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Diagnostic accuracy and practice effects in the National Alzheimer's Coordinating Center Uniform Data Set neuropsychological battery

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Abstract

Introduction: The Uniform Data Set (UDS) neuropsychological battery is frequently used in clinical studies. However, practice effects, effectiveness as a measure of global cognitive functioning, and detection of mild cognitive impairment have not been examined.
Methods: A normative total score for the UDS has been developed. Linear discriminant analysis determined classification accuracy in identifying cognitively normal and impaired groups. Practice effects were examined in cognitively normal and cognitively impaired groups.
Results: The total score differentiates between cognitively normal participants and those with dementia, but does not accurately identify individuals with mild cognitive impairment (MCI). Mean total scores for test-exposed participants were significantly higher than test-naive participants in both the normal and MCI groups and were higher, but not significantly so, in the dementia group.
Conclusion: The total score's classification accuracy discriminates between cognitively normal versus participants who have dementia. The total score appears subject to practice effects.

Keywords: Practice effects; Longitudinal data; Diagnostic accuracy; Aging; Cognitive testing

1. Introduction

The National Institute on Aging's (NIA) Alzheimer's Disease Centers (ADCs) have engaged in comprehensive, multidisciplinary Alzheimer's research since the 1980s. However, until 2005, individual centers developed their own research protocols, making data sharing somewhat problematic. The Uniform Data Set (UDS) [1] was incorporated into all ADCs in 2005 to standardize data collection across centers and disciplines. This battery was also designed to provide a brief assessment (i.e., 30–45 minutes) of multiple cognitive domains using at least one neuropsychological measure per domain with a target of differentiating between participants with normal cognitive functioning versus Alzheimer's disease (AD) [1]. However, the UDS was not specifically developed to distinguish cases with mild cognitive impairment (MCI) from cognitively normal controls or participants with dementia and may lack the depth and complexity necessary to discern subtle, preclinical cognitive changes.

Normative data for the UDS have been provided by Shirk and colleagues [2] in the form of a web-based calculator that generates z scores for each subtest adjusted for age, gender, and education. Data were provided for individual measures only and issues related to practice effects, global cognitive functioning, longitudinal tracking of cognitive change, and the ability to detect subtle cognitive impairment were not addressed. To optimize the use of cognitive measures in both clinical and research settings, a measure's usefulness in terms of diagnostic discrimination must be evaluated.

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Although differential diagnosis is routinely and successfully done in traditional neuropsychological clinics with thorough, comprehensive assessment techniques, many researchers seek concise batteries that retain the ability to adequately discriminate between the broad categories of cognitively normal, MCI, dementia, and other neurologic conditions.

Using a single, concise, comprehensive score, as opposed to interpreting performance on individual cognitive tests or cognitive domains, is valued for its simplicity and efficiency. As a result, screening measures, like the Mini-Mental State Exam (MMSE) [3] and the Montreal Cognitive Assessment (MoCA) [4], have become popular methods for screening participants for MCI or dementia. However, such brief screening instruments may not be sufficiently difficult, sensitive, or specific to detect MCI or very mild dementia, especially in the highly educated, high-functioning individuals typically representative of a volunteer research population [5]. In addition, dementia affects most higher order cognitive functions [6,7] to varying degrees, even in the earliest stages. Thus, the development of a composite index of cognition that mitigates ceiling and floor effects typically found with traditional, brief mental status exams may further the purpose of staging and detecting MCI and mild dementia.

There is precedent for combining test scores across multiple procedures to derive a unified total score reflecting global cognitive functioning. Chandler and colleagues [8] developed a total score for the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery using a control group of normally aging individuals and a clinical group of participants diagnosed with AD. They further validated the use of the total score for diagnostic purposes in a sample of normal controls and participants with MCI and AD. Chandler and colleagues reported that the total score accurately discriminated between normal cognition and impaired participants (with AD or MCI) and showed high 1-month test-retest reliability and concurrent validity with the MMSE and the Clinical Dementia Rating (CDR) scale [9].

The current study provides a method of determining global cognitive function, discriminating between normal and cognitively impaired groups, and examines the effect of repeated test administrations on longitudinal test data using ADC UDS data from the Sanders-Brown Center on Aging at the University of Kentucky. The total score for the UDS battery was derived from data provided by those participants determined to be cognitively normal at the initial UDS assessment [5,10].

2. Methods

2.1. Study overview

The ADC at Sanders-Brown Center on Aging, University of Kentucky, follows older research volunteers with detailed annual cognitive and clinical assessments, with, in most cases, brain donation at death. Participants may be either cognitively normal or impaired at study entry. Inclusion and exclusion criteria for cognitively normal participants, who enroll in the Biologically Resilient Adults in Neurological Studies (BRAiNS) project, have been described in detail previously [5,10]. Briefly, BRAiNS participants are volunteers $\geq$60 years of age who are free of neurologic disorders, major psychiatric conditions, substance abuse, and significant medical conditions affecting cognition at baseline assessment. All study procedures were approved by the institutional review board of the University of Kentucky, and all participants provided written informed consent. Given that these initially normally aging participants are followed longitudinally until death, cases of MCI and AD naturally developed over time. These participants were followed in a separate cohort until 2005, when the BRAiNS and clinical cohorts were combined under the UDS.

2.2. Participants

Participants in the current analysis included all UK-ADC participants with complete initial UDS assessments (N = 667). The UDS total score was developed on a subset of test-naive participants who were cognitively normal, $\geq$60 years of age, had a CDR Sum of Boxes score (CDR_{sob}) = 0, MMSE $\geq$ 25, and were free from clinically diagnosed cognitive impairment (n = 250). The CDR yields 2 scores (i.e., Global Score and Sum of Boxes) and is used to stage dementia severity based on interview responses from patients and informants. The Sum of Boxes score is a total score ranging from 0 to 18 based on the sum of 6 domain scores (i.e., orientation, judgment and problem solving, memory, home and hobbies, personal care, and community affairs) each rated from: normal (0); questionable or very mild dementia (0.5); mild dementia (1); moderate dementia (2); and severe dementia (3). These domains are then combined into a global CDR that ranges from 0 to 3 [11,12].

Because the information from the UDS procedures is used to diagnose participants clinically, for the purposes of group discrimination a coding scheme based on an optimal CDR_{sob} cut score suggested in a recent validation study [13] was used to assign classifications of "normal" (CDR_{sob} = 0), "questionable impairment" (CDR_{sob} = 0.5–2.0), or "dementia" ($CDR_{sob} > 2$) to the full sample of participants. Questionable impairment is referred to as MCI in what follows. All participants with a CDR_{sob} = 0 also received a CDR global score = 0.

2.3. Procedures

All participants completed the UDS neuropsychological measures at baseline. The UDS and its administration have been described in detail by Weintraub and colleagues [14]. Briefly, the currently recommended UDS battery [14] includes the MMSE [3], Wechsler Memory Scale—Revised (WMS-R) Logical Memory IA and IIA [15], WMS-R Digit