Classifying neurocognitive disorders: the DSM-5 approach

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Abstract | Neurocognitive disorders—including delirium, mild cognitive impairment and dementia—are characterized by decline from a previously attained level of cognitive functioning. These disorders have diverse clinical characteristics and aetiologies, with Alzheimer disease, cerebrovascular disease, Lewy body disease, frontotemporal degeneration, traumatic brain injury, infections, and alcohol abuse representing common causes. This diversity is reflected by the variety of approaches to classifying these disorders, with separate groups determining criteria for each disorder on the basis of aetiology. As a result, there is now an array of terms to describe cognitive syndromes, various definitions for the same syndrome, and often multiple criteria to determine a specific aetiology. The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) provides a common framework for the diagnosis of neurocognitive disorders, first by describing the main cognitive syndromes, and then defining criteria to delineate specific aetiological subtypes of mild and major neurocognitive disorders. The DSM-5 approach builds on the expectation that clinicians and research groups will welcome a common language to deal with the neurocognitive disorders. As the use of these criteria becomes more widespread, a common international classification for these disorders could emerge for the first time, thus promoting efficient communication among clinicians and researchers.

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Introduction

The nomenclature of neuropsychiatric disorders has a contentious history, with periodic attempts to bring cohesion to this diverse and disparate field. As an influential organization in this area, the American Psychiatric Association (APA) sought to publish a glossary for mental disorders in 1952 as the first edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-I).[1] This manual has since undergone multiple revisions. The third edition (DSM-III), published in 1979, deviated from earlier editions in that it provided explicit criteria for all disorders listed in the manual, signalling an emphasis on achieving reliable diagnoses. This volume proved to be highly influential, and was adopted by clinicians and researchers from around the world.

The fourth edition of DSM (DSM-IV), published in 1994, included a chapter on neurocognitive disorders entitled "Delirium, Dementia, and Amnestic and Other Cognitive Disorders."[2] The general description of dementia was that of a condition "characterized by the development of multiple cognitive deficits (including memory impairment) that are due to the direct physiological effects of a general medical condition, to the persisting effects of a substance, or to multiple etiologies." The cognitive effects needed to represent a decline from a previous level of functioning, and had to be severe enough to cause significant impairment in social or occupational functioning. Specific criteria for "dementia of the Alzheimer's type" and "vascular dementia" were included, with the latter similar to the contemporary description of multi-infarct dementia. DSM-IV did not include criteria for the predementia syndrome mild cognitive impairment (MCI), but did define similar conditions—namely, amnestic disorder, and age-related cognitive decline—in the appendix. The definitions of dementia in DSM-III and DSM-IV were influential in both research and clinical practice, and formed the basis of a wealth of epidemiological data.[3] The DSM-IV approach to classifying neurocognitive disorders also contained a number of limitations, which prompted a major revision in the fifth edition (DSM-5).[4]

Competing interests
The authors were members of the Neurocognitive Disorders Work Group for DSM-5. D.V.J. was President of the American Psychiatric Association from 2012–2013 when DSM-5 was published.

The DSM-5 process

The DSM revision process began in 1999, and followed the various steps listed in Figure 1 (Timeline). The Neurocognitive Disorders Work Group was appointed in 2008, and embarked on a 5 year process of biannual in-person meetings, and frequent teleconferences and electronic exchanges. The Work Group, comprising the authors of this paper, one other full-time member and two members in partial attendance, had representation from geriatric psychiatry, neurology, neuropsychiatry, neuropsychology and cultural psychiatry, and liaised with groups covering psychosis, neurodevelopmental disorders, mood disorders and other aspects of the DSM.

Key points

- The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) provides a framework for the diagnosis of neurocognitive disorders based on three syndromes: delirium, mild neurocognitive disorder and major neurocognitive disorder
- Major neurocognitive disorder is mostly synonymous with dementia, although the criteria have been modified so that impairments in learning and memory are not necessary for diagnosis
- DSM-5 describes criteria to delineate specific aetiological subtypes of mild and major neurocognitive disorder
- The diagnostic certainty of an aetiological diagnosis is based on clinical features and biomarkers, and can be qualified as probable or possible
- The DSM-5 criteria are consistent with those developed by various expert groups for the different aetiological subtypes of neurocognitive disorders
- Further validation in clinical practice is necessary, but we expect these criteria will have high reliability and validity, and widespread adoption will bring consistency to the diagnosis of diverse neurocognitive disorders

The Neurocognitive Disorders Work Group formally invited additional experts to act as external advisers, and informally consulted with other such experts internationally. Public comment was solicited on draft criteria posted on the DSM-5 website. Although the administrative procedures determined by the DSM-5 Task Force—comprising 31 leading experts in psychiatric research and practice, including the chairs of the 13 Work Groups—had to be followed, no intellectual constraints were imposed on the Work Group. The tasks of literature review and external liaison were shared by the Work Group members. The final criteria, designed to reflect the latest advances in scientific knowledge in this field, were reached by consensus of the members after considerable input from expert advisers. The final criteria were reviewed by several overarching DSM-5 panels, including a scientific review committee, a clinical and public health review committee, the Task Force, and a summit body, before final approval was granted by the APA Board of Trustees.[5]

The purpose of DSM-5

As the official classification system of the APA, the primary constituency of the DSM is mental health professionals based in the USA, who use it primarily for the purpose of diagnosing their patients and billing for their services. The DSM is also used extensively by psychiatric researchers for participant selection criteria, outcome measures and reliable communication of their work. The use of DSM, however, transcends professional and national boundaries, with widespread use by clinicians and researchers in a variety of settings internationally. The DSM-5 has received a chorus of criticism from many quarters, largely owing to its inability to meet all needs and expectations of a diverse group of users.[6] Most of this criticism is not related to the neurocognitive disorders cluster, but a few contentious aspects will be discussed below.

This Review presents an introduction to the DSM-5 approach of classifying the neurocognitive disorders. We cover the three major cognitive syndromes that form the basis of the neurocognitive disorders cluster, including the rationale for grouping these disorders together and the key criteria for each diagnosis. We also describe several aetiological subtypes of minor and major neurocognitive disorder, which replace DSM-IV diagnoses such as dementia of the Alzheimer type and dementia due to Parkinson disease.

The neurocognitive disorders cluster

In line with the descriptive approach to classification used in DSM-5, the cluster of neurocognitive disorders is characterised by the presence of cognitive deficits that are the most prominent and defining features of a given condition. Whereas cognitive impairment is present in many mental disorders—such as schizophrenia, bipolar disorder, major depression and obsessive compulsive disorder—it cannot be regarded as the defining feature of these disorders as it might be, for example, in Alzheimer disease (AD) or traumatic brain injury. The term 'cognitive' is used broadly in psychology to refer to thought and multiple related processes,[7] and the term 'neurocognitive' was applied to this cluster of disorders to emphasize that disrupted neural substrates lead to symptoms, and that, in most cases, such disruption can be reliably measured.[8] The disorders in the neurocognitive cluster are also characterized by 'acquired' deficits, which represent a decline from a previously attained level of functioning, and are not neurodevelopmental deficits present from birth or early life.

When referring to neurocognitive disorders, it is important to delineate the domains of cognitive function that are likely to be affected. Cognitive domains have been variously categorized by different authors,[9,10] and a complete consensus is lacking. For the purpose of classifying neurocognitive disorders, the Neurocognitive Work Group agreed on six principal domains of cognitive function—complex attention, executive function, learning and memory, language, perceptual–motor function, and social cognition (Figure 2)—each with subdomains. The DSM-5 provides examples of symptoms and observations for each domain, and of ways to objectively assess each domain, but avoids the endorsement of proprietary tests.

The newly included domain of social cognition is particularly noteworthy, as it recognizes the fact that, in some neurocognitive disorders, socially inappropriate behaviour can manifest as a salient feature. These symptoms can take the form of reduced ability to inhibit unwanted behaviour, recognize social cues, read facial expressions, express empathy, motivate oneself, alter behaviour in response to feedback, or develop insight. Deficits in social cognition were usually referred to as personality change in previous diagnostic criteria.[2]

Subdividing the cluster

The neurocognitive disorders cluster comprises three syndromes, each with a range of possible aetiologies: delirium, mild neurocognitive disorder and major neurocognitive disorder.

Delirium

This neurocognitive disorder is characterised by disturbance in attention that makes it difficult for the individual

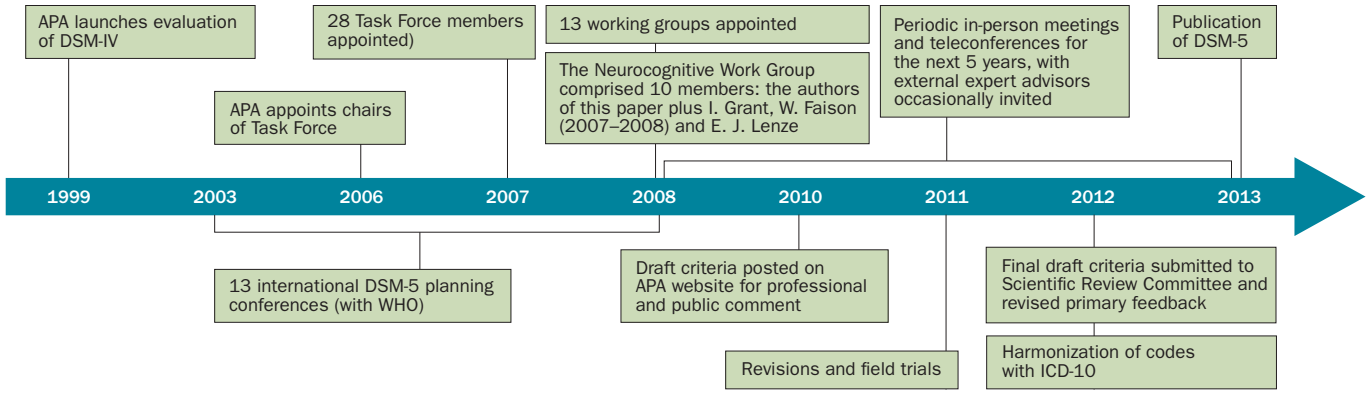

Figure 1 | Timeline of the DSM-5 consultation and revision process. Abbreviations: APA, American Psychiatric Association; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD-10, International Classification of Diseases 10th edition.

to direct, sustain and shift their focus. The individual is, therefore, likely to have reduced orientation to their environment, and at times to oneself. This symptom has sometimes been referred to as 'reduced level of consciousness' or confusional state,[11] although disturbance in awareness is a more accurate description. The disturbance of awareness tends to develop over hours to days, and typically fluctuates in the course of the day, often worsening in the evening. Delirium can be caused by an underlying medical condition, substance intoxication or withdrawal, exposure to toxins, or a combination of these factors. Patients may be hyperactive, hypoactive or have a mixed level of activity. The criteria for delirium are listed in Box 1.

Mild and major neurocognitive disorder

In this broad category of neurocognitive disorders, there is clear decline from a previous level of functioning in one or more of the key cognitive domains (Figure 2). Attention may be disturbed in these disorders, but, in contrast to delirium, this disturbance is not the core feature, and awareness of the environment is generally retained, except in very severely impaired patients. Therefore, the diagnoses of mild or major neurocognitive disorder are not made if the cognitive deficits occur in the context of persistent delirium, but can be made in patients for whom delirium manifests and then resolves.

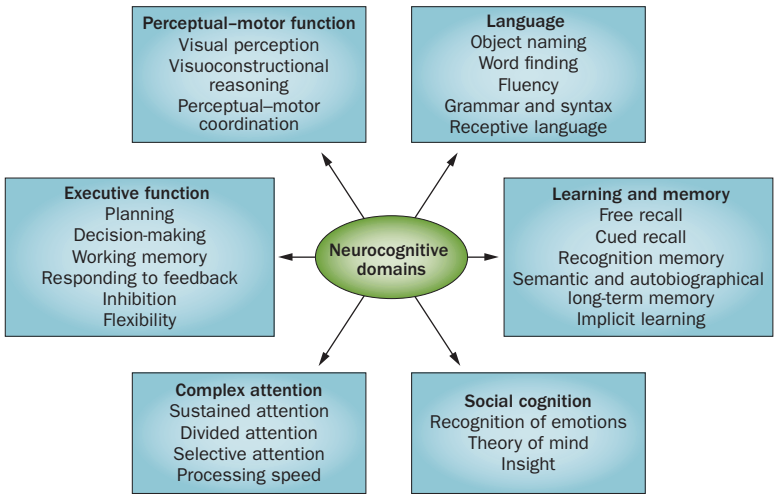

Figure 2 | Neurocognitive domains. The DSM-5 defines six key domains of cognitive function, and each of these has subdomains. Identifying the domains and subdomains affected in a particular patient can help establish the aetiology and severity of the neurocognitive disorder. Objective assessments are essential, but the DSM-5 does not name any proprietary tests. Abbreviation: DSM-5, Diagnostic and Statistical Manual of Mental Disorders 5th edition.

Mild neurocognitive disorder is a new addition to the DSM nomenclature, previously subsumed by the non-specific category of 'cognitive disorder not otherwise specified,' and represents a new framework for the commonly used diagnosis of MCI.[12] Major neurocognitive disorder mostly obviates the older concept of dementia, even though DSM-5 retains 'dementia' in parentheses to indicate that it may still be used (discussed further below). Mild and major neurocognitive disorders are categorical diagnostic constructs imposed on an underlying continuum of cognitive impairment from normality to severe impairment, as seen in the clinic and the population. Therefore, the structure of the DSM-5 criteria for mild neurocognitive disorder is parallel to that for major neurocognitive disorder, with the differences being the severity of cognitive deficits and functional impairment.

DSM-5 does not permit the diagnosis of mild or major neurocognitive disorders if the cognitive deficits can be better explained by another mental disorder, such as major depression or schizophrenia. This approach has been criticised by some commentators,[22] who argue that distinct neurocognitive disorders can be caused by mental disorders such as major depression, as implicit in the concept of depressive dementia. Under this framework, these neurocognitive disorders would be regarded as aetiological subtypes rather than as confounding factors. The argument in favour of the DSM-5 approach is that neurocognitive disorders are only diagnosed for conditions that have cognitive deficits as the core or defining feature: though psychiatric disorders should be considered in the differential diagnosis of neurocognitive disorders, distinct conditions should not be conflated.

Mild neurocognitive disorder

The use of the diagnosis of MCI has become commonplace in clinical practice, partly because many patients with cognitive decline now seek treatment earlier in the course of the disease, before a diagnosis of dementia is

Box 1 | Diagnostic criteria for delirium

A. A disturbance in attention (that is, reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).
B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.
C. An additional disturbance in cognition (for example, memory deficit, disorientation, language, visuospatial ability, or perception).
D. The disturbances in Criteria A and C are not better explained by another pre-existing, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.
E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (that is, due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple aetiologies.

Specify whether:
- Substance intoxication delirium
- Substance withdrawal delirium
- Medication-induced delirium
- Delirium due to another medical condition
- Delirium due to multiple aetiologies:
  - Specify if: acute (lasting a few hours or days); persistent (lasting weeks or months)
  - Specify if: hyperactive, hypoactive, mixed level of activity

Box 2 | Diagnostic criteria for mild neurocognitive disorder

A. Evidence of modest cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual–motor, or social cognition) based on:
   1. Concern of the individual, a knowledgeable informant, or the clinician that there has been a mild decline in cognitive function; and
   2. A modest impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.
B. The cognitive deficits do not interfere with capacity for independence in everyday activities (that is, complex instrumental activities of daily living such as paying bills or managing medications are preserved, but greater effort, compensatory strategies, or accommodation may be required).
C. The cognitive deficits do not occur exclusively in the context of a delirium.
D. The cognitive deficits are not better explained by another mental disorder (for example, major depressive disorder or schizophrenia).

justified. Furthermore, many brain diseases result in cognitive impairments that may not meet the threshold of functional impairment specified by the DSM-IV dementia diagnosis, but nonetheless have implications for the individual and those around them.

The move to diagnose neurocognitive disorders as early as possible emerged from the recognition of a long pre-dementia stage in neurodegenerative diseases, improvements in early diagnosis, and the increasing emphasis on early intervention to prevent or postpone dementia. Importantly, mild neurocognitive disorder is not always a precursor of major neurocognitive disorder, and the diagnosis has no requirement for further decline: there may be continued decline, as in the neurodegenerative disorders, or the impairment may be static, as in traumatic brain injury. The introduction of mild neurocognitive disorder has been criticized on the grounds that it medicalizes normality and might lead to many 'worried well' individuals with no disease being wrongly diagnosed, leading to unnecessary diagnostic tests and unproven treatments.[16] However, such criticism should not preclude the appropriate use of this diagnosis in the clinic.

The criteria for mild neurocognitive disorder are presented in Box 2. DSM-5 describes the level of cognitive decline in mild neurocognitive disorder to be "modest," leaving it up to the diagnostician to make the final judgement on the severity. As a guideline, test performance in mild neurocognitive disorder should fall in the range of 1–2 SD below the normative mean, or between the third and 16th percentiles, on tests for which appropriate norms are available. The DSM-5 does not specify which tests, or how many, should be administered per cognitive domain. In the absence of a formal neuropsychological assessment, the clinician may rely on 'bedside' assessments, but the objective demonstration of cognitive deficits is essential. In fact, because mild neurocognitive disorder needs to be distinguished from both normal cognitive ageing and major neurocognitive disorder (or dementia), even greater reliance on neuropsychological assessment is called for in mild than in major neurocognitive disorder. Serial assessments might be necessary to document decline, but the results must be interpreted cautiously in view of practice effects, variable test–retest reliability, and the dearth of normative data on cognitive decline.[21]

The DSM-5 criteria for mild neurocognitive disorder must be considered in the context of the other commonly used criteria for MCI: the Mayo Criteria,[16] the International Working Group (IWG) or the Key Symposium Criteria[18,19] and the National Institute of Aging–Alzheimer's Association (NIA–AA) Criteria.[20] The Mayo Criteria correspond best to what is referred to as amnestic MCI in the IWG Criteria, with the main objective of the diagnosis being the identification of AD at the predementia stage.[12] NIA–AA criteria were explicitly developed to enable researchers to diagnose MCI due to AD, but include a generic definition of MCI. The DSM-5 criteria for mild neurocognitive disorder are conceptually similar to both the NIA–AA and IWG criteria, requiring decline in one or more cognitive domains, with or without memory impairment.

The cognitive deficits in mild neurocognitive disorder do not interfere with the capacity for independence in everyday activities. Rather, the individual usually functions at a suboptimal level, with everyday tasks becoming more effortful owing to the engagement of compensatory strategies to maintain independence. The criterion of independent functioning represents the key distinction between the mild and major neurocognitive disorders, and relies on an insightful report by the individual and/or a family member, and a level of good judgement from the clinician.

Major neurocognitive disorder

The introduction of major neurocognitive disorder as an alternative term to dementia in DSM-5 was prompted by a number of reasons. Although we accept the long history of dementia in clinical medicine, as well as its familiarity

Box 3 | Diagnostic criteria for major neurocognitive disorder (or dementia)

A. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual–motor, or social cognition) based on:
   1. Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function; and
   2. A substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.

B. The cognitive deficits interfere with independence in everyday activities (that is, at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).

C. The cognitive deficits do not occur exclusively in the context of a delirium.

D. The cognitive deficits are not better explained by another mental disorder.

Specify:

- Without behavioural disturbance: if the cognitive disturbance is not accompanied by any clinically significant behavioural disturbance
- With behavioural disturbance (specify disturbance): if the cognitive disturbance is accompanied by a clinically significant behavioural disturbance (for example, psychotic symptoms, mood disturbance, agitation, apathy, or other behavioural symptoms). For example, major depressive disorder or schizophrenia

to the laity and policy makers, the limitations of this term should be recognized.[13] The term dementia is most commonly used to refer to older individuals—very often synonymously with AD—and is less likely to be used to describe younger people with severe cognitive deficits due to, for example, traumatic brain injury or HIV infection. The term has also acquired a pejorative connotation, and although a mere change in terminology is not sufficient to eliminate stigma, it might be a necessary first step. We expect that 'dementia' will continue to be used for elderly patients and in many clinical settings owing to familiarity and historical continuity, but we also expect that major neurocognitive disorder will be a more suitable diagnosis for many younger patients.

The DSM-5 criteria for major neurocognitive disorder (Box 3) have some noteworthy differences from the DSM-IV criteria for dementia. First, substantial decline in only one cognitive domain is sufficient for the diagnosis if the other criteria are met. As a consequence, the DSM-IV category of 'amnestic disorder' is now covered by major neurocognitive disorder. Second, memory impairment is not essential for the diagnosis. This change was made in recognition of the fact that many individuals with dementia not due to AD can have relatively intact memory, as is seen in patients with cerebrovascular disease,[14] frontotemporal degeneration[15] and some other conditions. Third, the functional criterion has been revised to reflect that the threshold for diagnosis of major neurocognitive disorder emphasizes loss of independence in daily living, in comparison with the DSM-IV requirement of impairment that "significantly interferes with work or social activities or relationships with others."

The determination of "significant" cognitive decline—that is, impairment sufficient to diagnose major neurocognitive disorder—is based on concern expressed by an individual or by an informant or clinician who knows the individual, and also on the demonstration of substantially impaired performance on an objective cognitive measure. A cognitive concern might not be voiced spontaneously, and might need to be elicited by careful questioning of the patient and/or significant others. The requirement of an objective measure is best met by formal neuropsychological assessment, with the performance being compared to normative data appropriate for the patient's age, educational attainment and cultural–linguistic background. If such an assessment is available, the performance typically falls at least 2 SD below the normative mean (or below the third percentile) on the test administered. As in mild neurocognitive disorder, patients for whom neuropsychological testing is not feasible, or appropriate norms are not available, can undergo a brief bedside assessment by the clinician to supply the objective data necessary for diagnosis. Competent interpretation of test performance is essential, and can be aided by prior administration of the same test so that decline can be assessed.

Aetiological subtypes

The DSM-5 classification was designed to complement the clinical process in which a diagnosis is made in two steps: a syndromal diagnosis is made first, and then potential causative factors are examined to attribute aetiology. Mild and major neurocognitive disorders are therefore subtyped according to aetiology.

In many patients with neurocognitive disorders, there is evidence for a causative disorder such as Parkinson disease, Huntington disease, traumatic brain injury, HIV infection or AIDS, or stroke. In other patients, the cognitive and behavioural symptoms manifest first, and the longitudinal course reveals aetiologies such as in AD, cerebrovascular disease, frontotemporal lobar degeneration and Lewy body disease. Occasionally, and especially in older individuals, there can be multiple causative factors, all of which should be recognized, but with primacy or salience assigned to one or two. For example, major neurocognitive disorder may be due to pathology produced by AD and cerebrovascular disease, which should both be diagnosed.

The principal aetiological subtypes for which diagnostic criteria are included in the DSM-5 are listed in Box 4. The aetiological subtype criteria are the same for both mild and major neurocognitive disorders, although establishing aetiology in mild neurocognitive disorder is more difficult and may, therefore, have to remain unspecified in many patients. For some of the aetiologies, the clinical features also determine the level of certainty in the aetiological diagnosis, with 'probable' representing a higher level of certainty than 'possible.'

The DSM-5 criteria were designed primarily for the clinician. Researchers can use the DSM-5 as well, although they may want to ensure a greater degree of specificity by adding additional requirements such as biomarkers, or by turning to alternative criteria. Some criteria stipulate that a 'definite' aetiological diagnosis requires neuropathological confirmation from autopsy or biopsy.[24,25] Considering that DSM-5 is a clinical

Box 4 | Subtypes with diagnostic criteria in DSM-5

- Alzheimer disease
- Frontotemporal lobar degeneration
- HIV infection
- Huntington disease
- Lewy body disease
- Parkinson disease
- Prion disease
- Substance and/or medication use
- Traumatic brain injury
- Vascular disease
- Another medical condition
- Multiple aetiologies
- Unspecified

classification and neuropathological criteria for many of the aetiological subtypes are lacking, 'definite' diagnostic criteria are not presented.

The usefulness of biomarkers for disorders associated with cognitive dysfunction has been increasingly recognized, and some biomarkers are specific enough to be of diagnostic value, and have, therefore, been incorporated into disease criteria. For example, the presence of mutations in the amyloid precursor protein gene (*APP*) or the presenilin genes (*PSEN1* and *PSEN2*) is considered causative for AD with an early onset, and expansion of the huntingtin gene (*HTT*) with 36 or more repeats of the CAG trinucelotide is of diagnostic salience for Huntington disease. Neuroimaging is particularly important in the neurocognitive disorders to determine vascular and frontotemporal degenerative aetiology. Imaging can support diagnosis of AD, but its specificity is not considered high enough to be explicitly included in the diagnostic criteria. Other biomarkers for AD diagnosis,[23] such as levels of amyloid-β_{42} and phosphorylated tau in cerebrospinal fluid, are in the research arena and not yet ready for the clinic.

Diagnostic criteria for most of the aetiological subtypes of neurocognitive disorders include the exclusionary criterion that the disturbance cannot be explained by another aetiology. This requirement reflects the nonspecificity of the clinical features; thus, the diagnostic process involves the consideration of all possible aetiologies and their systematic exclusion to arrive at the most likely cause.

Neurocognitive disorders might include impairments in one or more cognitive domains, and so it is possible to subtype them on the basis of the number (single or multiple) or type (for example, amnestic or nonamnestic) of affected domains—though DSM-5 does not explicitly use this approach. In the literature on MCI, use of such subtyping is common and supported by the IWG criteria,[18] which highlight amnestic MCI, especially with a "hippocampal memory profile," as being the likely precursor of an AD dementia diagnosis.[23,26] The salience of deficits in processing speed and frontal–executive functions is used as evidence to support small vessel disease as being a causative factor. However, the subtyping of neurocognitive disorders by cognitive profile is not very specific for aetiology in many settings. For major neurocognitive disorder, such subtyping may sometimes be relevant, as in the case of the DSM-IV diagnosis amnestic disorder being renamed as amnestic major neurocognitive disorder, though this approach to subtyping is not explicitly described in DSM-5.

It is useful to consider some risk factors when attempting to determine aetiology, but such factors are generally independent of aetiology and should not be conflated with the underlying pathology. For example, hypertension, diabetes, obesity and metabolic syndrome are risk factors for vascular neurocognitive disorder, but they also increase the risk for AD, and their presence is consistent with other aetiologies for neurocognitive disorder as well. Risk factors are therefore not included in the diagnostic criteria for the aetiological subtypes in DSM-5.

The development of the DSM-5 criteria for the various subtypes involved extensive discussions with experts from diverse fields to harmonize the DSM criteria with criteria developed by other expert groups, such as the NIA–AA,[20,27] the frontotemporal dementia expert group,[28,29] the consortium on DLB,[30] the VASCOG working group,[31] the Movement Disorder Study Task Force on Parkinson Disease[32] and the AIDS Task Force of the American Academy of Neurology.[33]

Neurocognitive disorder due to AD

AD is a neurodegenerative disorder with an insidious onset and gradual progression of cognitive deficits. In a typical case, decline in learning and memory is an early and predominant feature, and the decline is progressive, without extended plateaus. For the DSM-5 diagnosis of major neurocognitive disorder due to AD, decline in at least two cognitive domains is necessary, one of which should be learning and memory; for mild neurocognitive disorder due to AD, the learning and memory deficit is sufficient for diagnosis, although the characteristic profile of insidious onset and gradual progression is necessary. In the absence of evidence for mixed aetiology (such as cerebrovascular disease or another neurological disorder), or in the presence of a causative mutation in *APP*, *PSEN1* or *PSEN2* indicated by definite family history or genetic testing, insidious onset and gradual progression increase the certainty of the diagnosis to 'probable' in the case of major neurocognitive disorder. For mild neurocognitive disorder, a more conservative standard is warranted, and a 'probable' diagnosis is only reached if there is evidence of a causative mutation for AD, and a 'possible' diagnosis requires only the typical clinical features.

Biomarkers of AD have received much attention recently. The presence of the ε4 variant of apolipoprotein E is a risk factor for AD but not a diagnostic marker. Other markers include the demonstration of amyloid deposition in the brain using PET, reduced levels of amyloid-β_{42} and elevated levels of phosphorylated tau and total tau in the cerebrospinal fluid, hippocampal and temporoparietal atrophy on MRI, and temporoparietal hypometabolism on ^{18}F-fluorodeoxyglucose PET. Although these biomarkers are appropriate for research

studies,[20,23] their availability varies in clinical settings, and they have, in general, not been fully validated for clinical use. It is possible that some of these biomarkers, along with novel ones, will move into general clinical practice in the future. The approach taken by DSM-5 is consistent with the one adopted by the NIA–AA criteria for dementia[25] and MCI.[20]

Vascular neurocognitive disorder

After the diagnosis of mild or major neurocognitive disorder has been made, the criteria for this disorder focus on establishing cerebrovascular disease as the dominant—if not exclusive—aetiology. The concept of vascular neurocognitive disorder is broad and includes both ischaemic and haemorrhagic lesions, as well as changes due to small vessel disease. The diagnosis of vascular neurocognitive disorder can, therefore, be made in the absence of patient history or physical signs suggestive of stroke. In this case, the clinical features should suggest damage due to small vessel disease, including prominent disturbance in processing speed and frontal–executive function, and physical signs consistent with stroke or small vessel disease, such as hemiparesis, pseudobulbar palsy and visual field defects, and/or neuroimaging evidence such as multiple lacunar infarcts or extensive and confluent white matter lesions. The development or worsening of cognitive deficits following a cerebrovascular event increases the certainty of the diagnosis.

Structural neuroimaging using MRI or CT has an important role as supportive evidence, and MRI can, in fact, be used to exclude the presence of clinically significant parenchymal injury due to vascular pathology. A number of vascular risk factors that should raise the index of suspicion have been recognized,[34] but these factors should not be used as diagnostic criteria. No biomarkers of vascular neurocognitive disorder, other than neuroimaging, have been established. The diagnosis of probable vascular neurocognitive disorder is therefore made if the clinical syndrome is supported by neuroimaging, follows a documented cerebrovascular event, or if both clinical and genetic evidence of cerebrovascular disease is present, for example in patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy.

Frontotemporal neurocognitive disorder

This group of neurodegenerative disorders comprises a number of syndromal variants with insidious onset and gradually progressive impairment of behaviour, personality and/or language. The behavioural variant is characterized by symptoms such as disinhibition; apathy or inertia, which leads to inactivity and lack of effort; loss of sympathy or empathy; perseverative, compulsive, ritualistic behaviours or stereotypies; and hyperorality and dietary changes. In various neuropsychiatric syndromes, these features are commonly present in isolation, and so the presence of at least three features is necessary for the diagnosis of frontotemporal neurocognitive disorder. This pattern of cognitive impairment should be associated with prominent decline in social cognition and/or executive abilities, but with relative sparing of learning and memory, and perceptual–motor function.

Individuals with the language variant present with primary progressive aphasia, and three subtypes have been recognized: semantic, agrammatic or nonfluent, and logopenic. The characteristics of these subtypes have been described elsewhere.[28]

Diagnostic markers are well recognized for this group of disorders. Neuroimaging is suggestive of disproportionate frontal and/or temporal lobe involvement. In familial cases, a number of causative mutations have been identified in *C9ORF72*, and in genes coding for microtubule-associated protein tau (*MAPT*), granulins (*GRN*), TAR DNA-binding protein 43 (*TDP-43*), transitional endoplasmic reticulum ATPase (*VCP*), charged multivesicular body protein 2b (*CHMP2B*) and FUS protein (*FUS*). These criteria are consistent with those published by external expert groups,[28,29] but it must be pointed out that the identification of frontotemporal degeneration as the aetiology for mild neurocognitive disorder in the absence of genetic and/or neuroimaging evidence is not yet established. Probable frontotemporal neurocognitive disorder is only diagnosed in the presence of a causative mutation or neuroimaging evidence of disproportionate frontal and/or temporal lobe involvement. Frontotemporal neurocognitive disorder overlaps with progressive supranuclear palsy, corticobasal degeneration and motor neuron disease in terms of clinical and pathological profiles.

Neurocognitive disorder with Lewy bodies

Like AD, this disorder presents with cognitive impairment of insidious onset and gradual progression, but the early changes are in complex attention and executive function rather than in learning and memory. The DSM-5 diagnosis of neurocognitive disorder with Lewy bodies requires the presence of core and suggestive features. The three core features are fluctuating cognition with pronounced variations in attention and alertness, recurrent visual hallucinations that are well formed and detailed, and spontaneous features of parkinsonism subsequent to the development of cognitive decline. Further suggestive features are rapid eye movement (REM) sleep behaviour disorder and severe neuroleptic sensitivity.

The diagnosis of probable neurocognitive disorder with Lewy bodies requires two core features, or one suggestive feature with one or more core features. The presence of spontaneous parkinsonism is an important feature and, by convention, the major cognitive symptoms are observed at least 1 year before the motor symptoms. The parkinsonism must be distinguished from drug-induced extrapyramidal signs, as individuals with neurocognitive disorder with Lewy bodies can be very sensitive to neuroleptic drugs that are often used to treat their hallucinations and delusions. Assessment scales for fluctuations in attention and awareness have been developed. The assessment of REM sleep behaviour disorder may require a sleep study. Neuroimaging markers include low striatal dopamine transporter uptake on single-photon emission CT (SPECT) or PET, generalized low uptake on

SPECT or PET perfusion, or a metabolic scan showing reduced occipital activity. Brain CT or MRI should also show relative preservation of medial temporal structures, low uptake on ^{123}I-metaiodobenzylguanidine myocardial scintigraphy suggesting sympathetic denervation, and prominent slow-wave activity on EEG with transient waves in the temporal region.

Other subtypes

Criteria for a number of other aetiologies for neurocognitive disorders are described in the DSM-5 (Box 4). The criteria set for each has a common structure: first, the criteria for mild or major neurocognitive disorder must be met, and then the relevant aetiology must be established while excluding other possible causes. As an example, the criteria for neurocognitive disorder due to HIV infection require patients with cognitive dysfunction to have documented evidence of infection with HIV. Clinicians must then exclude possible causes not related to HIV, including secondary brain diseases such as progressive multifocal leukoencephalopathy or cryptococcal meningitis. Information and criteria for each subtype can be found in the DSM-5.[4]

Conclusions

DSM-5 is the first major attempt to classify the various neurocognitive disorders with sets of criteria that are internally consistent and use common terminology. The DSM-5 uses a clinical approach to diagnosis, and recognizes that the neurocognitive cluster is a heterogeneous group of disorders occurring throughout the lifespan. Providing a parallel format across the various disorders simplifies the approach to differential diagnosis. The DSM-5 also attempts to disentangle cause from consequence,[21] and is written in the recognition that multiple and nonexclusive factors may cause a given disorder. It makes explicit the fact that neurocognitive disorders lie on a continuum, and many individuals have a milder form of the disorder that is not severe enough to be called dementia. The DSM-5 does not imply that mild neurocognitive disorder will necessarily progress to major neurocognitive disorder.

The validity of these criteria has had only limited testing in clinical practice. However, as they represent a synthetic organization of available knowledge and are largely consistent with the criteria developed by external expert groups, their reliability and validity are likely to be high. The adoption of these criteria by an international group of clinicians with a broad range of specialties should foster greater consistency in the diagnosis of neurocognitive disorders and bring cohesion to this diverse field.

Review criteria

The DSM-5 criteria were arrived at by expert consensus. The Neurocognitive Disorders Work Group of the DSM-5 Task Force was appointed by the American Psychiatric Association. Each work group member was assigned to review the published literature in relation to one or more disorder, and draft criteria were reached by consensus after multiple in-person meetings and teleconferences. Input was sought from external advisers and members of expert groups, and general public comment was sought after publishing draft criteria on a website. The criteria were field-tested for reliability, revised multiple times, and scrutinized by several overarching DSM-5 panels before being finalized.

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Author contributions
All authors researched data for the article and made substantial contributions to discussion of the content, writing of the article and to review and/or editing of the manuscript before submission.