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Independent comparison of CogState computerized testing and a standard cognitive battery with neuroimaging

Michelle M. Mielke[a,b,*], Stephen D. Weigand[c], Heather J. Wiste[c], Prashanthi Vemuri[d], Mary M. Machulda[e], Davis S. Knopman[b], Val Lowe[d], Rosebud O. Roberts[a,b], Kejal Kantarci[d], Walter A. Rocca[a,b], Clifford R. Jack, Jr.,[d], Ronald C. Petersen[a,b]

[a]*Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA*
[b]*Department of Neurology, Mayo Clinic, Rochester, MN, USA*
[c]*Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA*
[d]*Department of Radiology, Mayo Clinic, Rochester, MN, USA*
[e]*Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN, USA*

Abstract

Background: Inexpensive, non-invasive tools for assessing Alzheimer-type pathophysiologies are needed. Computerized cognitive assessments are prime candidates.

Methods: Cognitively normal participants, aged 51–71, with magnetic resonance imaging, fluorodeoxyglucose-positron emission tomography (FDG-PET), amyloid PET, CogState computerized cognitive assessment, and standard neuropsychological tests were included. We first examined the association between the CogState battery and neuroimaging measures. We then compared that association to the one between standard neuropsychological z-scores and neuroimaging.

Results: Slower reaction times for CogState Identification and One Back, and lower memory and attention z-scores, were associated ($P < .05$) with FDG-PET hypometabolism. Slower time on the Groton Maze Learning Task and worse One Card Learning accuracy were associated ($P < .05$) with smaller hippocampal volumes. There were no associations with amyloid PET. Associations of CogState and neuropsychological Z-scores with neuroimaging were small and of a similar magnitude.

Conclusions: CogState subtests were cross-sectionally comparable to standard neuropsychological tests in their relatively weak associations with neurodegeneration imaging markers.

Keywords: Preclinical Alzheimer's disease; Neuropsychology; Computerized cognitive battery; Neuroimaging; Amyloid-beta; Hippocampal volume

1. Introduction

Evidence of amyloid (cerebrospinal fluid [CSF] amyloid-beta or amyloid imaging) and neurodegeneration (CSF tau, hippocampal volume, or fluorodeoxyglucose-positron emission tomography [FDG-PET] hypometabolism) are the defining components of the preclinical stages of Alzheimer's disease (AD) [1]. Psychometrically evident, subtle changes in cognition are proposed to occur later in the pre-clinical phase of AD (i.e., in stage 3) and have a stronger correlation with neurodegeneration compared with amyloid. Inexpensive, non-invasive tools for identifying the early stages of the Alzheimer-type pathophysiologic process, and subtle cognitive changes, are needed. Computerized tests may have logistic and cost advantages over standard pencil-and-paper tests. The aim of the present study was to examine the cross-sectional association between the CogState computerized cognitive battery and neuroimaging measures

*Corresponding author. Tel.: +1-507-284-5545; Fax: +1-507-284-1516.

E-mail address: mielke.michelle@mayo.edu

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of amyloid PET and neurodegeneration (hippocampal volume and FDG-PET) in cognitively normal individuals, aged 51–71 years, enrolled in the population-based Mayo Clinic Study of Aging. We then compared the cross-sectional relationship between CogState and neuroimaging to that between standard neuropsychological global- and domain-specific Z-scores and neuroimaging.

2. Methods

2.1. Participants

The Mayo Clinic Study of Aging (MCSA) is a population-based study of cognitive aging among Olmsted County, MN, residents that began in October 2004, and initially enrolled individuals aged 70 to 89 years. The details of the study design and sampling procedures have been previously published [2]. Given the importance of understanding risk factors and the development and progression of AD pathophysiology in middle-age, we expanded the study to also enroll a population-based sample of individuals aged 50–69 years using the same stratified random sampling methodology as in the original cohort. The Olmsted County population, aged 50-69 (n = 31,502), was sampled by 5-year age groups and sex on November 1, 2011. Of the 948 participants who enrolled in the study the first year, the present study includes 324 who were cognitively normal, completed a cognitive assessment (CogState computerized battery and standard pencil and paper battery) and also had a MRI within 5 months of the visit. Of the 324 individuals, 261 (81%) consented to additional amyloid imaging (Pittsburgh Compound B [PiB]-PET) and 259 (80%) to FDG-PET. There were no demographic or cognitive differences between those who did and did not consent to PET imaging.

2.2. Standard protocol approvals, registrations, and patient consents

The study protocols were approved by the Mayo Clinic and Olmsted Medical Center Institutional Review Boards. All participants provided written informed consent to participate in the study and in the imaging protocols.

2.3. Participant assessment

Study visits included a neurologic evaluation by a physician, an interview by a study coordinator, and neuropsychological testing administered by a psychometrist [2]. The physician examination included a medical history review, a complete neurological examination, and administration of the Short Test of Mental Status [3] and the Unified Parkinson's Disease Rating Scale [4]. The study coordinator interview included questions about memory to both the participant and an informant using the Clinical Dementia Rating scale [5]. A psychometrist administered a neuropsychological battery that included nine tests covering four domains: (1) **memory** (Auditory Verbal Learning Test Delayed Recall Trial [6], Wechsler Memory Scale-Revised Logical Memory & Visual Reproduction II) [7]; (2) **language** (Boston Naming Test [8] and Category Fluency) [9]; (3) **executive function** (Trail Making Test [TMT] B [10] and Wechsler Adult Intelligence Scale - Revised (WAIS-R) Digit Symbol subtest) [11]; and (4) **visuospatial skills** (WAIS-R Picture Completion and Block Design subtests) [11].

2.4. CogState computerized battery

Several computerized batteries are available, with advantages and limitations for each. We chose to include the CogState battery in the MCSA because it is brief (20 minutes); requires minimal administrative oversight and has a web-based platform; is easy to understand, even for non-English speakers and people with little computer experience (e.g., [12–14]); has minimal practice effects after initial familiarization (e.g., [13,15,16]); does not have ceiling or floor effects; and has good test-retest reliability (e.g., [13,15,16]). However, some limitations should be noted. For example, the card tasks have relatively low face validity as they are game-like and remote from traditional neuropsychological tests [17]. Furthermore, the four card tasks primarily load on only two factors – "learning efficiency" and "problem solving" [18,19].

The administration of the CogState computerized cognitive battery was overseen by the study coordinator and included four card tasks and the Groton Maze Learning Test (GMLT), which has previously been described in detail [13,18,20]. The four card tasks consisted of the following tests (in this order):

Detection (DET) task – a simple reaction time paradigm that measures psychomotor speed. Reaction time was the primary outcome measure.

Identification (IDN) task – a choice reaction time paradigm that measures visual attention. Reaction time was the primary outcome measure.

One Card Learning (OCL) task – a continuous visual recognition learning task that assesses memory and attention. Reaction time and accuracy were the primary outcome measures.

One Back (ONB) task – a task that assesses working memory and attention. Reaction time and accuracy were the primary outcome measures.

The GMLT was given after the four card tasks and is a hidden pathway maze learning test that measures problem solving, reasoning, recent memory, and executive function. The primary outcome measures were the number of moves per second.

Criterion and construct validity for these tests have been reported [14]. For example, performance on the Detect task correlated highly with the Grooved Pegboard Dominant Hand ($r = .81$, $P < .001$) and TMT Part A ($r = .70$, $P < .001$). Performance on the Identification task correlated highly with the Grooved Pegboard Dominant Hand