Our Mission: Helping to prepare Iowa’s health practitioners to care for our growing population of elders. E-NEWS is one of our methods of teaching through technology.

Each month, E-NEWS delivers abstracts from current multidisciplinary healthcare journal articles related to a specific geriatric topic. This month’s E-NEWS focuses on THE BASICS OF NEUROPSYCHOLOGICAL TESTING AND ITS ROLE IN THE DIAGNOSIS AND TREATMENT OF DEMENTIA.

THE BASICS OF NEUROPSYCHOLOGICAL TESTING AND ITS ROLE IN THE DIAGNOSIS AND TREATMENT OF DEMENTIA

In this issue of the E-NEWS, you will find abstracts for:

- A study that evaluates the suitability of neuropsychological tests in patients with vascular dementia.
- A study that examines staging of the cognitive decline in Alzheimer's disease using a detailed neuropsychological investigation of mild cognitive impairment and mild Alzheimer's disease.
- A study that tests predicting conversion from mild cognitive impairment to Alzheimer's disease using neuropsychological tests and multivariate methods.
- A study that investigates the clinical applicability and cutoff values for a neuropsychological assessment protocol for older adults with low formal education.
- An article that discusses the role of neuropsychological assessment in patients with dementing illness.
- A study that researches neuropsychological predictors of dementia in late-life major depressive disorder.
- A study that assesses the predictive value for future conversion to dementia (5-year period) of a comprehensive neuropsychological battery.
- A study that seeks to determine whether early onset Alzheimer's disease is associated with a distinct neuropsychological profile.
- An article that presents the neuropsychological profile of Alzheimer's disease.
- An article that addresses improving the accuracy and precision of cognitive testing in mild dementia.

The concept of vascular dementia (VaD) has evolved with the introduction of vascular cognitive impairment (VCI). VaD patients show predominantly frontal cognitive deficits. The executive area is particularly affected, while memory deficits are less frequent in patients with VaD than patients with AD. Several neuropsychological tests are available for the diagnosis and differentiation of dementias, but there are currently no tests developed specifically for VaD. We proposed to evaluate various neuropsychological tests, on the basis of evidence from different studies, in order to clarify the utility of the neuropsychological assessment in vascular dementia. Copyright © 2012 Elsevier B.V.


OBJECTIVE: The decline of episodic memory in Alzheimer’s disease (AD) is well established, but the exact appearance and staging of deficits in other cognitive domains is sometimes contentious. The current investigation attempted to elucidate the appearance of additional cognitive deficits in the non-episodic domains and to understand these deficits with respect to the known pathological staging of AD. METHODS: A cross-sectional investigation compared cognitively normal age-matched controls with patients with mild AD and mild cognitive impairment (MCI) using a detailed neuropsychological assessment. RESULTS: The systematic investigation of cognitive performance across the major cognitive domains demonstrates that the appearance of additional cognitive deficits in MCI and AD can be predicted, with impaired semantic cognition performance pre-empting the appearance of attention/executive dysfunction and visuospatial deficits in the majority of patients with MCI. CONCLUSIONS: This progressive pattern of cognitive deficits fits with the known pathological staging of AD, and the data further highlight the relative rarity of pure amnestic MCI. These results indicate that any neuropsychological test battery used to assess patients with MCI should include language and semantic memory tests in addition to typical episodic memory tests, as changes within this domain might be a sensitive indication of incipient AD. Copyright © 2011 John Wiley & Sons, Ltd.


Behavioral markers measured through neuropsychological testing in mild cognitive impairment (MCI) were analyzed and combined in multivariate ways to predict conversion to Alzheimer’s disease (AD) in a longitudinal study of 43 MCI patients. The test measures taken at a baseline evaluation were first reduced to underlying components (principal component analysis, PCA), and then the component scores were used in discriminant analysis to classify MCI individuals as likely to convert or not. When empirically weighted and combined, episodic memory, speeded executive functioning, recognition memory (false and true positives), visuospatial memory processing speed, and visuospatial episodic memory were together strong predictors of conversion to AD. These multivariate combinations of the test measures achieved through the PCA were good, statistically significant predictors of MCI conversion to AD (84% accuracy, 86% sensitivity, and 83% specificity). Importantly, the posterior probabilities of group membership that accompanied the binary prediction for each participant indicated the confidence of the prediction. Most of the participants (81%) were in the highly confident probability bins (.70-1.00), where the obtained prediction accuracy was more than 90%. The strength and reliability of this multivariate prediction method were tested by cross-validation and randomized resampling.

BACKGROUND AND OBJECTIVES: The neuropsychological exam plays a central role in the assessment of elderly patients with cognitive complaints. It is particularly relevant to differentiate patients with mild dementia from those subjects with mild cognitive impairment. Formal education is a critical factor in neuropsychological performance; however, there are few studies that evaluated the psychometric properties, especially criterion related validity, neuropsychological tests for patients with low formal education. The present study aims to investigate the validity of an unstructured neuropsychological assessment protocol for this population and develop cutoff values for clinical use. METHODS AND RESULTS: A protocol composed by the Rey-Auditory Verbal Learning Test, Frontal Assessment Battery, Category and Letter Fluency, Stick Design Test, Clock Drawing Test, Digit Span, Token Test and TN-LIN was administered to 274 older adults (96 normal aging, 85 mild cognitive impairment and 93 mild Alzheimer’s disease) with predominantly low formal education. Factor analysis showed a four factor structure related to Executive Functions, Language/Semantic Memory, Episodic Memory and Visuospatial Abilities, accounting for 65% of explained variance. Most of the tests showed a good sensitivity and specificity to differentiate the diagnostic groups. The neuropsychological protocol showed a significant ecological validity as 3 of the cognitive factors explained 31% of the variance on Instrumental Activities of Daily Living. CONCLUSION: The study presents evidence of the construct, criteria and ecological validity for this protocol. The neuropsychological tests and the proposed cutoff values might be used for the clinical assessment of older adults with low formal education.


Neuropsychological assessment has a distinct role in the detection and monitoring of cognitive and functional changes associated with dementing illness. Molecular, structural and functional neuroimaging studies have advanced our understanding of the anatomy and physiology underlying neurodegenerative disease; however, the overlap in pathological features of different dementia-associated diseases limits the information that can be obtained by these methods. Incorporation of information obtained from multiple sources can help to increase diagnostic and prognostic accuracy. Neuropsychological test findings provide unique value as biomarkers of dementia, as differentiators of disease topography and in the estimation of disease risk and trajectory. However, psychometric test properties—such as construct validity, stability and the use of appropriate norms—must be understood, because they influence both the application of neuropsychological tests and the interpretation of their results. Finally, measurement of cognitive strengths and weaknesses in patients at risk of dementia can be helpful to predict changes in functional abilities, design appropriate and effective interventions, and assist family and health-care providers in the planning of the patient's future care needs. This Review describes the key characteristics of neuropsychological testing in the assessment of patients at risk of dementia.


OBJECTIVE:: Major depressive disorder is a likely risk factor for dementia, but some cases of major depressive disorder in older adults may actually represent a prodrome of this condition. The purpose of this study was to use neuropsychological test scores to predict conversion to dementia in a sample of depressed older adults diagnosed as nondemented at the time of neuropsychological testing. DESIGN:: Longitudinal, with mean follow-up of 5.45 years. SETTING:: Outpatient depression treatment study at Duke University. PARTICIPANTS:: Thirty nondemented individuals depressed at the time of neuropsychological testing and later diagnosed with incident dementia; 149 nondemented individuals depressed at the time of neuropsychological testing and a diagnosis of cognitively normal. METHODOLOGY:: All participants received clinical assessment of depression, were assessed to rule out prevalent dementia at the time of study enrollment, completed neuropsychological testing at the time of study enrollment, and were diagnosed for cognitive disorders on an annual basis. RESULTS:: Nondemented, acutely depressed older adults who converted to dementia during the study period exhibited broadly lower cognitive performances at baseline than
acutely depressed individuals who remained cognitively normal. Discriminant function analysis indicated that 2 neuropsychological tests, Recognition Memory (from the Consortium to Establish a Registry for Alzheimer’s Disease neuropsychological battery) and Trail Making B, best predicted dementia conversion.

CONCLUSIONS: Depressed older adults with cognitive deficits in the domains of memory and executive functions during acute depression are at higher risk for developing dementia. Some cases of late-life depression may reflect a prodrome of dementia in which clinical manifestation of mood changes may co-occur with emerging cognitive deficits.

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The use of neuropsychological tests to detect cognitive decline in the initial phases of Alzheimer’s disease (AD) has faced significant limitations, namely the fact that most cohort studies of conversion to dementia had relatively short follow-up periods. The aim of the present study is to assess the predictive value for future conversion to dementia of a comprehensive neuropsychological battery applied to a cohort of non-demented patients followed-up for 5 years. Participants (n = 250) were selected from the Cognitive Complaints Cohort (CCC) having cognitive complaints, assessment with a comprehensive neuropsychological battery, and a follow-up period of 5 years (unless patients have converted to dementia earlier). During the follow-up period (2.6 ± 1.8 years for converters and 6.1 ± 2.1 years for non-converters), 162 patients (64.8%) progressed to dementia (mostly AD), and 88 (35.2%) did not. A Linear Discriminant Analysis (LDA) model constituted by Digit Span backward, Semantic Fluency, Logical Memory (immediate recall), and Forgetting Index significantly discriminated converters from non-converters (λ Wilks = 0.64; χ²(4) = 81.95; p < 0.001; RCanonical = 0.60). Logical Memory (immediate recall) was the strongest predictor with a standardized canonical discriminant function coefficient of 0.70. The LDA classificatory model showed good sensitivity, specificity and accuracy values (78.8%, 79.9% and 78.6%, respectively) of the neuropsychological tests to predict long-term conversion to dementia. The present results show that it is possible to predict, on the basis of the initial clinical and neuropsychological evaluation, whether non-demented patients with cognitive complaints will probably convert to dementia, or remain stable, at a reasonably long and clinically relevant term.

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Alzheimer's disease (AD) in younger patients is associated with a higher prevalence of atypical symptoms. We examined neuropsychological performance according to age-at-onset. We assessed cognition in 172 patients with AD (81 early and 91 late onset) in five cognitive domains (memory, language, visuo-spatial functioning, executive functioning, attention). Dementia severity was assessed using the Mini-Mental State Examination (MMSE) and global cognitive decline using Cambridge Cognitive Examination (CAMCOG). Analyses of variance were performed with age-at-onset as between-subjects factor, and gender and education as covariates. Analysis was repeated after stratification for dementia severity (based on median MMSE). In early onset AD, age (mean ± SD) was 60 ± 4 years; 44 (54%) were female. In late onset AD, age was 72 ± 5 years; 47 (52%) were female. Dementia severity and global cognitive decline did not differ between groups (early onset: MMSE: 20 ± 5, CAMCOG: 69 ± 15, late onset: MMSE: 21 ± 5, CAMCOG: 70 ± 15; p > 0.05). Early onset patients performed worse than late onset patients on visuo-spatial functioning (p < 0.01), executive functioning (p < 0.001), and attention (p < 0.01). Late onset patients performed worse on memory, although not significantly (p = 0.11). Stratification for dementia severity showed that in mildly demented early onset patients, memory function was remarkably preserved compared to late onset patients (p < 0.01). In moderate AD, differences in memory function disappeared, but early onset patients performed worse on visuo-spatial functioning (p < 0.01), executive functioning (p < 0.001), and attention (p < 0.01) than late onset patients. Adjustment for APOE left results unchanged. In conclusion, early onset AD presents with a different cognitive profile and the disease course seems different. Relative sparing of memory function in early stages stresses the need to adequately test other cognitive domains.

Neuropsychological assessment has featured prominently over the past 30 years in the characterization of dementia associated with Alzheimer disease (AD). Clinical neuropsychological methods have identified the earliest, most definitive cognitive and behavioral symptoms of illness, contributing to the identification, staging, and tracking of disease. With increasing public awareness of dementia, disease detection has moved to earlier stages of illness, at a time when deficits are both behaviorally and pathologically selective. For reasons that are not well understood, early AD pathology frequently targets large-scale neuroanatomical networks for episodic memory before other networks that subserve language, attention, executive functions, and visuospatial abilities. This chapter reviews the pathognomonic neuropsychological features of AD dementia and how these differ from "normal," age-related cognitive decline and from other neurodegenerative diseases that cause dementia, including cortical Lewy body disease, frontotemporal lobar degeneration, and cerebrovascular disease.


The CAMCOG, ADAS-cog, and MMSE, designed to grade global cognitive ability in dementia have inadequate precision and accuracy in distinguishing mild dementia from normal ageing. Adding neuropsychological tests to their scale might improve precision and accuracy in mild dementia. We, therefore, pooled neuropsychological test-batteries from two memory clinics (ns = 135 and 186) with CAMCOG data from a population study and 2 memory clinics (n = 829) and ADAS-cog data from 3 randomized controlled trials (n = 713) to estimate a common dimension of global cognitive ability using Rasch analysis. Item difficulties and individuals' global cognitive ability levels were estimated. Difficulties of 57 items (of 64) could be validly estimated. Neuropsychological tests were more difficult than the CAMCOG, ADAS-cog, and MMSE items. Most neuropsychological tests had difficulties in the ability range of normal ageing to mild dementia. Higher than average ability levels were more precisely measured when neuropsychological tests were added to the MMSE than when these were measured with the MMSE alone. Diagnostic accuracy in mild dementia was consistently better after adding neuropsychological tests to the MMSE. We conclude that extending dementia specific instruments with neuropsychological tests improves measurement precision and accuracy of cognitive impairment in mild dementia.


Next Month’s Issue:

New Diagnostic Tools for Understanding Dementia

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