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Mild Neurocognitive Disorder: An Old Wine in a New Bottle

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Abstract: The American Psychiatric Association has recently published the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5). The DSM-IV category “Dementia, Delirium, Amnestic, and Other Cognitive Disorders” has undergone extensive revision. DSM-5 has renamed this category as “Neurocognitive Disorders” (NCD), which now covers three entities: delirium, major NCD, and mild NCD. The DSM-IV version of mild NCD resembles the DSM-5 version in name only. DSM-IV defined mild NCD based on a single criterion, whereas DSM-5 defines mild NCD by using several cognitive and related criteria. The main difference between mild NCD and the Key International Symposium criteria of mild cognitive impairment (MCI) is that the research work that led to the construct of MCI primarily involved elderly study participants (even though age was not part of the definition of MCI), whereas mild NCD includes acquired cognitive disorders of all age groups. DSM-5 essentially discusses the epidemiology and diagnostic markers of mild NCD by drawing congruence between MCI and mild NCD. The DSM-5 definition of mild NCD is anchored on four criteria and two specifiers. The four criteria refer to cognitive changes, functional activities, and exclusion of delirium and competing mental disorders. The two specifiers are the presumed etiologies of mild NCD and the presence or absence of behavioral problems. While the category “mild NCD” may improve reliability of diagnoses, it has yet to withstand scientific scrutiny to be considered a valid construct. This article reviews the DSM-5 criteria for mild NCD, compares them with the Key International Symposium MCI criteria, and discusses the pros and cons of the mild NCD construct.

Keywords: cognitive disorders, dementia, DSM-5, mild cognitive impairment, mild neurocognitive disorder

The American Psychiatric Association has recently published the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5).¹ Like all its predecessors, DSM-5 follows a theme of describing a constellation of signs and symptoms under “Criterion A.”

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The other criteria typically describe the presence or absence of a departure from baseline functioning and the exclusion of other medical or mental conditions that can account for the signs and symptoms described under Criterion A. Additionally, pertinent specifiers such as probable etiologies or severity of symptoms are included. One of the categories that underwent substantial revision is the chapter “Dementia, Delirium, Amnestic, and Other Cognitive Disorders” in DSM-IV.² DSM-5 has renamed this category “Neurocognitive Disorders,” and it covers three entities: delirium, major neurocognitive disorder, and mild neurocognitive disorder. The focus of this article, mild neurocognitive disorder, was first introduced in DSM-IV under the category “Cognitive Disorder Not Otherwise Specified.” The DSM-IV version of mild neurocognitive disorder, however, resembles the DSM-5 version of mild neurocognitive disorder (mild NCD) in name only. Mild NCD in DSM-IV was essentially defined by one single criterion (i.e., neuropsychological testing) or by “quantitative clinical assessment,” whereas the DSM-5 version of mild NCD is based on several cognitive and related criteria.

The American Psychiatric Association initiated the DSM-5 review process in 1999. Chairs of the task force were appointed in 2006, and members of the work group were named in 2007.³ The draft criteria were posted on the APA

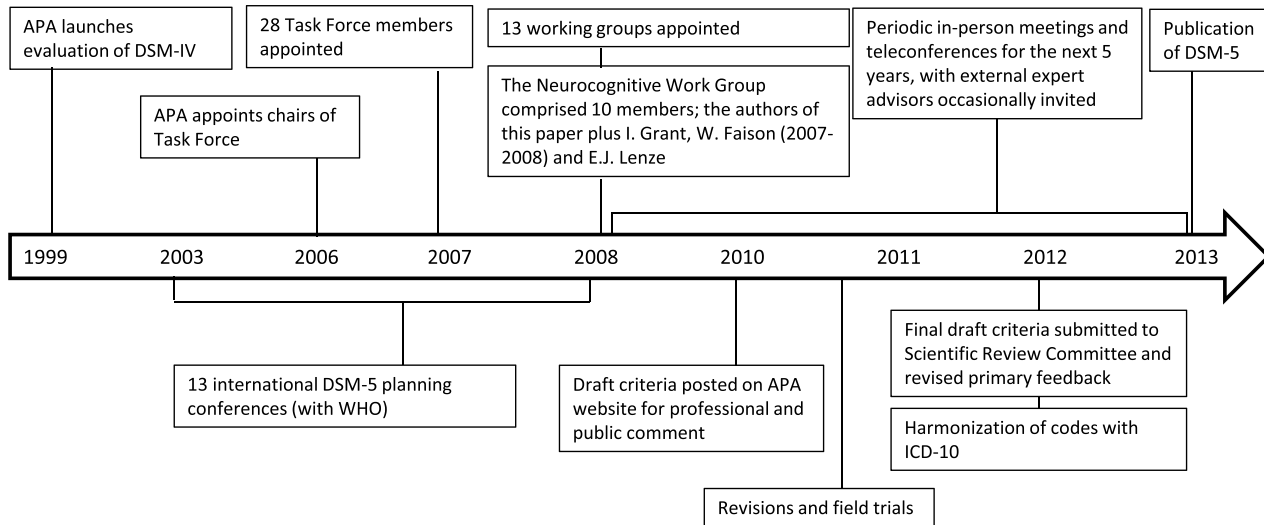


Figure 1. Timeline of DSM-5 consultation and review process. Reprinted, with permission, from *Nature Reviews. Neurology*.³

website in 2010 to get feedback from professionals and the public (Figure 1).

The DSM-5 task force⁴ extensively reviewed the literature and particularly paid “due consideration”⁵ to the international criteria of mild cognitive impairment (MCI) published after a 2003 Key Symposium held in Stockholm.^{6,7} The result is that the DSM-5 version of mild NCD, in more ways than not, resembles the widely used international criteria of MCI. For example, subjective complaint by the patient, informant, or clinician—preferably confirmed by a neuropsychological test—is one of the criteria used to define mild NCD. The other criteria of mild NCD, as discussed elsewhere in this article, are also almost identical to the international criteria of MCI (Table 1).

This leaves open the question as to whether mild NCD is an “old wine in a new bottle.” Indeed, the DSM-5 task force

has referred to mild NCD as an entity that has “most frequently been described as mild cognitive impairment.”¹² The main difference between MCI and mild NCD is that the research work that led to the construct of MCI took place in the context of geriatric populations (even though age was not part of the definition of MCI), whereas mild NCD encompasses acquired cognitive disorders of all age groups. Since the clinical, epidemiological, neuropsychological, and biomarker research on MCI is so extensive, it is reasonable and appropriate for the task force to have used MCI as a template to define mild NCD.

The goal of this article is to review the DSM-5 criteria for mild NCD, to compare them with the Key Symposium criteria for MCI, and to further discuss the pros and cons of the mild NCD classification. In order to understand mild NCD, one may need to examine the historical genesis of the

Table 1

Diagnostic Criteria: Mild Neurocognitive Disorder Versus Mild Cognitive Impairment

Criteria ^a	Original Mayo Clinic ^{8,9}	Expanded/Key Symposium ^{6,7}	NIA-AA ¹⁰	DSM-5 ¹
Self- or informant-reported memory complaint	X			
Self- or informant-reported cognitive complaint		X	X	X
Objective memory impairment	X			
Objective cognitive impairment		X	X	X
Essentially preserved general cognitive functioning	X			
Preserved independence in functional abilities	X	X	X	X
No dementia	X	X	X	X

NIA-AA, National Institute on Aging–Alzheimer’s Association work group; DSM-5, *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed.; X, criterion required.

^a Core clinical criteria according to major definitions are listed.

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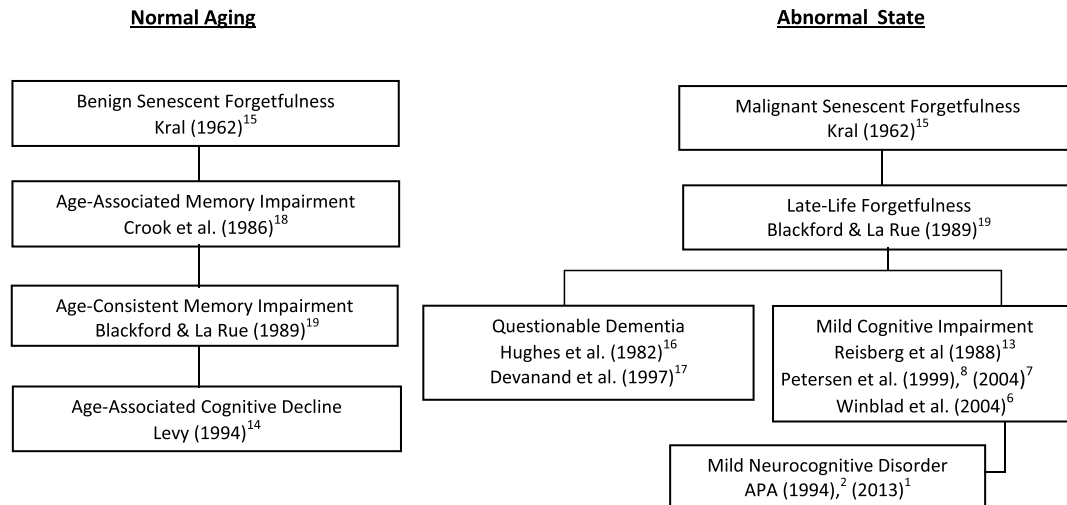


Figure 2. Boundary conditions and terms to describe the gray zone between normal cognitive aging and dementia.²⁰ Modified and reprinted, with permission, from *Geriatric Neuropsychology: Assessment and Intervention*.²¹

concept of MCI and related constructs that describe the intermediate stage between normal cognitive aging and dementia.

THE GRAY ZONE BETWEEN NORMAL COGNITIVE AGING AND DEMENTIA

The research agenda of the field of aging and dementia has evolved over time. The initial goal of clinicians and researchers was to understand the clinical and epidemiological characteristics of dementia and to delineate its probable causes. Clinicians and investigators noted, however, that some elderly persons were neither demented nor cognitively normal, leading researchers to investigate the gray zone between normal cognitive aging and dementia. Experts coined various terms to describe that gray zone, including MCI,^{6-8,13} aging-associated cognitive decline,¹⁴ benign senescent forgetfulness,¹⁵ questionable dementia,^{16,17} malignant senescent forgetfulness,¹⁵ age-associated memory impairment,¹⁸ age-consistent memory impairment,¹⁹ late-life forgetfulness,¹⁹ and cognitive impairment no dementia²⁰ (Figure 2).

From among these constructs and terms, MCI is perhaps the most empirically investigated and widely cited construct, as is evident from the exponential increase in the number of publications pertaining to MCI (Figure 3).

Individuals with MCI show a cognitive impairment that is greater than expected for their age and educational level but does not meet the commonly used criteria for dementia. It must also be noted that both MCI and mild NCD refer to cognitive syndromes and not to any specific disease state. The reader is referred elsewhere for a detailed review of MCI.⁹

Introduction of the construct of MCI substantially contributed to the field of cognitive aging and dementia. In clinical settings, the diagnosis of MCI has implications for patients and their caregivers and clinicians. Most importantly, patients and their caregivers can plan for future medical and socioeconomic challenges.¹² From a research perspective, the MCI construct has been the subject of several observational and interventional studies. As a high-risk group for dementia, MCI patients present an opportunity to test novel medications at an earlier stage of disease progression,²³ with the

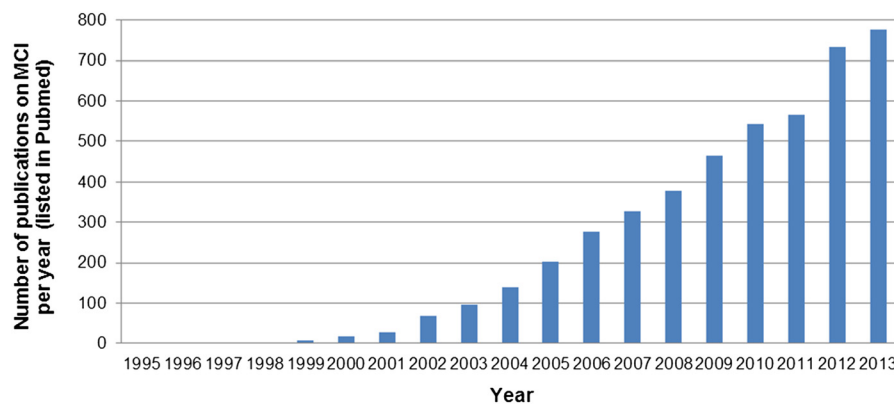


Figure 3. Number of publications on “mild cognitive impairment” listed in PubMed by calendar year. Modified and reprinted, with permission, from *American Journal of Geriatric Psychiatry*.²²

hope of providing a better chance to slow the progression of cognitive decline. In addition, patients could potentially be diagnosed earlier, and at a stage that would allow them to make conscious decisions about themselves and their property if their underlying diseases lead to progression to dementia. Prior to the year 2000, fewer than 50 articles on the subject of MCI were published per year. Following the publication of the original MCI criteria in 1999, the number of publications grew exponentially. By 2010, the number of publications had increased to more than 500, and in 2013 the number exceeded 700.

Even though the international criteria of MCI^{6,7} are the most widely cited publications on the gray zone between normal aging and dementia, not all investigators have agreed with this construct.¹¹ For some, MCI was synonymous with early-stage Alzheimer's disease (AD).²⁴⁻²⁷ Furthermore, the field was not satisfied that a pre-dementia state had been reliably and helpfully identified. Rather, advances in epidemiologic, neuroimaging, and biomarkers research led to research on identifying asymptomatic dementia, particularly asymptomatic AD. Thus, the focus of research evolved from dementia to MCI and, more recently, to identifying the asymptomatic phenotype of AD.^{10,28} To date, biomarker-based criteria are mainly used for research purposes,^{10,29} although they are increasingly being used in clinical practice.

MILD NEUROCOGNITIVE DISORDER

As noted earlier, DSM-5 has now classified acquired neurocognitive disorders of all age groups under three major headings: delirium, major NCD, and mild NCD. The key distinction between major and mild NCD is that persons with major NCD experience a substantial decline in function (loss of independence) as a result of profound cognitive impairment, whereas subjects with mild NCD experience only a modest cognitive decline and, as a result, function relatively independently.⁵ One typically follows a time-honored diagnostic algorithm of first diagnosing major or mild NCD via the DSM-5 criteria, and then using the specifiers to define the etiology.¹² Thus, the components of major and mild NCD criteria are classified under four categories of criteria (criteria A, B, C, and D) and three specifiers (etiologies, presence or absence of behavioral problems, and severity of functional decline). Details of the criteria and specifiers are discussed below.

Criterion A refers to cognitive impairment in one or more domains (e.g., complex attention, executive function, learning and memory, language, perceptual-motor, and social cognition). Criterion A is further divided into two parts. The first part refers to a cognitive concern reflecting a change from a previous level of cognitive function, as reported by the patient, an informant, or a clinician. Of note, DSM-IV did not have a criterion for subjective complaint;⁵ the introduction of this criterion in DSM-5 was based primarily on data from MCI research. The second subheading of criterion A specifies that the cognitive impairment is preferably confirmed by

neuropsychological testing or quantitative clinical assessment. If the individual's performance is two or more standard deviations below the mean within the appropriate norms, the person would be considered as having major NCD. For a diagnosis of mild NCD, the performance typically ranges 1–2 standard deviations below age- and education-adjusted norms. This range is based on the assumption that normal cognitive performance falls within one standard deviation above or below the mean; however, since normative data may not be available, one may need to rely on clinical judgment to make a diagnosis of mild NCD. DSM-5 also states that neuropsychological testing may not be available or appropriate in every case. Therefore, quantitative clinical assessment may also be performed, though DSM-5 does not explicitly state what it means by quantitative clinical assessment. We are left to assume that quantitative assessment includes clinical evaluation with bedside cognitive-screening tests.³⁰⁻³³ DSM-5 generally recommends that, whenever possible, clinicians should interpret any neuropsychological testing performance in light of the patient's previous task performance. In contrast to a simple comparison with normative values, this procedure allows for a more accurate estimate of the trajectory of each individual's cognitive decline. It should also be noted that both subjective concern and objective evidence are required for a diagnosis of a NCD.

Criterion B refers to whether or not there is a departure from baseline function. Persons with major NCD have substantial decline in activities of daily function, whereas individuals with mild NCD essentially function independently although doing so may require greater effort or compensation strategies. Criterion C refers to the exclusion of delirium. Hence, a person who is in an acute confusional state or delirium should not be diagnosed with major or mild NCD. Criterion D refers to the exclusion of a competing mental disorder that can account for the findings. For example, syndromes such as major depressive disorder need to be ruled out before making a diagnosis of NCD.

In addition to criteria A, B, C, and D, DSM-5 describes three specifiers: (1) etiologies, (2) presence or absence of behavioral abnormalities, and (3) severity of symptoms. The etiologic specifiers have identified underlying diseases such as AD, frontotemporal lobar degeneration, Lewy body disease, vascular disease, traumatic brain injury, substance/medication use, HIV infection, prion disease, Parkinson's disease, Huntington's disease, "another medical condition," multiple etiologies, and unspecified. For example, a patient can be diagnosed with major NCD due to AD. In the old parlance, such a condition would have been characterized as dementia due to AD. Furthermore, in DSM-5, one can specify the etiology of impairment of a specific cognitive domain (e.g., language impairment due to frontotemporal lobar degeneration). The second specifier refers to the presence or absence of behavioral abnormalities. In both major and mild NCD, several behavioral abnormalities such as psychotic or mood symptoms, sleep disturbances, agitation, apathy, and

other symptoms may be noted in a patient. In such cases, the clinician or researcher needs to document the behavioral abnormality (e.g., mild NCD with apathy). Finally, the last specifier focuses on the severity of functional decline. The severity specifier is primarily applicable for major NCD because, by definition, mild NCD is not associated with functional decline to the point of impairing independent living. The severity specifier is mentioned here to clearly distinguish between major NCD and mild NCD. DSM-5 classifies the severity of symptoms in major NCD into three categories: mild (impairment only in instrumental activities of daily living), moderate (impairment in basic day-to-day functions such as clothing and feeding), and severe (completely dependent on others).

EPIDEMIOLOGY, RISK FACTORS, AND DIAGNOSTIC MARKERS OF MILD NEUROCOGNITIVE DISORDER

By definition, major and mild NCD refer to acquired cognitive disorders of all age groups. However, the current DSM-5 manual mainly discusses the epidemiology, risk factors, and diagnostic markers of NCD by drawing congruence between dementia and major NCD, and between MCI and mild NCD. Therefore, while reviewing the sections on epidemiology, risk factors, and diagnostic markers of mild NCD as discussed below, the reader should keep in mind that most evidence stems from research on MCI. Clinicians and researchers should also keep in mind that even though DSM-5 has broadened the age range for major and mild NCD, it remains important that the z-score cutoffs for tests are to be interpreted in the context of other risk factors such as age.

Risk Factors

The traditional confounders or risk factors for major and mild NCD are age, sex, and education. The risks for neurodegenerative and cerebrovascular diseases are elevated with increasing age, thus making age a strong risk factor for both major and mild NCD. Occupation and education are other important risk factors; for example, a person who has a

demanding occupational or recreational activity is more likely to notice a cognitive decline, especially at a mild level. There are also a number of risk factors for the various subtypes of major and mild NCD. For example, apolipoprotein E (APOE) $\epsilon 4$ is a well-known risk factor for major or mild NCD due to AD.³⁴ Genetic mutations, several risk genes, vascular risk factors (e.g., stroke and hypertension), and family history are other risk factors for several major or mild NCD subtypes. Environmental and lifestyle factors such as physical exercise and mentally stimulating activities have also been associated with decreased risk of major or mild NCD of various subtypes.^{35–37}

Diagnostic Markers

NEUROPSYCHOLOGICAL TESTS As proposed in criterion A, the diagnosis of NCD is based on subjective complaint reflecting a cognitive decline and is preferably confirmed by standardized and valid neuropsychological testing or by clinical evaluation. This procedure allows for an accurate assessment of relevant cognitive functions and may therefore indicate a decline in one or more domains. For example, the Rey Auditory Verbal Learning Test³⁸ is a psychometric test that measures learning and recall that represents the memory domain. Another test that measures memory is the Wechsler Memory Scale–Revised (WMS-R).³⁹ Similarly, tests for language (e.g., Boston Naming Test,⁴⁰ category fluency⁴¹), executive function (e.g., trail-making test,⁴² digit symbol substitution test of the Wechsler Adult Intelligence Scale–Revised [WAIS-R]⁴³), and visuospatial function (e.g., Picture Completion and Block Design subtests of the WAIS-R) can be employed to objectively measure cognitive function.

BIOMARKERS AND NEUROIMAGING There are biomarkers for several etiological subtypes of major and mild NCD. Extensive research is conducted in Alzheimer's NCD in which chemical and neuroimaging biomarkers are used to investigate that disease from the asymptomatic phase all the way to major NCD due to AD (Figure 4). The biomarker research of AD is

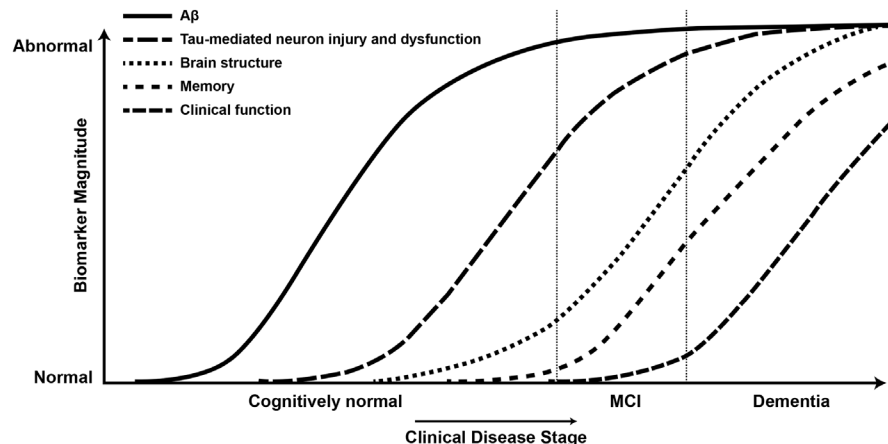


Figure 4. Dynamic biomarkers of the Alzheimer's pathological cascade. A β , β -amyloid; MCI, mild cognitive impairment. Reprinted with permission from *Lancet Neurology*.⁴⁴

anchored upon the study of amyloid- β ($A\beta$), tau-mediated neuron injury, and neuronal loss. $A\beta$ is measured by employing various types of ligands developed for amyloid positron emission tomography.⁴⁵ Additionally, $A\beta$ is measured by using cerebrospinal fluid $A\beta_{42}$,⁴⁶ whereas tau-mediated neuronal injury and dysfunction is identified by CSF tau, phosphorylated tau, or fluorodeoxyglucose positron emission tomography (FDG-PET). Neuronal atrophy is measured by structural magnetic resonance imaging. Computerized tomography and magnetic resonance imaging are commonly used to visualize cortical atrophy in brain regions that are pertinent to NCD.^{44,47–50} Functional neuroimaging techniques can be particularly informative when the structural neuroimaging is normal. For example, glucose hypometabolism can be detected in AD signature areas by using FDG-PET. Similarly, amyloid deposition in the brain can be visualized by using various types of PET ligands.²⁸

Epidemiology

The prevalence of mild NCD, which is congruent with MCI, is dependent on age and the underlying etiology, and ranges between 3% and 22%.^{51–53} This variability is attributable to methodological differences; clinical-based convenience samples tend to report higher prevalences than population-based studies. Similarly, the incidence of mild NCD is about 1%–6% per year; again, this variability is largely due to methodological differences between studies that generated these epidemiological indices.⁵⁴

ETIOLOGIES OF MILD NEUROCOGNITIVE DISORDER

The National Institute on Aging–Alzheimer’s Association task force reviewed the research work involving biomarkers and neuroimaging pertaining to MCI. The task force coined the term “MCI due to AD.”¹⁰ This entity constitutes a subset of MCI; other types of MCI may not be caused by AD. While some of the biomarkers await validation, the construct of MCI due to AD has spurred further research regarding diagnostic biomarkers. The DSM-5 construct does not distinguish, however, between major and mild NCD when it discusses etiologies. Accordingly, DSM-5 lists ten causes of major or mild NCD: (1) AD, (2) frontotemporal lobar degeneration, (3) Lewy body disease, (4) vascular disease, (5) traumatic brain injury, (6) substance/medication-induced, (7) HIV infection, (8) prion disease, (9) Parkinson’s disease, and (10) Huntington’s disease. In addition to the ten specific etiologies, DSM-5 has also created three other etiological categories: (1) major or mild NCD due to multiple etiologies, (2) major or mild NCD due to “another medical condition,” and (3) major or mild NCD with unclear etiology. If a patient meets the criteria for mild NCD and if the medical workup indicates that the cause is due to brain tumor, then the official DSM-5 diagnosis will be “mild NCD due to another medical condition.” In clinical or research settings, is it possible for a clinician to be specific and to state mild NCD due to brain

tumor? The answer is yes. The cornerstone of clinical practice is that one identifies a syndrome and looks for a specific etiology.

The Role of Biomarkers and Laboratory Investigation in Clarifying Etiologies

If there is genetic, biochemical, neuroimaging, or clinical evidence for AD, then the etiology will be considered probable (e.g., mild NCD due to probable AD in a patient with clinical and deterministic genetic mutation). When the diagnosis is less firm, the clinician would make a diagnosis of mild NCD due to possible AD.

Other Features

In addition to its overview of diagnostic features, DSM-5 specifies the following: associated features supporting a diagnosis; prevalence estimates; development and course; risk and prognostic factors; culture-related diagnostic issues; diagnostic markers; functional consequences; differential diagnosis; and comorbidity.

THE PROS AND CONS OF THE CONSTRUCT OF MILD NEUROCOGNITIVE DISORDER

Sachs-Ericsson and Blazer⁵⁵ discuss the rationales and benefits of introducing mild NCD from the patient’s perspective and also from the perspective of the scientific community. The scientific advances include biomarker changes indicating that the pathophysiology underlying NCD due to AD starts long before clinical symptoms become apparent. The authors justifiably argue that this scientific advance suggests the need to intervene early, if and when treatments are developed, and to target the presymptomatic stage or early mild NCD.⁵⁵

One important contribution of DSM-5 is its elimination of the obligatory requirement to have memory impairment in the diagnosis of any type of dementia. For example, memory impairment was a necessary criterion for the DSM-IV diagnosis of vascular dementia, whereas in DSM-5, the obligatory requirement for involvement of the memory domain is eliminated.⁵⁶ DSM-5 has thus rectified the “Alzheimer’s-centric” criteria of DSM-IV. DSM-5 also introduced additional cognitive domains that were not present in DSM-IV: complex attention and social cognition (in addition to the DSM-IV domains of language, memory, executive function, and visuospatial function). DSM-IV used categories that describe cortical lesions such as aphasia, apraxia, and agnosia as cognitive disturbances, whereas DSM-5 has eliminated these terms and instead listed cognitive domains (i.e., complex attention, executive function, learning and memory, language, perceptual-motor, and social cognition).

Another weakness of DSM-IV was the absence of criteria to objectively assess cognitive decline by using neuropsychological testing.⁵⁶ In DSM-5, the following criterion is added: “A substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing.” Another major change pertains to a substantial revision of

“cognitive disorder not otherwise specified.” This DSM-IV category underwent marked change in order to further elaborate mild NCD, which also includes MCI.

One of the advantages of mild NCD is that it offers a more structured diagnostic approach. First, the clinician needs to decide whether the cognitive impairment is mild or major NCD; the next step is to identify possible etiology; and the last step is to document the presence or absence of behavioral abnormalities.

DSM-5 is criticized for failing to include biomarkers as one part of the diagnostic procedure. The DSM-5 diagnostic criteria mainly rely on observations of behavior and cognition without taking into consideration specific neuroimaging or biomarker investigations.⁵⁷ Therefore, although DSM-5 may be useful for clinicians in diagnosing diseases and planning appropriate treatment, it stops short of incorporating biomarkers into the diagnostic criteria.⁵⁷ DSM-5 does mention biomarkers, however, for some specifiers of NCD. We also anticipate that once validation studies are conducted, then biomarkers will most likely be included into the diagnostic criteria of mild NCD.

Another criticism of DSM-5 pertains to the use of the term “neurocognitive disorders.” Rabins and Lyketsos⁵⁶ argue that the prefix “neuro” could lead to the impression that some cognitive disorders do not result from brain disease. They thus recommended the use of the term “acquired cognitive disorders” to be dissimilar from cognitive disorders being present from birth or childhood. Indeed, the DSM-5 work group on NCD⁴ had initially considered using the term “acquired cognitive disorders,” as suggested by Rabins and Lyketsos.⁵⁶ The work group noted, however, that the term “neurocognitive” has several advantages, including the avoidance of potential misclassification errors that can be associated with “cognitive disorders.” For example, the term “cognitive” is widely used in various contexts in the field of psychiatry and psychology (e.g., cognitive therapy, cognitive symptoms of schizophrenia, cognitive errors, cognitive strategy). The work group also identified precedents for its adoption of the term “neurocognitive” (e.g., HIV-associated neurocognitive disorders).⁴ In our opinion, either term could have served the discipline equally well. Perhaps the term “neurocognitive” is a constant reminder of keeping in mind that cognitive disorders implicate the brain as the neuroanatomic source of thoughts and emotions.

The replacement of “dementia” by the term “major NCD” was also met with some criticism,⁵⁶ although DSM-5 stated that “dementia” may still be used if preferred. Some argue that the widespread use of “dementia” by both the lay public and professionals has essentially led to its “destigmatization.” Therefore, it will be rather confusing for the public to drop dementia and replace it with major NCD. The authors also argue that the term “major NCD” may sound awkward in day-to-day parlance. For example, instead of saying dementia with Lewy bodies, one has to say major NCD due to Lewy body disease. In our opinion, both arguments are correct

because DSM-5 has not “banned” the term “dementia”; instead, it has introduced “major NCD” as an alternative to “dementia.” Therefore, those who prefer to use the “dementia” can do so.

One source of debate and argument pertains to age. Some argue that one of the main reasons for replacing the terms “dementia” and “MCI” with “major” and “mild NCD” is that both dementia and MCI are associated with acquired geriatric disorders,⁵ whereas major and mild NCD are acquired cognitive disorders of all age groups. This classification, however, may potentially lead to “lumping” together different diseases. For example, a 20-year-old football player with concussion and cognitive problems could be diagnosed with mild NCD (due to traumatic brain injury). A person aged 80 years with insidious onset and gradually progressing cognitive decline and who has minimal loss of independence could also be diagnosed with mild NCD (due to AD).

Some authors have further argued that the distinction between major and mild NCD may not be reasonable as cognitive and functional decline are usually described as being a continuum without having categorical cutoff points.⁵⁸ Additionally, the commonly used screening instruments may not be sensitive enough to accurately classify patients into these two categories, which can cause wrong diagnoses and lead to confusion among patients and clinicians alike.⁵⁹ Additionally, more detailed diagnostic criteria (i.e., criteria for frontotemporal dementia) have been published recently and get more into the theory of mind and other behavioral symptoms than does DSM-5.⁶⁰ More generally, there is a lack of clarity with regard to the clinical assessment of NCD. For example, DSM-5 fails to specifically and tangibly define what it means by “quantitative clinical assessment.” Clinicians may thus have to resort to available means of “quantitative clinical assessment”—which opens the door to disparate types of cognitive screening tools (ones that may not necessarily have been validated) and introduces variability into the quantitative clinical assessment of NCD.

Initial empirical work on mild NCD has already begun. Investigators from Spain and UK⁶¹ have reported that the prevalence of mild NCD as diagnosed by DSM-5 criteria was only half that as diagnosed by the Mayo Clinic criteria in the same population. In an editorial comment on that study, conducted by the “Zaragoza group,” John Breitner⁶² discusses that contrary to hopes and expectations, DSM-5 mild NCD was less sensitive than MCI in identifying individuals at the earliest stage of cognitive decline. Breitner thus argues that DSM-5 should have relied more on biomarkers or genes to detect early stages of cognitive decline than on defining cognitive dysfunction based on clinical features. Furthermore, he posed the following challenge to the DSM-5 work: “Has the APA’s preferred method of relying on consensus opinion in fact produced a perverse result? Should the experts instead have relied

on studies such as those of the Zaragosa group in formulating their diagnostic terminology?” In fairness to DSM-5, the various work groups exhaustively reviewed the literature, duly considered the existing empirical work, and sought input from both scientific and lay public in defining the various diagnostic categories. In this sense, DSM-5 was not entirely a product of “consensus opinion.” The study by the Zaragosa group heralds the beginning of the empirical work needed to validate DSM-5 constructs.

CONCLUSION

The initial impetus for developing the *Diagnostic and Statistical Manual of Mental Disorders* was to establish standard and universal criteria for mental disorders. In particular, the goal was to have a clinical and research system that can reliably diagnose mental disorders across the globe. The initial edition was published in 1952, and the fourth edition (DSM-IV) in 1994. Recent, substantial scientific advances have been made in the field of aging and dementia that have prompted the revision of cognitive disorders. DSM-5 dropped the term “dementia” and replaced it with “major NCD.” The cognitive disturbances that do not lead to a substantial functional decline were classified under “mild NCD.” The formulation of the diagnostic criteria for mild NCD was developed by paying “due attention” to the international criteria of MCI published in 2004.^{6,7}

The construct of “neurocognitive disorders” as proposed in DSM-5 will need to withstand rigorous scientific scrutiny and validation prior to being universally accepted by clinicians and researchers.

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