, clinical judgment) (ie, true positives/total number of impaired cases). Specificity refers to the MMSE's ability to correctly identify those individuals who previously have been classified as cognitively intact (ie, true negatives/total number of cognitively intact cases). Sensitivity and specificity data can be used to derive a likelihood ratio [sensitivity/(1-specificity)] that may be helpful in interpreting a MMSE score for an individual from a particular population (eg, community, hospital), provided the prevalence of the cognitive impairment is known for the population. (For further information see Refs. 62 and 63).

It is also important to determine how well a positive or negative test result actually predicts the presence or absence of impairment. If someone obtains a MMSE score of 22, for instance, what is the probability that cognitive impairment actually exists? The predictive value of a positive test is the ratio of correctly identified positive cases to the total number of positive cases (ie, true positives/[true positives + false positives]), while the negative predictive value refers to the ratio of correctly identified negative cases to the total number of negative cases (true negatives/[true negatives + false negatives]).

Table 2 shows 25 experiments for which sensitivity

TABLE 2. CRITERION VALIDITY FOR MMSE USING 23/24 CUT-OFF SCORES

Sample	Groups	n	Age*	Mean Score	Criteria	Results**
Dementia Subjects						
Folstein et al ¹	1. Cognitively intact	63	74	28	Psychiatric diagnosis	Sensitivity = 100% Specificity = 100% Positive prediction = 100% Negative prediction = 100%
Exp 1	2. Dementia	29	80	10		
Exp 2	Dementia	8	76	7	Psychiatric diagnosis	Sensitivity = 100%
Exp 3	Dementia	9	74	12	Psychiatric diagnosis	Sensitivity = 100%
Anthony et al ⁴⁵	1. Cognitively intact	74	20-89+	26	DSM-III	Sensitivity = 87% Specificity = 82% Positive prediction = 60% Negative Prediction = 95%
	2. Dementia or delirium	23	20-80+	15		
Goldschmidt et al ⁶⁴	1. Cognitively impaired	23	55	20	Clinical assessment	Sensitivity = 100%
Folstein et al ¹⁸	1. Cognitively intact (no clinical diagnoses)	106	65+		DSM-III	Sensitivity = 100% Specificity = 62% Positive prediction = 44% Negative prediction = 100%
	2. Dementia	32	65+			
Comparison 1	1. Cognitively intact (clinical diagnoses)	90	65+		DSM-III	Sensitivity = 100% Specificity = 46% Positive prediction = 40% Negative prediction = 100%
	2. Dementia	32	65+			
Kay et al ³⁴	1. Cognitively intact	235	70-80+		DSM-III	Sensitivity = 69% Specificity = 89%
	2. Dementia (mild, moderate & severe)	39	70-80+			
Comparison 2	1. Cognitively intact	235	70-80+		DSM-III	Sensitivity = 100% Specificity = 85%
	2. Dementia (moderate & severe only)	13	70-80+			
Davous et al ⁶⁵	1. Cognitively intact (functional disorders & neurology)	56	70***	27	DSM-III NINCDS-ADRDA	Sensitivity = 93% Specificity = 100% Positive prediction = 100% Negative prediction = 95%
	2. Dementia	44	74	15		
Comparison 2	1. Cognitively intact (psychiatric illness)	33	57	26	DSM-III NINCDS-ADRDA	Sensitivity = 93% Specificity = 82% Positive prediction = 87% Negative prediction = 90%
	2. Dementia	44	74	15		
Fisk and Pannill ⁶⁶	1. AD	113	77	15	DSM-III	Sensitivity = 89%
Foreman ⁴⁴	1. Cognitively intact	33	66-85		DSM-III	Sensitivity = 82% Specificity = 80% Positive prediction = 80% Negative prediction = 82%
	2. Dementia or delirium	33	66-85			
Huff et al ⁶⁷	1. Cognitively intact	86	63	29	NINCDS-ADRDA	Sensitivity = 44%
	2. AD	79	67	22		
Pfeffer et al ⁶⁸	1. AD	162	65+		DSM-III-R NINCDS-ADRDA	Sensitivity = 20%
Jackson and Ramsdell ⁶⁹	1. Cognitively intact	38		27	Clinical assessment	Sensitivity = 85% Specificity = 87% Positive prediction = 98% Negative prediction = 43%
	2. Dementia	294		15		
Kafonek et al ⁴⁹	1. Cognitively intact	22	77		DSM-III	Sensitivity = 79% Specificity = 86% Positive prediction = 92% Negative prediction = 66%
	2. Dementia or delirium	47	77	14***		
O'Connor et al ³²	1. Cognitively intact	285	75+	20	CAMDEX	Sensitivity = 86% Specificity = 92% Positive prediction = 55%
	2. Dementia or delirium	196	75+	13		

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TABLE 2. CONTINUED

Sample	Groups	n	Age*	Mean Score	Criteria	Results**
Knopman and Ryberg ⁷⁰	1. Cognitively intact	55	74	29	NINCDS-ADRDA	Sensitivity = 54% Specificity = 96% Positive prediction = 88% Negative prediction = 80% Sensitivity = 57%
	2. AD	28	74	23		
Reed et al ⁷¹	1. AD	21	70	20	NINCDS-ADRDA	
Black et al ⁷²	Comparison 1	1. Cognitively intact	80	70+	Clinical assessment plus AGE CAT#	Sensitivity = 100% Specificity = 66%
		2. Dementia (probable & definite)	31	70+		
	Comparison 2	1. Cognitively intact	80	70+	Clinical assessment	Sensitivity = 89% Specificity = 70%
		2. Dementia (probable (definite & mild))	47	70+		
Galasko et al ²¹	1. Cognitively intact	74	70	29	NINCDS-ADRDA	Sensitivity = 68% Specificity = 100% Positive prediction = 100% Negative prediction = 76%
	2. AD	74	71	20***		
Jorm et al ²⁹	1. Cognitively intact	45	80		DSM III	Sensitivity = 76% Specificity = 73%
Murden et al ²²	1. Cognitively intact	148	60-99		Research criteria	Sensitivity = 96% Specificity = 81% Positive prediction = 79% Negative prediction = 97%
	2. Dementia	110				
Neurological and Psychiatric Subjects						
DePaulo and Folstein ⁷⁴	1. Cognitively intact	26	44	28	Clinical assessment	Sensitivity = 50% Specificity = 100% Positive prediction = 100% Negative prediction = 55%
	2. Cerebral lesions	42	56	23		
Dick et al ⁴⁷	1. Cognitively intact	93	49		Clinical assessment	Sensitivity = 76% Specificity = 96% Positive prediction = 90% Negative prediction = 88%
	2. Neurological & cognitive impairment	50	54			
Lautenschlaeger et al ⁷⁵	1. Non-organic		64-92		Clinical assessment	Sensitivity = 76% Specificity = 64%
	2. Organic		64-92			
Schwamm et al ⁷⁶	1. CNS lesion (excluded dementia & delirium)	30	54	22	Clinical assessment	Sensitivity = 52%
Chandler and Gerndt ⁷⁷	1. Mixed psychiatric without cognitive impairment or depression	102		28	DSM-III & NINCDS-ADRDA	Sensitivity = 33% Specificity = 91% Positive prediction = 31% Negative prediction = 92%
	2. Mixed organic mental disorder with cognitive impairment	12	53	24		
Faustman et al ⁷⁸	1. Mixed psychiatric without cognitive impairment	76		29	Luria-Nebraska Neuro-Psychological Battery	Sensitivity = 21% Specificity = 96% Positive prediction = 50% Negative prediction = 87%
	2. Mixed psychiatric with cognitive impairment	14		27		

Note: See text for explanation of sensitivity, specificity, positive prediction, and negative prediction.

Note: DSM III (Diagnostic and Statistical Manual of the American Psychiatric Association-Third Edition); NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association).

* Single age score represents mean age. Pair of age scores represents range of ages.

** Prediction ratios are unadjusted for estimated prevalence rates.

*** Estimated by authors.

AGE CAT is a computer program for analyzing scores on the Geriatric Mental Status (GMS) exam.

and specificity data were cited or could be derived from information in the article. Only studies that used the criterion score of 23 or less (23/24) are included.

Sensitivity: Dementia Subjects Anthony et al⁴⁵ were the first to employ the 23/24 cut-off score to determine the sensitivity of the MMSE. The cut-off criterion was based on data originally reported by Folstein et al¹ that suggested that a high, if not perfect, level of sensitivity would occur if the cut-off criterion was set at 23/24. Anthony et al⁴⁵ selected 99 of 101 consecutive admissions to a general medical ward who were classified as either cognitively impaired or intact based on the presence/absence of delirium or dementia as assessed by a psychiatrist using DSM-III⁷³ criteria. The MMSE correctly identified 20 of the 23 impaired patients (87% sensitivity). Table 2 shows that similar levels of sensitivity have been reported in approximately 75% of comparisons using dementia patients. A related and perhaps more critical clinical question is how well does a positive test score predict the presence of dementia. Inspection of the positive prediction data reveals that in approximately 70% of the studies, a MMSE score of less than 23 was associated with the diagnosis of dementia in at least 79% of the cases.

The major variable that appears to differentiate between high and low MMSE sensitivity is the level of cognitive impairment in the dementia groups. The probability of obtaining high levels of sensitivity increases as impairment increases. For example, all studies with a mean MMSE score of 15 or less for the demented subjects report relatively high levels of sensitivity. The two studies with a mean MMSE score greater than 20^{67, 70} for the impaired group reported low levels of sensitivity (44% and 68%). In addition, higher sensitivity has been reported with hospital or clinic samples relative to community surveys. This trend probably reflects the over-representation of moderate and severe cognitive impairment compared to community samples.

Sensitivity: Neurological and Psychiatric Subjects As shown in Table 2, the sensitivity of the MMSE for general neurology and psychiatry patients usually is low, ranging from 21% to 76%. Two reasons are frequently cited for this. Probably because of its bias toward verbal items, the MMSE is relatively insensitive to damage in the right hemisphere, causing an increase in false negatives.^{47, 76, 79, 80} As well, the language items are too simple to detect mild impairments.^{21, 35, 47, 76, 81} In addition, according to Chandler and Gerndt⁷⁷ the heterogeneity of neurological patients makes it difficult to identify cognitive impairment. It should be noted that a high degree of variability also exists in the positive predictive values, with scores ranging from 31% to 100%.

Specificity Most studies report moderate-to-high levels of specificity, indicating the members of the control group are readily identified by a score greater than 23. The negative predictive value of the MMSE is also relatively high due to the low number of false negative cases. Table 2 shows that the composition of the control group is an important factor in determining specificity. Two studies^{18, 65} have shown lowered spec-

ificity when psychiatric patients are included in the comparison group. Davous et al⁶⁵ reported 100% specificity when the control group consisted of patients with neurological or "functional" disorders, but only 82% when psychiatric patients were used. A similar trend was reported by Folstein et al¹⁸ in a community survey. Specificity was 62% for elderly subjects without a clinical diagnosis and 46% for a mixed group of community-dwelling subjects diagnosed as having some type of a DSM-III condition. As discussed later, the demographic characteristics of the sample also affect specificity levels.

Correlation with Other Tests*

The degree to which the MMSE is correlated with other tests measuring cognitive functioning provides evidence of construct validity. These correlations are reviewed below.

Cognitive Screening Tests Correlations ranging from -0.66 to -0.93 were obtained from the studies^{27, 28, 48, 50, 65} that compared the MMSE with either the original 26-item Blessed Information-Memory-Concentration test (BIMC)⁸² or the shortened 6-item Blessed Orientation-Memory-Concentration test (BOMC).⁸³ The negative sign occurs because the MMSE adds the number of correct answers while the Blessed sums the number of errors. Given the high degree of overlap in items, the high correlation is not unexpected. Additional research has shown that correlations generally falling within the .70 to .90 range exist between MMSE scores and those obtained from a representative sample of other cognitive screening tests administered to a variety of different types of subjects.^{29, 42-44, 84-93}

Intelligence and Memory Tests Since the MMSE originally was designed to assess the construct of general cognitive ability, Folstein et al¹ compared MMSE scores to those obtained on the Wechsler Adult Intelligence Scale.⁹⁴ They found a correlation of .78 with the Verbal Scale and .66 with the Performance Scale. Comparable findings have been reported in several other studies using a variety of different types of subjects.^{25, 47, 60, 78, 95-97} The failure of some studies to obtain significant correlations^{24, 96} occurred where the average MMSE score was 27 or above and probably reflects a range restriction due to the truncated distribution of scores. Moderate-to-high correlations were also obtained with the Wechsler Memory Scale.^{95, 97}

Neuropsychological Tests Modest-to-high correlations between scores on the MMSE and those obtained on various cognitive tests (eg, Trails B, WMS, digit span, story recall, word list recall) used in neuropsychological assessments have been reported.^{37, 46, 50, 78, 87, 95, 98, 99} These results are consistent with a report by Morris et al⁵⁰ that factor analysis of several neuropsychological tests loaded on three different factors, and the MMSE loaded equally on all factors.

* A summary table containing the correlations between MMSE scores and those obtained on other tests is available on request.

Activities of Daily Living (ADL) Measures The relationship between cognitive deficits and ability to function independently is critical in dementia. Impaired occupational or social function has been shown to covary with severity levels, and the degree of impairment may serve as a criterion for the diagnosis of dementia (eg, DSM-III). Thus, MMSE scores should correlate with measures of functional capacity, such as those obtained with the Blessed Dementia Rating Scale (BDRS),⁸² that assess an individual's everyday activities, habits, and personality. Correlations between MMSE scores and those obtained from ADL scales generally range from .40 to .75, indicating that lower MMSE scores are related to decreased independence.^{19, 49, 50, 100-107} The ECA Piedmont Health Survey¹⁰⁷ provides the most extensive ADL data. MMSE scores from 1,637 community-dwelling individuals were correlated (.48) with instrumental activities (eg, cooking, caring for finances) but not with physical activities (eg, dressing, eating). The higher correlation obtained with instrumental, rather than physical, ADLs has been reported in several studies.^{66, 103, 108, 109} Thus, scores on the MMSE are sensitive to a decline in more cognitively demanding functional behavior that is independent of physical health and mobility.

Finally, since the BDRS originally was validated against postmortem neuropathological changes,^{82, 110} the high degree of relationship between the MMSE and BDRS provides indirect evidence that MMSE scores are correlated to histopathological findings. This speculation is supported by the $-.70$ correlation that existed between MMSE scores and plaque counts.¹¹¹

Longitudinal Studies

Longitudinal studies with Alzheimer's patients provide additional evidence of construct validity. Since AD is a progressive disease where cognitive functions decline over time, MMSE scores should decline with serial testing. Longitudinal studies using test-retest intervals ranging from 1 month to 3 years show that MMSE scores for dementia patients, the majority classified as AD, significantly declined over time.^{50, 52, 56, 58, 71, 80, 92, 112-120} Although the rate of decline varied between and within studies, it generally fell between 2 and 5 points per year. Moreover, the rate of decline in 1 year was not correlated with that occurring during the following year.⁸⁰

A substantial degree of variability occurred in those studies employing Alzheimer's patients. While some of the test-retest variability is related to the uneven progression of AD and the heterogeneity of subjects produced by differences in the duration of illness, age of onset, and subclass of AD, the content and psychometric properties of the MMSE are contributing factors as well. The verbal items (eg, recall of three words, 7s/WORLD) that make the MMSE sensitive to the profound decline in memory that occurs in moderately demented patients^{80, 112, 118, 121} lose their discriminability as the severity of the illness increases. Thus, as the lower limits of the scale are approached, the MMSE becomes less sensitive to the progressive decline of

functioning that occurs with AD. Several studies have reported that scales evaluating functional competence, such as ADL measures, assess a wider range of functions than the MMSE and are more appropriate for longitudinal studies involving severely demented patients.^{19, 80, 100, 121, 122}

Other Evidence of Construct Validity

MMSE scores also correlate with other measures that reflect severity of AD, thus providing additional evidence of construct validity. These include urinary incontinence,^{104, 123} mortality,^{105, 112, 124, 125} changing health status,¹⁰⁵ abnormal behavioral change,^{104, 118, 126, 127} hearing impairment,^{56, 120} length of time in hospital,¹²⁸⁻¹³⁰ and extrapyramidal signs.¹³¹ However, some studies have shown that neuropsychological measures, such as drawing a 3-dimensional cube, were related to behaviors such as wandering and urinary incontinence, which were not correlated with MMSE scores.^{98, 132}

Influence of Demographic and Social Variables

Educational Level MMSE scores repeatedly have been shown to be related to educational attainment. This association between years of education and MMSE performance has been reported in studies using hospital patients,⁴⁷ a mixed sample of dementia and cognitively intact subjects,¹³³ individuals randomly sampled from the community,^{2, 6, 16, 17, 30, 31, 36, 40, 107, 128, 134} and subjects screened to exclude delirium and dementia.^{17, 22, 45, 108, 135} The importance of education was revealed by regression analyses as well, showing that education accounted for more variance than other demographic variables including gender, race, and social class.^{2, 107, 133, 134} In addition, education levels affected the distribution of errors across individual items and categories of items.^{22, 31, 36, 45, 133, 134, 136} Some studies, however, have failed to find such a relation.^{19, 24, 60, 90, 137} This may be due, at least in part, to sampling biases caused by an overrepresentation of individuals with either high education or severe cognitive impairment, the latter causing a restricted range of very low MMSE scores.

A central issue emerging from these results is whether the effects attributed to education represent a measurement error or a risk factor. The prevalent view is that education introduces a psychometric bias leading to a misclassification of individuals from different educational backgrounds, and this bias should be corrected by employing norms stratified for education. This position assumes that education reflects a stable characteristic that is not associated with any type of underlying pathology and, as such, does not constitute a risk factor. To a large degree, this view is based on evidence showing that low educational levels increase the likelihood of misclassifying normal subjects as cognitively impaired (ie, false positives). This is particularly evident when subjects have fewer than 9 years of education.^{22, 45} Higher education levels also may produce classification errors. Fillenbaum et al.¹⁰⁷ speculated that higher education levels may mask mild impairment, and O'Connor et al.³² found that all dementia

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patients with an MMSE score of 24 or greater (ie, false negative) had relatively high levels of education. Thus, evidence from cross-sectional studies shows that number of years of education affects both sensitivity and specificity.

Results from longitudinal studies provide further evidence that while education is associated with low MMSE scores, it is not associated with either the diagnosis of AD or the rate of cognitive decline that occurs as the severity of AD increases. Three studies^{22, 134, 138} have reported that although educational levels and MMSE scores were correlated, number of years of education was not related to the diagnosis of dementia. This is consistent with other reports showing that education is not associated with dementia.^{139, 140} Additionally, several longitudinal studies have reported that education was not associated with the rate of decline.^{22, 80, 112} Similar effects have been reported from studies using measures other than the MMSE to assess rate of cognitive change in AD patients.¹⁴¹⁻¹⁴³ While these results do not conclusively demonstrate that education solely reflects a psychometric bias, they do suggest that substantial potential for misclassification exists, prompting several authors to recommend that education levels, particularly 8 years or less, be considered when interpreting MMSE scores.^{31, 36, 40, 45, 51, 79, 107, 133, 144, 145}

Although little doubt exists that educational levels lead to potential misclassification, several authors caution that education may not exclusively represent a detection bias but also may reflect etiologic factors critical in a process eventually resulting in dementia.^{17, 134, 146-148} Lower education levels could, for example, contribute to the incidence of dementia because education is associated with various biological risk factors typically associated with multi-infarct dementia, such as hypertension, obesity, and serum cholesterol. Moreover, the failure of education to be etiologically related to one type of cognitive impairment, say Alzheimer's disease, does not necessarily mean that education will be unrelated to other types of cognitive impairments, such as vascular dementia. Thus, modification of the cut-off score to compensate for educational biases in one sample does not justify using the same criterion for another sample, unless justified by empirical results for that sample. Berkman¹⁴⁶ suggests that adjusting for education level at the time of initial screening decreases, if not eliminates, the possibility of exploring the hypothesis that education constitutes a risk factor for dementia. Furthermore, it reduces the possibility of investigating the relationship between education and cognitive impairment caused by factors other than dementing illness. The importance of Berkman's warning is underscored by preliminary results from the East Boston study suggesting that rate of AD may be higher among individuals with few years of schooling.¹⁴⁷ Thus, it appears likely that education represents both a psychometric bias and a risk factor, differing only in degree (for further discussion see Refs. 30, 40, 144, 146-148).

Age Numerous studies have shown that MMSE scores decrease as age increases. This relationship has

been reported in community surveys employing random sampling procedures,^{2, 18, 31, 34, 36, 40, 107, 134} studies in which subjects did not suffer from dementia, delirium, or depression,^{17, 24, 45, 51, 137} and studies that tested hospital or clinic patients.^{17, 35, 149} Most of this age-related change begins about age 55 or 60 and then dramatically accelerates over the age of 75 or 80.^{16, 40} These age effects persist when subjects are stratified by education level,^{16, 18, 31, 40} demonstrating that the age effect is not simply due to cohort differences in educational attainment.

The finding that older adults tend to have lower MMSE scores than younger adults suggests that fixed, age-independent cut-off scores (eg, 23/24) may underestimate cognitive impairment with younger adults or over-estimate it with older adults. Evidence showing that dementia frequently is overestimated in older normals supports this notion.^{18, 45, 145} However, since age generally is viewed as a risk factor for dementia,^{134, 146, 147} all age effects cannot be merely dismissed as representing only psychometric bias. The matter is further complicated by the finding from longitudinal studies that rate of cognitive deterioration in Alzheimer's patients appears to be independent of age.¹²¹

Conflicting evidence exists concerning the degree to which age interacts with education. While some studies^{16, 31} report that age-related impairment in scores is greater for subjects with lower educational levels, others¹⁷ conclude that declines for age and education are independent. In addition, several studies have reported that age and education do not uniformly affect all items.^{2, 16, 17, 24, 31, 36, 45, 134} These and other results suggest that the association between total MMSE performance, age, and education is complex, but nevertheless one that should be considered in interpreting MMSE performance.

Gender In a summary report containing data from approximately 20,000 individuals participating in the ECA study, George et al⁴⁰ concluded that no meaningful gender differences existed in the prevalence of cognitive impairment. Other studies indicate that even when differences were statistically significant, they did not account for a substantial portion of variance and generally were not substantively important.^{16-18, 24, 45, 51, 107, 118, 150}

Race/Ethnicity and Social Class The most widely cited study on the effects of race/ethnicity on MMSE performance analyzed interview responses from over 3,000 English and Hispanic residents of Los Angeles.³⁶ Both English and Spanish versions of the MMSE were used. Analysis of individual items revealed that Hispanics performed significantly lower on many items. A more recent report of the results from all ECA centers⁴⁰ indicates that race/ethnicity exerts a significant effect on the distribution of MMSE scores. The finding that racial effects tend to be maintained within different educational levels suggests that education cannot explain all race/ethnicity effects. However, Murden et al²² reported contradictory findings that MMSE performance was not affected by race. Effects

of social class and socioeconomic status on MMSE scores also have been observed.^{17, 34, 150, 133}

ANALYSIS OF INDIVIDUAL ITEMS

Various analyses, including frequency distributions of the errors, part-total correlations, item analyses, and stepwise regression analyses, have been employed to investigate the relationship between individual items and total MMSE score. Analyses of individual items from studies containing normal subjects (ie, large community surveys or ones in which participants were screened to eliminate obvious cases of dementia and delirium) revealed that most errors generally occurred in only four of the seven cognitive domains: recall of three words, serial 7s/WORLD, pentagon, and orientation to time.^{2, 16, 21, 24, 31, 34, 40, 137} Although the relative contribution of each domain varied from study to study, recall of three words usually produced the greatest number of errors. Errors rarely occurred for orientation to place, registration, and individual language questions.

Analyses of individual items for Alzheimer's patients again indicated that the same four cognitive domains consistently produced the greatest number of errors.^{2, 19, 21, 27, 28, 135, 151} The relative difficulty of these items varied across studies, with the exception that the greatest percentage of errors generally occurred for recall of three words. The failure to observe a consistent rank order of difficulty for the other three domains is attributable, at least in part, to differences in dementia severity that existed between studies. Although there are reports that orientation to place is highly predictive of total MMSE scores,²¹ this finding is not consistent and may depend on whether subjects were tested in a familiar (eg, home) or unfamiliar (eg, hospital) environment.^{37, 56, 57}

We are aware of only two studies that directly compared the performance of normals and Alzheimer's patients on each item. Brayne and Calloway¹³⁴ reported that "normal" subjects scored significantly higher than dementia patients on all MMSE items except "no ifs, and, or buts" and naming two objects (watch, pencil). Galasko et al,²¹ employing a paired-comparison procedure for different age and education levels, compared scores from healthy controls with those obtained by Alzheimer's patients. As expected, the differences between the "normal" and moderate-to-severe groups increased on the same items that had previously best discriminated between mild AD and normals. In addition, a significant difference occurred for the language items. Thus, it appears that although the language items are useful in distinguishing between normals and Alzheimer's patients, they are much less discriminating than are the other four categories and are most sensitive to individual differences among patients with moderate-to-severe AD. This finding is consistent with previous findings showing that items are differentially sensitive to disease severity.^{19, 119, 152-154}

Three studies were undertaken to determine if the seven rationally derived cognitive categories could be validated through factor analysis.^{27, 28, 119} Although each study yielded a two factor solution, the items

contained in each factor varied among the studies. Nevertheless, the results from the studies are important since they show that the set of cognitive domains measured by the MMSE is certainly less than the seven categories into which the questions usually are grouped.

Finally, studies have determined if serial 7s and reverse spelling of WORLD represent equivalent tasks. The overwhelming weight of the data shows they are not comparable. Spelling WORLD backward consistently produces higher scores than does counting backward by sevens.^{16, 19, 21, 33, 36, 37, 45, 137, 155-158} Moreover, Holzer et al¹⁶ reported a correlation between serial 7s and WORLD of only .37, with WORLD having a higher correlation with the total score than serial 7s (.47 vs .39). Finally, studies on the effects of age, education, and gender on performance on these two items have been inconsistent.^{22, 32, 36, 45, 155, 156}

SUGGESTED MODIFICATIONS TO THE MMSE

Several attempts have been made to improve the sensitivity and specificity of the MMSE. Some studies have explored altering the cut-off score, but without much success. In general, changing the cut-off points alters both the sensitivity and specificity of the test, increasing one while decreasing the other.^{21, 32, 34, 45, 72, 77}

A second approach has been to compensate in some manner for various ages and/or educational levels.^{2, 22, 24, 45, 51, 133, 145, 159} One strategy is to assume that the MMSE is valid only if the person has 9 or more years of schooling.^{22, 105, 133, 145} Another tack is to generate normative data, stratified for age and/or education.^{24, 51} Although using different cut-off scores for various ages and educational levels has its merits, it also suffers the same problem noted above—attempts to increase sensitivity usually decrease specificity.

A third avenue is using multivariate procedures to differentially weight existing MMSE items.^{2, 16, 21, 31, 36, 38, 137, 144, 160} For example, Cullum et al,¹³⁷ using a stepwise regression analysis with highly educated normal subjects aged 50 to 80, reported that recall of three words and orientation to time correlated .87 with total score. Galasko et al,²¹ employing a logistic-regression model with AD patients, found that the sum of the scores for recall of three words and orientation to place resulted in sensitivity and specificity levels that were similar to those produced by total MMSE scores. Magaziner et al³¹ generated a series of prediction equations for different age groups and educational levels. However, results from several studies make the generality of these equations questionable.¹⁶¹⁻¹⁶³

A fourth alternative is to modify the content of the MMSE.^{2, 21, 22, 36, 45, 81, 144} One way to modify the MMSE would be to exclude questions particularly sensitive to age, education, and culture or to add questions less sensitive to these demographic variables. Another approach would involve eliminating items with little diagnostic utility and/or adding items known to be sensitive to cognitive impairment. The need for more adequate language items, for example, has been mentioned by several authors.^{35, 47} In some instances, sup-

plementary items have been employed. For example, Galasko et al²¹ found that adding a word fluency task decreased error rates and increased the sensitivity of the MMSE from 79.2% to 87.5% for mild AD. Mayeux et al⁸¹ created a modified version of the MMSE (mMMS) by adding digit span, recall of four US presidents, confrontational naming, sentence for repetition, and copy of two additional designs. The mMMS correlated .89 with the MMSE, has a test-retest reliability of .95,^{81, 103, 131, 165} and has been employed in several dementia studies.

The most extensive revision of the MMSE was undertaken by Teng et al.¹³⁵ The Modified Mini-Mental State Examination (3MS) maintains the MMSE's basic format while extensively modifying its content. It contains four new test items, an expanded range of scores (0-100 rather than 0-30), and modified scoring procedures allowing assignment of partial credit on some items. Subsequent research⁵¹ demonstrated that the 3MS possesses higher reliability and validity than the MMSE. Additional information on the psychometric properties of the 3MS should be forthcoming since it currently is being used to assess cognitive impairment in the Canadian Study on Health and Aging,¹⁶⁶ an epidemiological survey sponsored by the Health and Welfare Canada.

A fifth alternative has been to include the MMSE as part of a battery of tests. For example, Pfeffer et al¹⁶⁷ developed the Mental Function Index (MFI) by using a discriminant function analysis to obtain weighted scores for the MMSE, the Symbol Digit Modalities Tests,¹⁶⁸ and the Raven Subtest B.¹⁶⁹ The combined sum of the weighted scores yielded 93% sensitivity for demented patients and 80% specificity for normals. Similar values were obtained in a follow-up study.⁴⁶ However, substantially lower levels of sensitivity have been reported.^{26, 70} In addition, Mowry and Burvill²⁶ noted that high refusal rates and administrative time also contraindicate the MFI's use as a screening device.

SUMMARY AND RECOMMENDATIONS

The MMSE was developed as a screening test to quantitatively assess the severity of cognitive impairments and to document cognitive changes that occur over time. The research reviewed over the past 26 years indicates, to a large degree, that the MMSE has been able to fulfill these goals. Examination of its psychometric properties shows moderate-to-high levels of reliability, with test-retest reliability higher than measures of internal consistency. Items measuring recall of three words, copy pentagon, 7s/WORLD, and orientation to time appear to be the most sensitive to both normal aging and dementing illnesses. The MMSE, like many measures of cognitive ability, is affected by demographic factors. Of these, age and education exert the greatest effect. Criterion validity measures show high levels of sensitivity for moderate-to-severe levels of dementia. Construct validation studies demonstrate that MMSE scores correlate highly with those obtained from other types of cognitive screening tests as well as from psychological and neuropsychological tests measuring intelligence, memory,

specific types of cognitive abilities, and activities of daily living. Other evidence shows the MMSE to be correlated with AD pathology. Longitudinal research with dementia patients illustrates its ability to serially document cognitive change.

However, the MMSE is not without problems. Perhaps the most frequently cited shortcoming relates to its lack of sensitivity to mild cognitive impairment and its failure to adequately discriminate patients with mild AD from normal patients. Attempts to improve the sensitivity, including altering the cut-off scores, differentially weighting existing items, modifying the content of the items, or using supplementary items, have met with mixed success. The MMSE also has received its share of criticism because of its insensitivity to progressive changes occurring with severe Alzheimer's disease. Moreover, inconsistencies in the way it is administered, scored, and interpreted make cross-study comparison difficult. The content of the MMSE is highly verbal, lacking sufficient items to adequately measure visuospatial and/or constructional praxis. Hence, its utility in detecting impairment caused by focal lesions, particularly those residing in the right hemisphere, is uncertain. Items designed to measure language functions also tend to be overly simplistic and tend to be insensitive to mild linguistic deficits, hence increasing the number of false negative errors.

Some of the shortcomings may have occurred because the MMSE, in its current form, is expected to provide too many different types of screening functions. It may be unrealistic to expect a single version of the test to meet all of these demands. Different types of screening applications (eg, AD) may require different versions of the MMSE. Thus, it also may be more efficient to employ one set of cut-off scores for a hospital-based geriatric clinic and a different set for epidemiological surveys. Since altering cut-off scores typically increases either the sensitivity or specificity while the other decreases, the selection of the specific criterion score may depend on a cost-benefit analysis to assess the relative importance of increased numbers of false positives or false negatives.

In view of the above, we feel the following recommendations are warranted when the MMSE is employed in a clinical setting.

(1) The MMSE should be used as a screening device for cognitive impairment or a diagnostic adjunct in which a low score indicates the need for further evaluation. It should *not* serve as the sole criterion for diagnosing dementia or to differentiate between various forms of dementia. However, MMSE scores may be used to classify the severity of cognitive impairment or to document serial change in dementia patients.

(2) The following three cut-off levels should be employed to classify the severity of cognitive impairment: no cognitive impairment = 24-30; mild cognitive impairment = 18-23; severe cognitive impairment = 0-17.

(3) The MMSE should not be used clinically unless the person has at least a grade eight education and is fluent in English. While this recommendation does not discount the possibility that future research may show

that number of years of education constitutes a risk factor for dementia, it does acknowledge the weight of evidence showing that low educational levels substantially increase the likelihood of misclassifying normal subjects as cognitively impaired.

(4) Serial 7s and WORLD should not be considered equivalent items. Both items should be administered and the higher of the two should be used. In scoring serial 7s, each number must be independently compared to the prior number to insure that a single mistake is not unduly penalized. WORLD should be spelled forward (and corrected) prior to spelling it backward. The scoring procedures employed by either Morris et al¹³ or Teng et al²³ are recommended.

(5) The words apple, penny, and table should be used for registration and recall. If necessary, the words may be administered up to three times in order to obtain perfect registration, but the score is based on the first trial.

(6) The "county" and "where are you" orientation to place questions should be modified. The name of the county where a person lives should be asked rather than the name of the county where the testing site resides, and the name of the street where the individual lives should be asked rather than the name of the floor where the testing is taking place.

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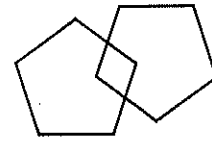
APPENDIX

Mini-Mental State Examination (MMSE)

Questions	Points
1. What is the: Year? Season? Date? Day? Month?	5
2. Where are we: State? County? Town or City? Hospital? Floor?	5
3. Name three objects (Apple, Penny, Table), taking one second to say each. Then ask the patient to tell you the three. Repeat the answers until the patient learns all three.	3
4. Serial 7s. Subtract 7 from 100. Then subtract 7 from that number, etc. Stop after five answers. <i>Alternative: Spell WORLD backwards.</i>	5
5. Ask for the names of the three objects learned in # 3.	3

- 6. Point to a pencil and watch. Have the patient name them as you point. 1
- 7. Have the patient repeat "No ifs, and, or buts". 3
- 8. Have the patient follow a three-stage command: "Take the paper in your right hand. Fold the paper in half. Put the paper on the floor". 3
- 9. Have the patient read and obey the following: "CLOSE YOUR EYES". (Write it in large letters). 1

- 10. Have the patient write a sentence of his or her own choice. 1
- 11. Have the patient copy the following design (overlapping pentagons). 1



Total points = 30

(MSE)

	Points
y?	5
vn	5
y, h. ne ne	3
n p	5
s. ts	3