

PERSPECTIVE

The role of neuropsychological assessment in the evaluation of patients with cognitive-behavioral change due to suspected Alzheimer's disease and other causes of cognitive impairment and dementia

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Abstract

The Alzheimer's Association convened a Diagnostic Evaluation, Testing, Counseling and Disclosure Clinical Practice Guideline workgroup to help combat the major global health challenges surrounding the timely detection, accurate diagnosis, and appropriate disclosure of mild cognitive impairment (MCI) or dementia due to Alzheimer's disease (AD) or other diseases that cause these types of cognitive-behavioral disorders. The newly published clinical practice guidelines are proposed as a structured approach to evaluation. The purpose of the present article is to provide a clinical perspective on the use of neuropsychology within the new framework and practice guidelines outlined under the Diagnostic Evaluation, Testing, Counseling and Disclosure of Suspected Alzheimer's Disease and Related Disorders (DETeCD-ADRD) recommendations for primary care and specialty care. Neuropsychological evaluation is a critical component in supporting early and accurate diagnosis and staging, characterizing the clinical profile, assessing trajectory over time, and providing recommendations specifically tailored to the individual and their care team.

KEYWORDS

Alzheimer's disease, best practices, dementia, diagnosis, guidelines, mild cognitive impairment, neuropsychology

Highlights

- Reviews the neuropsychological evaluation component of the new framework and clinical practice guidelines outlined under the Alzheimer's Association clinical practice guidelines for the Diagnostic Evaluation, Testing, Counseling and Disclosure of Suspected Alzheimer's Disease and Related Disorders (DETeCD-ADRD).
- Examines the utility of neuropsychological evaluation in the assessment of Alzheimer's Disease and Related Disorders (ADRD).

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- Supports a basis for neuropsychology in early and accurate diagnosis and staging, characterizing the clinical profile, assessing trajectory over time, and providing recommendations specifically tailored to the individual and their care team.

The Alzheimer's Association clinical practice guideline for the Diagnostic Evaluation, Testing, Counseling and Disclosure of Suspected Alzheimer's Disease and Related Disorders (DETeCD-ADRD) focuses on recommendations that encourage timely, accurate, and effective diagnosis, staging, and disclosure for individuals living with cognitive-behavioral decline.^{1,2} The guidelines provide a structured and well operationalized, yet person-centered, evaluation plan for clinicians in primary and subspecialty care, with the important goal of empowering providers to confidently approach the diagnostic evaluation and disclosure process with their patient and care partner dyads. Furthermore, these recommendations are offered at a time when the financial, societal, and ethical benefits of timely detection, accurate diagnosis, and effective management are being increasingly realized, with dementia prevalence increasing as the population ages, and with the emergence of disease-modifying treatments being implemented in clinical practice. Thus the timely detection, accurate diagnosis, appropriate disclosure, and proper management of mild cognitive impairment (MCI) or dementia due to Alzheimer's disease (AD) or Alzheimer's disease and related dementias (ADRD), is of the utmost importance. In this Perspective, we use ADRD to refer to diseases such as the group of frontotemporal lobar degenerations (tauopathies and TAR DNA-binding protein-43 (TDP-43) proteinopathies) and cortical Lewy body disease, and specifically discuss the importance of incorporating neuropsychology, as detailed in recommendation 14 of the practice guidelines.

The clinical practice guidelines (CPG) provide a multitiered, three-step approach to diagnostic formulation, allowing for a structured but individualized process. As outlined in the primary articles, the steps include (1) to delineate the cognitive functional status (i.e., the overall level of impairment); (2) to characterize the patient's cognitive-behavioral syndrome; and (3) to generate and narrow the differential diagnosis of the brain disease(s) or disorder that is the likely cause(s) of the patient's cognitive-behavioral syndrome, recognizing the importance of differentiating AD from ADRD or other diseases, disorders (e.g., mood disorders), conditions (e.g., sleep apnea), and factors (e.g., effects of medications or alcohol) that may cause or contribute to cognitive or behavioral symptoms. A similar approach and diagnostic framework have been proposed to address ongoing challenges in dementia nomenclature.³

As it currently stands, the rate of timely diagnosis and appropriate disclosure is inadequately low and is especially protracted for individuals with so-called "atypical" dementia syndromes such as behavioral variant frontotemporal dementia and primary progressive aphasia⁴ or dementias of early onset.⁵ It is the hope that these recommendations will be prioritized by providers and resourced by health care

systems to be seamlessly integrated into practice. The aim is to aid clinicians in diagnosing the illness in a timely manner, and to define the symptom profile and the likely underlying disease so that a patient-centered care plan can be developed to optimize quality of life for the patient and family, and to improve outcomes in care settings. With respect to neuropsychology, the guidelines suggest that a more comprehensive evaluation can be especially beneficial when office-based cognitive assessment is not sufficiently informative or in cases with a level of complexity that leaves the clinician with residual uncertainty surrounding interpretation—we agree that this is well supported by the interpretation of evidence and consensus (as detailed and supported in the CPG evidence review, rationale, and processes), and informed by the principles of good care practices. Indeed, neuropsychological evaluation is critical in these cases and can significantly aid in the assessment of the level of severity of functional status and cognitive syndrome, and in narrowing the probable underlying etiology. Furthermore, we find the positioning, details, and logistics well balanced and appropriate surrounding the addition of neuropsychological evaluation in AD and ADRD care. Specifically, (1) when and where in the evaluation process neuropsychological assessment is necessary; (2) in whom there may be most benefit; (3) what should ideally be assessed, reported, and communicated; and (4) the general "how" to incorporate neuropsychological evaluation in the flow of a patient-centered and clinician-orchestrated process in various clinic settings. It is our belief that the overall CPG provides a structured approach with sufficient leeway for clinician proficiency and judgment.

The field of neuropsychology has a long history of dedication to timely diagnosis and clarification of the cognitive-behavioral syndrome in not just AD but also related disorders, and to providing patient-centered recommendations tailored to the individual's particular strengths and weaknesses, environment, and support network. The addition of biomarkers over time has quelled some of the need for localization, one of the original goals for neuropsychology as outlined by Alexander Luria in the 1960s,⁶ and for determination of the underlying neuropathological entity or entities that are propagating decline. However, no biomarker can establish the diagnosis of MCI or dementia—these remain clinical constructs that require integration and individualized interpretation of accurate clinical history and measures. Neuropsychological evaluation has been shown consistently to improve the diagnostic accuracy surrounding clinical diagnoses of MCI or dementia due to ADRD, and longitudinal assessment has been shown to improve prognostic accuracy beyond brief cognitive assessments.^{7,8} In addition, neuropsychological evaluation can accurately delineate an individual's cognitive functional status at even mild disease stages.^{9,10} Thus, although biomarker determination is crucial

in today's evaluative processes, neuropsychology will continue to be of value to accurately delineate the clinical syndrome, to inform regarding the likelihood of the primary driver and contributors, and to provide the added benefit of clear staging, all of which are important in clarification of differential diagnosis, prognosis, future planning, and the management of cognitive-behavioral decline.¹¹

An evaluation, ideally, should be structured around a referral question guided by a standardized mental status examination, which assists the referring provider in determining whether referral for further testing is appropriate and, if so, to define the referral question for the neuropsychologist. For any clinician, brief cognitive assessments can provide a quick estimate of an individual's cognitive function and identify those individuals who would benefit from a more detailed cognitive evaluation.¹² However, the referral question may be different for primary care as opposed to specialty care clinicians, as the complexity that prompts a referral for primary care may be less than that required by specialty care. In addition, primary care providers often face significant time limitations that constrain their assessments, which can translate to less well-defined or well-sourced referrals and may require a more comprehensive approach to evaluation in order to address a broader referral question. Nonetheless, limitations in clinicians' bandwidths are widespread across disciplines and clinical settings (primary, specialty, and subspecialty care), and consequently neuropsychological evaluation can provide an added level of comprehensive diagnostic clarification and individualized patient care, filling a much-needed gap. Neuropsychological evaluations are comprehensive, often taking several hours depending on the referral question, and optimally provide a more refined, quantitative assessment of an individual's history and level of functioning cognitively, behaviorally, and in daily life. The examination allows for a targeted assessment of change across various aspects of cognition, and it typically includes standardized and normed evaluation of premorbid functioning, and the domains of learning and memory, attention, executive functioning, visuospatial functioning, and language, which cannot be obtained through brief standardized assessments or bedside examination. An evaluation also often assesses mood and psychological functioning, which may be otherwise overlooked, although these factors can have implications for both current cognitive functioning and risk for decline.¹³ Similarly, the neuropsychologist is allowed the time, reimbursed by insurance in the context of medical necessity, to gather a comprehensive and detailed history from a review of records, and an interview with the individual and their care partner, which can provide additional important information as well as assist in goal-setting and future planning. Overall, the history and cognitive profile taken together can be greatly informative in clarifying the individual's cognitive profile and the underlying neurological basis of their presenting symptoms and behavior, and in communicating the results to both the patient and the referring provider.¹⁴

We agree with the CPG workgroup that the neuropsychological evaluation can prove exceptionally useful when working with individuals with suspected cognitive decline, but whose level of decline may not be sufficiently detectable during the mental status examination or on brief validated cognitive assessments.¹⁵ It is not uncommon for an individual who subjectively suspects cognitive decline as compared

to their baseline functioning to perform well within normal limits on routine office-based screening.⁸ This most often occurs in individuals with high historical functioning, achievement, and/or education, and can contribute to considerable delays in diagnosis, future planning, and appropriate treatment and care. Conversely, the neuropsychological evaluation is also beneficial when there is a question of decline, or brief evaluation is not normal, but there are complicating developmental or cultural factors that interfere with interpretation of brief assessments. The neuropsychologist not only has the ability to take a comprehensive history that can aid in interpretation and formulation, but also to objectively measure decline in relation to estimated historical functioning through utilizing standardized testing and normative data, while simultaneously taking into account that normative standards may not be entirely appropriate for the individual's baseline, culture, or education. Although limitations in normative samples utilized in neuropsychology are well recognized and can pose a challenge, a neuropsychologist's clinical acumen can add an additional level of nuance to interpretation in these cases, and strides are being made in creating more-appropriate cross-cultural neuropsychological batteries.¹⁶ Moreover, studies have shown that neuropsychological evaluation provides an additional layer of diagnostic certainty in individuals with above average intelligence and of varying racial and cultural backgrounds.¹⁶⁻¹⁸ Ultimately, it is important for primary care and specialty care alike to appreciate that the interpretation of brief cognitive assessments, such as the Mini-Mental State Examination (MMSE)¹⁹ or Montreal Cognitive Assessment (MoCA)²⁰ can be particularly difficult in cases confounded by factors such as race/ethnicity, culture/primary language, education level, quality of education, level of life achievement, prior medical history, sensory difficulties (e.g., primary vision or hearing impairments), history of neurodevelopmental disorder (e.g., intellectual disability or learning disorder), prominent psychiatric comorbidities, or underlying complicating factors (e.g., sleep disorder).²¹ Thus, despite limitations, we agree with the recommendation and rationale provided in the CPG that a more extensive evaluation in these cases is often paramount to accurately determine and characterize the extent of cognitive change over time, while also providing a more thorough assessment of cognitive functioning across domains and recommendations for further workup, monitoring, and individual care.

The provision of recommendations tailored to the patient's specific cognitive-behavioral profile and level of functioning is also of the utmost importance when considering the quality of life of the individual and their care partner. A neuropsychological evaluation and feedback can assist the family to appreciate the patient's level of impairment and to begin planning for future care and needs. Often, an individual's family or loved ones become frustrated and overwhelmed by behavioral or cognitive changes they observed but had difficulty understanding or managing. The evaluation can help delineate which activities of daily living the patient may need assistance with at the time of the assessment and suggest accommodations to support the individual's maximal level of functioning within their environment, a task that is especially challenging for early-onset dementia.²² For example, as expressed in the CPG, neuropsychologists furnish additional value to the care of patients when they provide, as an integral component of the evaluation

and feedback process, tailored recommendations to help compensate for areas of impairment such as memory or executive functions, help effectively communicate findings, and deliver recommendations for further assessment (e.g., of home safety, driving, dysphagia) and management. In addition, a full evaluation can help guide medical decision-making for individuals who are at risk for delirium in the context of preexisting dementia.

Also of importance when considering the role of neuropsychology in the assessment of cognitive-behavioral change or suspected AD/ADRD is assessing cognitive trajectory and symptom progression over time. A repeat neuropsychological evaluation provides the opportunity to update diagnostic considerations and recommendations appropriately to meet the patient's changing profile and needs. In the context of an underlying neurodegenerative condition, commonly an individual with subjective cognitive concerns and minimal presumed cognitive decline on initial evaluation will have symptoms that progress over time, and having the ability to closely assess interval changes is critical to ensure a more timely diagnosis and appropriate care.⁷ Furthermore, the assessment of change over time can help clarify differential diagnosis when factors such as language or cultural barriers make initial interpretation more challenging. Finally, most individuals lack a neuropsychological baseline for comparison when symptoms first appear. Thus older individuals are encouraged to consider obtaining baseline neuropsychological testing at the time of subjective cognitive concerns, before the onset of overt cognitive-behavioral changes or major symptoms. Evaluations are reimbursable through Medicare and other payors upon medical necessity, which includes when there are mild or questionable deficits on standard mental status testing or when even subtle concerns are raised in clinical interviews. The frequency of repeat assessments should be dictated by the neuropsychologist. If there are abnormalities raising concern for future decline, a re-evaluation in 1 year is recommended. Alternatively, an evaluation may be normal, although subjective cognitive decline or other factors may increase the risk of cognitive change; in these instances, a 2-year re-evaluation may be more appropriate. In all cases, as the CPG delineates, there is an opportunity to promote brain-healthy behaviors and to help reduce modifiable risk factors for dementia as part of the neuropsychological evaluation and feedback process.

Overall, although the advancements of biomarkers are a great benefit to the field and the diagnosis of underlying etiologies, a neuropsychological evaluation provides critical information surrounding an individual's current level of functioning, the specific cognitive and behavioral symptoms they are experiencing, and its impact. Not only can neuropsychology play an essential role in timely diagnosis, especially in particularly challenging cases, and in turn, assist in early intervention and management and achieving shared goals, but it can also, importantly, help identify, predict, and mitigate health, financial, and safety risks involved. As recommended in the primary articles, when further diagnostic confidence is required by the clinician, subsequent referral to neuropsychological evaluation to clarify the cognitive-behavioral syndrome and further aid in etiological considerations is important to provide the best possible patient-centered

care. Above, we have discussed the supporting evidence for these recommendations, along with recommendations for repeat assessment; the importance of tailored recommendations and future planning; and some important limitations in the field of cross-cultural neuropsychology that are being addressed, although should continue to be focused on in future directions. Individual neuropsychological profiles can differ significantly, even when the same underlying pathophysiology is at play. Clear delineation of the level of severity and symptomatology, along with tailored recommendations specific to an individual's own unique background, presentation, and profile, can vastly improve the lives of an individual living with cognitive-behavioral change and their loved ones, and positively impact overall outcomes. We believe that the DETeCD-ADRD recommendations provide a well-supported clinical framework for evaluation and disclosure that appropriately integrates neuropsychological evaluation in the pathway, and which, when implemented, will provide an important step in closing the gap in this important direction.

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The authors have nothing to report.

CONFLICT OF INTEREST STATEMENT

Dr. Shaughnessy serves as a consultant for Eisai. Dr. Weintraub is on the Board of Trustees of Toolbox Assessments, Inc. Author disclosures are available in the [Supporting Information](#).

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SUPPORTING INFORMATION

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