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Computerized Cognitive Assessment of Mild Cognitive Impairment in Urban African Americans

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Few objective cognitive assessment tools have been validated for mild cognitive impairment (MCI) in African Americans despite higher prevalence of disease. This preliminary study evaluated discriminant validity of a computerized cognitive assessment battery for MCI in an urban African American cohort. Twenty-seven participants with MCI and 22 cognitively healthy individuals completed a multidomain battery (Mindstreams, NeuroTrax Corp, New Jersey). Mild cognitive impairment participants performed more poorly than cognitively healthy participants in all domains, with significant differences in memory ($P = .003$; $d = 0.96$), executive function ($P = .046$; $d = 0.64$), and overall battery performance ($P = .041$; $d = 0.63$). Adjustment for intelligence quotient (IQ) yielded significant differences in memory ($P < .001$; $d = 1.34$), executive function ($P = .007$; $d = 0.86$), attention ($P = .014$; $d = .80$), and overall performance ($P = .001$; $d = 1.09$). Such a validated battery may help to address an important clinical need in this population.

Keywords: cognitive assessment; mild cognitive impairment; MCI; African American; computerized battery

Introduction

Early detection of dementia hinges upon the diagnosis of mild cognitive impairment (MCI),[1-3] a pre-dementia state with a prevalence rate of 3% to 19% and a conversion rate to dementia of 5% to 16% per year.[4] A key feature of MCI is documented cognitive impairment in at least 1 cognitive domain.[1-3] Thus, objective cognitive assessment is central to MCI diagnosis, most commonly evaluating memory, executive function, attention, language, and visuospatial skill.[5,6] Assessment has traditionally been accomplished with paper-based neuropsychological tests, but recent years have seen the advent of computerized testing.[7-12] Such testing has been shown valid for MCI and early dementia[7,10,11,13] as well as other neurological disorders,[14-17] and has opened the possibility of providing broad assessment while overcoming many of the logistical and practical difficulties of neuropsychological referral.[12] Further, computerized testing affords enhanced precision and objectivity, providing such advantages as millisecond-level response time measurement and a uniform testing experience unaffected by such subjective factors as tester mood and tone of voice.

Many studies have found a higher prevalence and incidence of MCI[18] and dementia[19-22] in African Americans, and 1 study reported greater interest in screening and treatment for MCI among African Americans.[23] However, while there have been efforts to develop cognitive assessment tools suitable for African Americans (eg, Refs 24-27), such tools have yet to be formally validated for MCI in this population.

One reason for the paucity of validated assessment tools for MCI in African Americans may be the tendency for their misidentification as MCI on the basis of scores computed from largely white reference samples.[28,29] Indeed, numerous studies in multiple conditions have shown poorer cognitive scores for African Americans relative to their white

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counterparts, even after controlling for such variables as age, education, and premorbid functioning[29-34] (for reviews see Refs 35 and 36). These poorer scores are evident even on nonverbal tests often considered to be "culture fair" or "culture free"[28,37,38] and have variously been attributed to differences in schooling and acculturation[39] as well as biological/genetic factors.[19]

A popular approach for improving the validity of neuropsychological testing in African Americans has been to utilize ethnicity-specific norms.[24,25] However, given that educational and cultural experiences of African Americans vary with geographic and socioeconomic factors, norms established in one region may not be applicable to all African Americans.[26,29] Further, such an approach is incompatible with the view that neuropsychological norms should be representative of the general population.[40] A better approach might be to adjust for education and other fundamental variables (eg, premorbid intelligence) that may underlie apparent ethnicity differences.[26,40] Indeed several studies have found education alone[41,42] or in combination with other variables[27,29,35,43] to account for performance differences on neuropsychological tests between African American and white individuals.

The present preliminary study, therefore, sought to evaluate the discriminant validity of a computerized cognitive assessment battery for MCI[7] in an urban African American cohort. To enhance validity, an internal control group of cognitively healthy African Americans was used, adjustment was made for years of education, and a correction[44] for low IQ was applied.

Method

Participants

Participants were 49 elderly individuals over the age of 60 (minimum age: 60.7 years) recruited from local advertisements, an inner-city specialty clinic (Alzheimer's Disease and Memory Disorders Clinic, State University of New York, Brooklyn, New York), and an inner-city primary care clinic (Family Practice Clinic, State University of New York, Brooklyn, New York). Participants were examined at the specialty clinic and diagnosed with MCI ($N = 27$; age: 69.2 ± 6.5 years; education: 10.3 ± 3.7 years; 7 male) or as cognitively healthy ($N = 22$; age: 67.6 ± 4.6 years; education: 13.6 ± 3.2 years; 4 male) by consensus of a neurologist (HC) and a neuropsychologist (M-YJ). Diagnosis of MCI followed Petersen and colleagues[1-3] and included the following features: (1) a complaint of defective memory; (2) normal activities of daily living; (3) a deficit documented by performance on a standardized neuropsychological test; and (4) absence of dementia. Healthy elderly had no memory complaint and demonstrated normal performance on standardized neuropsychological tests. Standardized neuropsychological tests considered as part of the diagnostic process included some combination of the following: Mini-Mental State Examination orientation subtest; California Verbal Learning Test II; Rey-Osterrieth Complex Figure; Boston Naming Test (15-item version); selected items from the sentence repetition and commands subtests of the Boston Diagnostic Aphasia Examination, Judgment of Line Orientation, Clock Drawing Test, letter, category, and design fluency and card sorting subtests from the Delis-Kaplan Executive Function System, Wisconsin Card Sorting Test, digit span subtest from the Wechsler Adult Intelligence Scale III, Symbol Digit Modalities Test, word list and visual reproduction subtests from the Wechsler Memory Scale III, and Trailmaking Test. Magnetic resonance imaging (MRI) results as well as scores on the Wechsler Test of Adult Reading and the Geriatric Depression Scale were also considered as part of the diagnostic process. Diagnoses were made blind to participant identity and independently of the computerized cognitive testing results. Participants with current or significant history of neurological or psychiatric disease, suffering from terminal illness, or taking psychoactive medications were excluded. Participants with history of significant head trauma, alcoholism, cocaine or heroin abuse, or HIV were also excluded. All participants completed Mindstreams in English, their most comfortable spoken ("primary") language. Years of education for participants who immigrated to the United States from Caribbean countries (cognitively healthy: $N = 14$; MCI: $N = 16$) was determined based upon estimated equivalence to the United States education system. Institutional Review Board approval was obtained and informed consent was obtained from all participants.

Procedure

All participants completed a Mindstreams (NeuroTrax Corp) battery designed to detect mild impairment[7,12] in their primary language. The NeuroTrax computerized assessment system has been described elsewhere.[7,11] In brief, Mindstreams consists of commercial software that resides on the local testing computer and serves as a platform for interactive cognitive tests that produce accuracy and reaction time (RT; millisecond timescale) data. Once tests are run on the local computer, data are automatically uploaded to a central server, where calculation of

Table 1. Mindstreams Tests for Detection of Mild Impairment, Cognitive Domains Tested, and Outcome Parameters Produced

Mindstreams Test	Cognitive Domains Tested	Outcome Parameter Types
Go-NoGo Response Inhibition	Executive function, attention	Accuracy, average response time, response time standard deviation, errors of commission, errors of omission
Verbal Memory	Memory	Accuracy
Non-Verbal Memory	Memory	Accuracy
MPST	Nonverbal IQ	Accuracy
Stroop Interference	Executive function, attention	Accuracy, average response time, response time standard deviation
Finger Tapping	Motor skills	Inter-tap interval, tap interval standard deviation
Catch Game	Executive function, motor skills	Time to make first move, time to make first move standard deviation, average direction changes per trial, average error for missed catches, mean weighted accuracy
Staged Information Processing Speed	Attention, information processing speed	Accuracy, average response time, response time standard deviation
Verbal Function	Verbal function	Accuracy (rhyming, naming)
Visual Spatial Processing	Visual spatial	Accuracy

Abbreviation: IQ, intelligence quotient; MPST, Mindstreams Problem Solving Test.

outcome parameters from raw single-trial data, data normalization, and report generation occur. Thus administration, scoring, and results generation are automated and standardized.

Cognitive domains assessed by the computerized battery included memory (verbal and non-verbal), executive function, visual spatial skills, verbal function, attention, information processing, and motor skills.[7] All responses were made with the mouse or with the number pad. Patients were familiarized with these input devices at the beginning of the battery, and practice sessions prior to the individual tests instructed them regarding the particular responses required for each test.

The tests comprising the battery (Table 1) have been shown to detect cognitive impairment in elderly individuals in multiple cognitive domains.[7] Tests were administered in the same fixed order for all participants. Outcome parameters varied depending on the test (Table 1). To minimize differences in age and education and to permit averaging performance across different types of outcome parameters (eg, accuracy, RT), each NeuroTrax outcome parameter was normalized according to stratifications of age and education. Normalization for the current study was performed relative to the 1124 cognitively healthy research participants comprising the Mindstreams normative database as of this study (from, eg, Refs. 7, 13-17).

Normalized subsets of outcome parameters were averaged to produce 7 summary scores as follows, each indexing a different putative cognitive domain:

MEMORY: mean accuracies for learning and delayed recognition phases of Verbal and Non-Verbal Memory tests

EXECUTIVE FUNCTION: performance indices (accuracy divided by RT) for Stroop Interference test and Go-NoGo Response Inhibition test, mean weighted accuracy for Catch Game

VISUAL-SPATIAL: mean accuracy for Visual Spatial Processing test

VERBAL: weighted accuracy for verbal rhyming test (part of Verbal Function test)

ATTENTION: mean reaction times for Go-NoGo Response Inhibition and choice reaction time (a non-interference phase of the Stroop test) tests, mean standard deviation of reaction time for Go-NoGo Response Inhibition, mean reaction time for a low-load stage of Staged Information Processing Speed test, mean accuracy for a medium-load stage of Staged Information Processing Speed test

INFORMATION PROCESSING SPEED: performance indices (accuracy divided by RT) for various low- and medium-load stages of Staged Information Processing Speed test; weighted average, with harder levels weighted more than easier levels

MOTOR SKILLS: mean time until first move for Catch Game, mean inter-tap interval and standard deviation of inter-tap interval for Finger Tapping test

These 7 index scores served as the primary dependent variables for the present analysis. A Global Cognitive Score (GCS) computed as the average of these index scores served as a secondary dependent measure.[8,11,13-17]

Forty-six participants (21 cognitively healthy; 25 MCI) completed the Mindstreams Problem Solving Test (MPST), a test of nonverbal IQ co-normed and administered together with the cognitive tests (Table 1). Three participants did not complete MPST as they demonstrated an inability to differentiate similar from dissimilar figures when screened prior to testing. The Mindstreams Problem Solving Test is a test similar to and correlated with[44] the Raven's Progressive Matrices,[45] a standard paper-based measure of analytic intelligence and the ability to solve problems involving new information, without relying on acquired knowledge or skills. Such tests are designed to load highly on Spearman's general intelligence factor (*g*) but have low cultural, language, and educational bias, making them prime estimates of premorbid intelligence. During MPST, pictorial puzzles of gradually increasing difficulty are presented. Each puzzle consists of a 2 × 2 array containing black-and-white geometric figures with a certain spatial relationship among them and a missing figure. Participants must choose the best fit for the fourth (missing) figure from among 6 possible alternatives. Solving the puzzles requires problem solving and abstraction abilities. Given that MPST performance was poor (cognitively healthy: 82.3 ± 16.7; MCI: 80.2 ± 14.1), an adjustment for premorbid IQ based on MPST score[44] was applied to the Mindstreams outcome parameters, and between-groups comparisons were run for the index scores and GCS as computed from the original and adjusted outcome parameters. The IQ-adjustment involved comparison of actual and expected outcome parameter performance, with expected performance computed from the correlation between MPST (the "hold" test) and the outcome parameter for the relevant normative stratification[44] (for a similar approach, see Refs 46 and 47). The IQ-adjusted scores are intended to give a better indication of true cognitive status.

Statistical Analysis

Between-group comparisons were made by univariate analysis of covariance (ANCOVA). Age, education, and gender were potential covariates. Each of these was included as a covariate in a separate analysis when a between-group difference was observed for the potential covariate ($P < .05$) along with a within-group correlation between the potential covariate and performance ($P < .10$) or vice versa. An interaction term was included in the ANCOVA when significant at $P < .10$ to correct for differential effects of the covariate across study groups and of study group across values of the covariate. Note that a conservative criterion (ie, $P < .10$) was adopted for inclusion of the interaction term to increase the likelihood that cases of inequality of covariance would be detected and corrected for. If heterogeneity of variance was indicated by a significant Levene's test, homogeneity of variance was achieved via standard transformations (eg, square, reciprocal).[11,48] In cases of persistent heterogeneity of variance in the absence of covariates, a nonparametric Mann-Whitney *U* test was used. Effect sizes (Cohen *d*) were computed for each comparison. Two-tailed statistics were used throughout, and $P < .05$ was considered a significant between-group difference. All statistics were computed with SPSS statistical software (SPSS Inc, Chicago, IL).

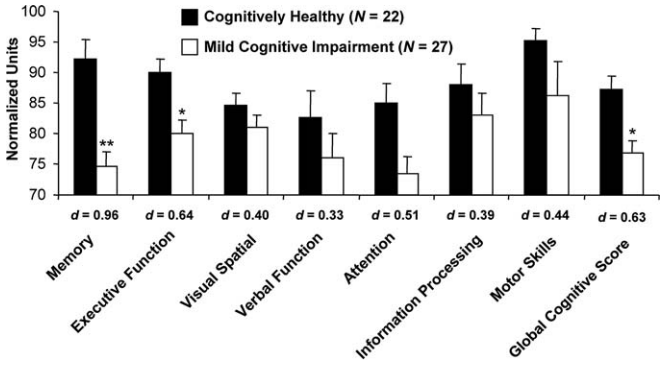

Figure 1. Index score and Global Cognitive Score performance (mean + standard error) for cognitively healthy and mild cognitive impairment (MCI) participants. Data is normalized by age and years of education and then fit to an intelligence quotient (IQ)-style scale (mean: 100, standard deviation: 15). * indicates $P < .05$ and ** indicates $P < .01$ versus healthy controls. Effect sizes (Cohen *d*) are given.

Results

Mild cognitive impairment participants were similar in age ($P = .334$) and gender ($P = .518$) but had significantly fewer years of education ($P = .002$) relative to cognitively healthy participants. Thus education was included as a covariate in the between-groups models when a within-group correlation was significant at the $P < .10$ level.

Mean performance was poorer for MCI as compared with cognitively healthy participants (Figure 1) for all index scores and the GCS, with significant differences for Memory ($P = 0.003$), Executive Function ($P = 0.046$), and the GCS ($P = 0.041$). A large effect ($d > 0.8$) was found for Memory ($d = 0.96$), with

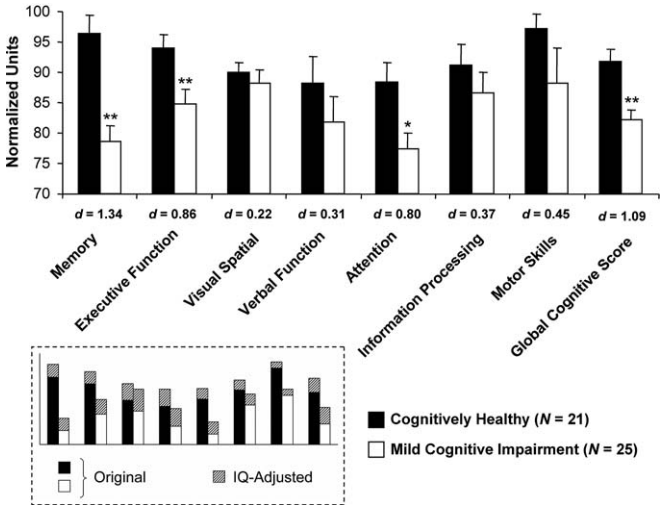

Figure 2. Intelligence quotient (IQ)-adjusted index score and Global Cognitive Score performance (mean + standard error) for cognitively healthy and mild cognitive impairment (MCI) participants. Data is normalized and IQ-adjustment applied by age and years of education and then fit to an IQ-style scale (mean: 100, standard deviation: 15). * indicates $P < .05$ and ** indicates $P < .01$ versus healthy controls. Effect sizes (Cohen d) are given, and comparison between original and IQ-adjusted scores is shown (inset).

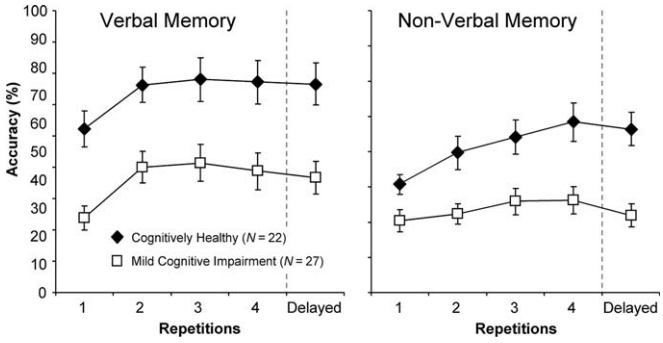

Figure 3. Raw memory test performance. Mean accuracy (mean + standard error) for each of the 4 immediate repetitions and the delayed repetition from Verbal (left) and Non-Verbal (right) memory tests for cognitively healthy (filled diamonds) and mild cognitive impairment (MCI) participants (open squares).

medium effects ($0.5 < d \leq 0.8$) for Executive Function, Attention, and the GCS, and small effects ($0.2 < d \leq 0.5$) for Visual Spatial, Verbal Function, and Information Processing (Figure 1). Correlations with education were significant at the $P < .10$ level for Memory, Executive Function, Attention, and the GCS, necessitating its inclusion as a covariate in between-groups analyses of these scores.

As anticipated based upon prior work,[44] adjustment for premorbid IQ resulted in higher cognitive scores for participants with below-average performance on the MPST, and lower scores for participants with above-average MPST performance. Moreover, the adjustment behaved similarly in the cognitively healthy and MCI groups. Given that most participants in both groups scored poorly on the MPST, application of the adjustment resulted in a net increase in scores relative to the unadjusted scores for both groups (Figure 2, inset). Critically, application of the adjustment eliminated correlations with education significant at the $P < .10$ level for all Mindstreams scores, obviating the necessity to include it as a covariate in the between-groups models. Use of adjusted scores and omission of the education term resulted in larger between-group differences. Significant differences and large effects were obtained for Memory ($P < .001$; $d = 1.34$), Executive Function ($P = .007$; $d = 0.86$), Attention ($P = .014$; $d = 0.80$), and the GCS ($P = .001$; $d = 1.09$; Figure 2).

To further examine the large between-group difference in Memory, Figure 3 shows raw accuracy performance for the Verbal and Non-Verbal Memory tests that contribute to the Memory index score. On the Verbal Memory test, MCI participants performed at a lower level, with both groups performing most poorly for the first repetition followed by improved performance that remained stable for the subsequent repetitions. On the Non-Verbal Memory test, MCI participants also performed at a lower level but seemed to show little learning relative to healthy participants, who showed marked learning across all 4 immediate repetitions.

Discussion

The present findings support good discriminant validity for MCI in a small, urban African American cohort who completed a multidomain battery of computerized cognitive tests. To enhance validity (1) a comparison group with similar ethnic and demographic characteristics was used; (2) outcomes were adjusted for age and education; (3) analyses included education as a covariate when correlated with performance; and (4) analyses were repeated following adjustment for IQ. In line with the current clinical concept of MCI[3], impairment was not limited to memory but was evident in multiple domains, most prominently executive function. The IQ-adjustment raised scores in a similar fashion for healthy and MCI groups, consistent with prior

work.[44] Adjusted scores were not correlated with education, making covariation unnecessary, and resulting in improved discriminant validity, with large effects for memory, executive function, attention, and overall battery performance. To our knowledge, no other studies to date have formally validated neurocognitive tests for MCI in an African American cohort.

In several studies,[41,42] the authors found no difference in cognitive performance between African American and white individuals when years of education was controlled. This finding is consistent with the suggestion that ethnicity is most often a surrogate variable for education and other more fundamental variables that influence test scores.[40] In other studies, adjustment for education eliminated only a portion, if any, of the difference between African Americans and whites.[29,35,27,43] Thus adjustment for education is a minimal requirement for valid assessment of African Americans,[36] but additional mediating variables (eg, premorbid intelligence) should be controlled for as well.[34]

In the current study, age- and education-adjusted scores were used as the primary outcomes and an adjustment for premorbid IQ applied to these scores.[44] The obtained improved validity with application of an IQ-adjustment is consistent with findings of several studies,[49,50] showing that compared with education-adjusted scores, IQ-adjusted scores better predict progressive cognitive decline in elderly individuals. Use of a nonverbal estimate of premorbid intelligence rather than a reading test measure (eg, NART, WRAT; see, eg, Refs 51 and 52) was motivated by the demonstrated misestimation using these methods[53-58] and inapplicability in patients with significant articulatory or visual acuity problems.[44,59]

One limitation of the present results is the small sample size. A related limitation is that the participants may not be representative of the general population of African Americans due to possible referral bias, but this limitation is unlikely to affect the discriminant validity demonstrated. Another limitation is that factors other than age, education, and premorbid intelligence that have been shown to account for performance in African Americans were not available (eg, socioeconomic status, comborbidities). Future studies should evaluate discriminant validity in a large, randomly-selected cohort and account for the impact of additional confounding variables. Such studies should also evaluate discriminant validity in other cultural/socioeconomic groups. Finally, longitudinal follow-up is needed to evaluate ability to predict conversion to dementia.

In conclusion, the present preliminary study extends prior work on the validity of a set of computerized cognitive tests for MCI[7,10,11] to an urban African American cohort. The study further demonstrates improved discriminant validity with application of a recently-developed automatic adjustment for premorbid IQ.[44] The tests thus appear well suited to address the clinical need for early detection in African Americans, a population that has been shown to have a high prevalence of MCI and dementia.[18-22]

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