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Comparison of the Memory Performance Index With Standard Neuropsychological Measures of Cognition

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Abstract

The Mild Cognitive Impairment Screen (MCIS) is a computer-based cognitive assessment designed for clinical and research use in detecting amnestic mild cognitive impairment (aMCI). Performance on the MCIS is reported as the Memory Performance Index (MPI). However, the comparability between the MPI and traditional neuropsychological tests in detecting aMCI, and in differentiating it from Alzheimer's disease (AD) and normal aging has not been examined. A cross-sectional study was conducted to assess the validity of the MPI relative to standard neuropsychological measures. Participants included 12 individuals diagnosed with aMCI, 49 with mild AD, and 25 healthy elderly. The MCIS significantly discriminated among aMCI, AD, and healthy elderly controls. The MCIS is effective in detecting aMCI, and in discriminating it from cognitive changes observed in AD and normal aging. The MCIS may be a valuable tool in the identification of elderly at high risk for dementia due to its ease-of-use and brief administration time.

Keywords

Mild Cognitive Impairment, Dementia, Alzheimer's Disease, Screening, Memory

Introduction

Early detection of Alzheimer's disease is increasingly important. Since cognitive symptoms are currently classified along a spectrum of "mild cognitive impairment" (MCI) through overt dementia, numerous instruments have been evaluated in terms of their ability to detect and discriminate among this range of conditions. Memory impairment is a cardinal feature of early AD, and the amnestic form of Mild Cognitive Impairment (aMCI) is often considered a prodromal stage of AD. The National Institute of Aging's Consortium to Establish a Registry for Alzheimer's Disease's (CERAD) "Word List Memory" (WLM) test, a subtest within the consortium's neuropsychological battery, has been shown to be a relatively sensitive test of memory for detecting MCI.[1-3] The WLM test consists of 3 immediate-recall trials of a 10-word list, followed by an interference task lasting several minutes, and then a delayed-recall trial with or without a delayed-cued-recall trial.

The Mild Cognitive Impairment Screen (MCIS), derived from the WLM, differentiates cognitive changes associated with normal aging from aMCI as well as dementia due to AD and related disorders.[4] The MCIS is a brief, electronically scored, verbally administered test that uses correspondence-analysis in calculating a patient's memory capabilities, which is then reported as the Memory Performance Index (MPI). The MCIS has been validated in both academic and community clinical settings and in multiple languages.[5,6] In this article, the comparability between the MCIS and a battery of traditional neuropsychological tests (Dementia Rating Scale, Mini-Mental State Examination (MMSE), Wechsler Memory Scale (WMS), Clock Draw, Digit span, Letter Fluency Test (FAS)), Trails A, Trails B, Boston Naming test, Wisconsin Card Sort Test (WCST), California Verbal Learning Test (CVLT), and Wechsler Adult Intelligence Scale (WAIS)[7-17] in detecting MCI was examined.

Materials and Methods

Sample

Data were collected and analyzed from 86 volunteers, aged 65 to 93 (normal [n = 25]; MCI [n = 12]; AD [n = 49]) recruited from the UCSD Shiley-Marcos Alzheimer's Disease Research Center (ADRC) and Memory Screening Clinic. Alzheimer's Disease Research Center participants are healthy elderly recruited from the local community and from memory screening programs and memory disorder clinics. This study used consecutive normals that were evaluated during the same time period as the aMCI and AD patients. Participants were all newly diagnosed (within 6 months) of this study. The study

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Table 1. Demographic Summary of the Participant Population

	Overall (N = 86)	Normal (N = 25)	MCI (N = 12)	AD (N = 49)	*P* Values[a]
Sex	50 Male, 36 Female	11 Male, 14 Female	8 Male, 4 Female	31 Male, 18 Female	.230
Age	77.1 (9.5)	80.3 (8.6)	74.8 (9.0)	76.4 (9.8)	.201
Years Ed.	15.4 (2.7)	16.3 (2.4)	14.7 (2.5)	15.2 (2.8)	.227

Abbreviation: MCI, mild cognitive impairment.
[a] *P* values for a one-way ANOVA, by group, for the corresponding comparison.

originally recruited 100 participants, but there was incomplete data on 14 of the participants. The protocol was reviewed and approved by the UCSD institutional review board. All research participants and caregivers gave written informed consent. Surrogate consent was used if criteria were met for its use. Potential volunteers completed a baseline evaluation consisting of structured interviews, neurological examinations, and mental status exams, as well as an extensive battery of neuropsychological tests. The ADRC battery of evaluations included tests of memory for verbal and visual material, attention/psychomotor speed, language abilities, spatial abilities, and executive functioning. Participants also completed a demographic / medical history form, an assessment of instrumental activities of daily living (IADLs), and the Clinical Dementia Rating Scale. There were no statistically significant differences with regard to medical health or education between the normal, MCI or AD participants. After completing the aforementioned protocol, the participants' data were reviewed by an independent panel of 6 board-certified dementia specialists, and an ADRC consensus diagnosis is reached. The MCIS was administered within 90 days of the ADRC battery. A minimum of 60 days must have elapsed before the MCIS was administered. The UCSD ADRC Consensus Diagnosis has been shown to be 92% accurate for AD as compared to neuropathological diagnosis.[18]

Statistical Methods

Comparisons between diagnostic groups (eg, normal, aMCI, probable AD) and also between individuals with normal and nonnormal MPI performance were performed using chi-square analysis, one-way analysis of variance, Kruskal-Wallis, Games-Howell test, and a-priori *t*-tests. Bivariate correlations and linear regressions were calculated between MPI scores and other neuropsychological measures. Sensitivity and specificity of the MPI, relative to the ADRC Consensus Diagnosis, was also calculated. All statistical analyses were conducted using SPSS version 17.0.

The MPI scoring algorithm uses correspondence analysis, a technique that creates weighted scores from the subject's full WLM performance profile, which consists of the pattern of recalled and not recalled words across 4 trials. The method by which the MPI scoring algorithm was derived is fully described elsewhere.[4]

Briefly, the algorithm produces an optimally weighted combination of values, which are then used in a logistic regression to predict each participant's probability of cognitive impairment. The value derived from the logistic regression (the logistic regression score) represents a participant's full WLM performance profile as a single value that has an unwieldy range from a negative number to a positive number that is hard to work with. Therefore, the logistic regression score was translated onto a scale, the MPI, of 0 to 100, with 50 making the cut point between impaired (<50) and normal (>50).

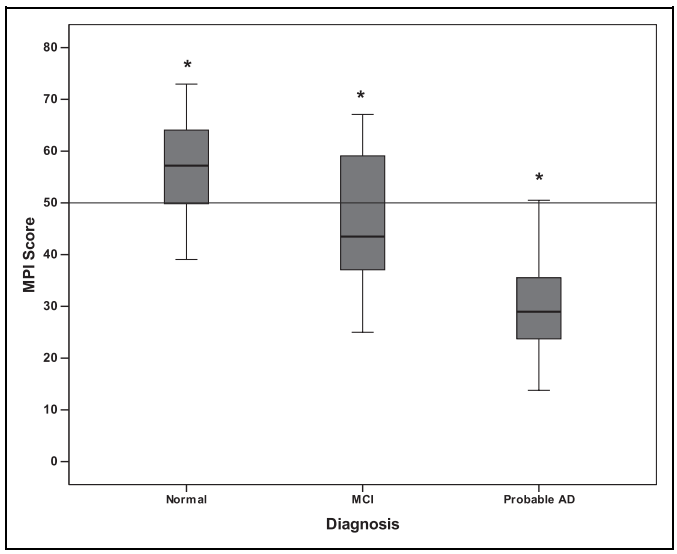

Figure 1. Comparison of classification of participants based on Memory Performance Index (MPI) and consensus Alzheimer's Disease Research Center (ADRC) diagnosis.

Results

A demographic summary of the participant population appears in Table 1. Of the participants 42% were women. The mean age of the participants was 77.1 years and mean education was 15.4 years. There were no statistically significant differences across the diagnostic groups for age or years of education; the groups differed significantly in terms of mean MMSE score, Trails B time, Trails B errors, and CVLT score (all $P < .001$). As can be seen in Figure 1, the diagnostic groups also differed significantly on MPI score ($P < .001$). A priori *t* tests between MPI normal individuals versus MPI impaired individuals showed no significant differences in terms of age, education, and Digit Span, whereas significant differences were noted on the MMSE ($P < .001$), CVLT—Long Delay ($P < .001$), Trails B Time ($P < .001$), and Trails B Errors ($P = .008$).

Table 2. Neuropsychological Summary of the Subject Population

	Overall	Normal	MCI	AD	*P* Values[a]	MPI Corr.[b]
MPI	40.3 (16.1)	56.7 (9.8)	46.2 (14.1)	30.5 (11.0)	<.001	n/a
DRS–total	124.5 (19.9)	139.5 (3.2)	137.8 (5.7)	111.8 (19.5)	<.001	0.514[c]
MMSE	25.2 (5.0)	29.3 (1.2)	28.9 (1.8)	22.2 (4.7)	<.001	0.546[c]
WMS-R logical Memory story B–Delayed	6.9 (6.2)	13.3 (4.5)	7.0 (3.6)	2.4 (3.3)	<.001	0.609[c]
Digit span total–Raw	16.6 (13.7)	15.6 (3.4)	15.6 (4.3)	17.6 (19.0)	.826	−0.008
FAS score	37.8 (14.4)	47.6 (10.7)	43.6 (13.4)	30.2 (12.3)	<.001	0.483[c]
Trails A–time	54.2 (33.5)	37.2 (15.8)	46.9 (33.5)	68.3 (36.9)	.001	−0.433[c]
Trails A–errors	0.6 (2.9)	0 (0)	1.0 (3.5)	0.89 (3.6)	n/a	−0.087
Trails B–time	161.4 (95.8)	94.0 (50.3)	104.83 (56.0)	232.9 (82.3)	<.001	−0.615[c]
Trails B–errors	2.6 (5.7)	0 (0)	0 (0)	5.4 (7.4)	n/a	−0.486[c]
WAIS-R digit Symbol raw	44.1 (21.8)	46.9 (11.1)	41.8 (11.8)	43.0 (28.1)	.724	0.231[c]
Boston–total correct	25.3 (12.8)	27.4 (2.4)	27.3 (3.6)	23.4 (17.2)	.391	0.206
WCST–Perseverative errors	3.3 (6.3)	0.4 (1.2)	0.4 (0.8)	6.2 (7.9)	.001	−0.413[c]
CVLT–Lisa A–trials 1-5 raw	32.8 (16.8)	50.7 (15.2)	36.9 (9.5)	21.7 (8.2)	<.001	0.749[c]
CVLT–Short Delay free recall	5.2 (5.0)	10.6 (3.7)	4.9 (3.2)	1.5 (2.3)	<.001	0.721[c]
CVLT–long delay free recall	5.0 (5.0)	10.4 (3.3)	5.2 (3.9)	1.3 (2.2)	<.001	0.737[c]
CERAD–delayed recall	2.9 (3.1)	7.1 (2.3)	4.0 (1.7)	1.0 (1.5)	<.001	0.655[c]
ANART–estimated premorbid IQ	115.9 (8.1)	120.9 (5.0)	117.8 (3.9)	113.4 (8.8)	.004	0.305[c]
WAIS-R–vocabulary raw score	51.9 (11.1)	59.1 (7.2)	54.4 (7.8)	47.1 (11.4)	<.001	0.463[c]

Abbreviations: CERAD, Consortium to Establish a Registry for Alzheimer's Disease's; MPI, Memory Performance Index; WMS-R, Wechsler Memory Scale—Revised Manual; ANART- American National Adult Reading Test.

[a] *P* values for a one-way ANOVA, by group, for the corresponding neuropsychological test.

[b] Pearson correlation between the MPI score and the corresponding neuropsychological test.

[c] $P < .05$.

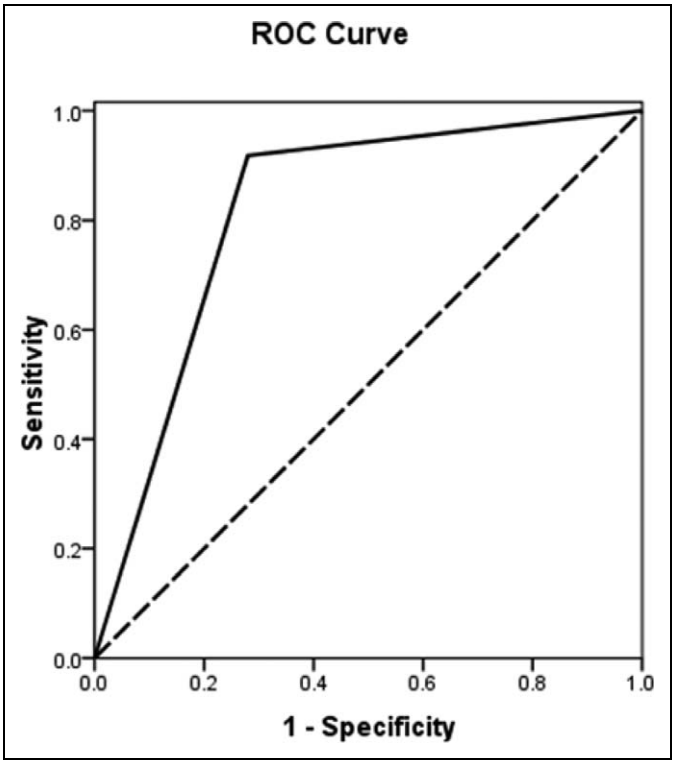

Figure 2. Receiver operator characteristic curve.

Memory Performance Index—Correlations and Group Differences

As anticipated, the MPI showed statistically significant correlations with several neuropsychological measures, as shown in Table 2. In particular, the MPI correlated well with measures of memory functioning such as Trails B time ($r = –.615$, $P < .001$), Trails B errors ($r = –.486$, $P < .001$), MMSE ($r = .546$, $P < .001$), DRS Total ($r = .514$, $P < .001$), WMS-R Delayed Logical Memory ($r = .609$, $P < .001$), WCST Perseverative Errors ($r = –.413$, $P = .001$), and CVLT Long Delay Free Recall ($r = .737$, $P < .001$).

Binary Classification and Receiver Operating Characteristic Curve

To compare the classifications provided by the ADRC Consensus Diagnosis versus the MPI, binary classifications were calculated and compared. Specifically, a 2 × 2 matrix was generated to compare the ADRC Consensus Diagnosis of normal versus nonnormal (eg, MCI or probable AD) versus the MPI score considered Normal ($\geq$51) versus Non-normal ($\leq$50). Relative to the neuropsychological assessment, the MPI accurately classified 74 of the 86 subjects (86%). More specifically, the matrix classified 56 individuals as True Positive (TP), 18 as True Negative (TN), 7 as False Positive (FP), and 5 as False Negative (FN). The calculated Sensitivity (TP / [TP + FN]) was 0.918. The calculated Specificity (TN / [TN + FP]) was 0.72. The Positive Predictive Value (TP / [TP + FP]) was 0.889. The generated receiver operating characteristic

(ROC) curve, Figure 2, had an area under the curve of 0.819 (95% confidence interval lower bound 0.706, upper bound 0.932).

Discussion

The clinical diagnosis of dementia is based on subjective cognitive complaints, impaired cognitive function on objective testing, and functional decline. Mild cognitive impairment is a clinical diagnosis in which deficits in cognitive function are evident but not of sufficient severity to warrant a diagnosis of dementia. Given that the number of elderly is predicted to increase steeply, there is a need for standardized cognitive assessment tools that deliver high-quality information and are practical for routine clinical use. The present study evaluated the discriminant validity of the MCIS in distinguishing individuals with aMCI from healthy elderly, as well as AD. From traditional neuropsychological testing, particularly strong results were obtained for parameters assessing memory, executive function, visual spatial skills, and verbal function. The MCIS provided the same level of discrimination, but using only verbal memory performance as the indicator.

The current findings are consistent with previous studies that have identified traditional neuropsychological tests that accurately detect dementia. Many such studies have found standard tests of verbal- and non-verbal memory and executive function to be very good discriminators. Others have found verbal fluency to be an excellent predictor, which is what was observed in this study. Regarding study limitations, our results may not be broadly generalizable, as the majority of our patients were recruited from specialty care centers. Also, the number of aMCI cases relative to normal and AD patients was relatively low, and including more patients with aMCI would lend more certainty to our findings. Finally, population-based studies with longitudinal follow-up, pathological confirmation of diagnosis, and comparison with a wider array of traditional tests are required to fully establish the validity of the MPI in aMCI detection. Another limitation of the MCIS is its inability to directly assess the underlying pathology leading to cognitive impairment, that is, biological markers of AD such as beta-amyloid levels, tau protein levels, and hippocampal volumes as assessed by neuroimaging. Based on previously published reports, we suggest that a future study with the MCIS could longitudinally follow participants recruited from a community setting, incorporating such biomarkers. Shankle and colleagues administered the MCIS to more than 100 000 individuals in a community setting and found a significant relationship between MPI scores and dementia severity (as measured by Functional Assessment Staging Test).[19] Other reports have also demonstrated the feasibility of administration of an electronic assessment as part of a longitudinal aging study with independently living participants, particularly in conjunction with common assessments (ie, MMSE, clinical dementia rating [CDR], etc.) and groups of varying clinical severity.[20] Hypothetically, such a study with the MCIS would not only extend the current findings but could potentially show the relationship between MPI scores over time and their association with conversion from one diagnostic category to another. Overall, the MCIS may be a useful screening tool for meaningful memory impairment, as documented by an independent extensive evaluation that included detailed neuropsychological testing and a formal Consensus Diagnosis.

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Declaration of Conflicting Interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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