NEUROCOGNITIVE DISORDERS

A Proposal from the DSM-5 Neurocognitive Disorders Work Group:
Dilip Jeste (Chair), Deborah Blacker, Dan Blazer, Mary Ganguli, Igor Grant, Jane Paulsen, Ronald Petersen, and Perminder Sachdev

INTRODUCTION:

The DSM-5 Neurocognitive Disorders Work Group proposes that a new category of Neurocognitive Disorders replace the DSM-IV Category of "Delirium, Dementia, Amnestic, and Other Geriatric Cognitive Disorders".
The defining characteristics of these disorders are that their core or primary deficits are in cognition and that these deficits represent a *decline from a previously attained level of cognitive functioning*; the latter feature distinguishes them from the neurodevelopmental disorders in which a neurocognitive deficit is present at birth or interferes with development. However, it is possible to develop a neurocognitive disorder superimposed on a neurodevelopmental disorder, for example Alzheimer's disease in a patient with mental retardation associated with Down Syndrome.

This section includes three broadly defined syndromes.
(1) Delirium,
(2) Major Neurocognitive Disorder,
(3) Minor Neurocognitive Disorder.

Disorders in this section are attributable to changes in brain structure, function, or chemistry. The etiologies of these syndromes, when known, are to be coded as subtypes. Typically, the etiology is more likely to be identifiable in Delirium and Major Neurocognitive Disorder than in Minor Neurocognitive Disorder, although this will vary across etiologic subtypes.

Delirium is distinguished from Minor or Major Neurocognitive Disorder based on its core characteristics, a disturbance in level of awareness and the ability to direct, focus, sustain, and shift attention. While some level of disturbance of awareness and attention can be observed in all Neurocognitive Disorders, particularly in the more severe form of Major Neurocognitive Disorder, these disturbances are not prominent in Major or Minor Neurocognitive Disorder (the *relative absence* of this disturbance was previously referred to as "clear consciousness"). However, delirium can, and frequently does, co-exist with Major or Minor Neurocognitive Disorder.

The distinction between Major and Minor disorders is primarily one of severity, with the threshold for Major Neurocognitive Disorder encompassing a greater degree of cognitive impairment and hence a loss of independence in instrumental activities of daily living. In most progressive disorders such as the neurodegenerative disorders and some forms of vascular cognitive impairment, Minor and Major may be earlier and later stages of the same disorder. In these settings, the differences may involve impairment in additional cognitive domains as well as more severe impairment within the domains as the patient crosses from the Minor to Major level of impairment. However, Neurocognitive Disorders of other etiologies may involve nonprogressive deficits (as in the sequelae of a traumatic brain injury or stroke), waxing and waning impairment (e.g., as in multiple sclerosis), or improvement (as in successful treatment of HIV or prolonged abstinence from substances of abuse).

We will first list and briefly describe the principal domains to be considered in diagnosis of these conditions, providing examples of *symptoms or observations* that reflect minor and major impairments in each domain and may be elicited from the patient or a knowledgeable informant or observed during the interview. We also offer specific examples of *objective assessments than can be used to document and quantify the degree of impairment (including assessment of changes over time or in response to intervention*). It should be noted that these domains are not entirely independent, their boundaries are indistinct and definitions in the literature are variable. We have given examples of tasks and assessments to help clarify what we mean by each domain. However, many tasks listed for a given domain (not only in everyday life but in the setting of formal neuropsychological testing) require adequate level of performance in other domains. For example, attention is required for most tasks; at least minimal levels of receptive language are required to understand instructions, and more intact language is required for many tasks; list learning

tasks are aimed at testing memory but also draw on executive ability and language, because memory is easier if the items are grouped by category. Nevertheless, the recognition of impairment in specific domains is critical for the differential diagnosis of subtypes of neurocognitive disorder.

Cognitive Domain	Examples of Symptoms or Observations	Examples of Assessments
Complex attention (sustained attention, divided attention, selective attention, processing speed)	Major: Increased difficulty in environments with multiple stimuli (TV, radio, conversation), easily distracted by competitive events in the environment. Unable to attend unless input is restricted and simplified. Difficulty holding recent memory in working mind, such as recalling phone numbers or addresses just given, or reporting back what was just said. Unable to conduct math calculations in head. All thinking takes longer than usual and components to be processed must be simplified to one or a few. Minor: Normal tasks take longer than previously. Begin to find errors in tasks regularly conducted; find work needs more double-checking than previously. Find that thinking is easier when not competing with other things (radio, TV, other conversations, cell phone, driving).	Sustained attention: maintenance of attention over time--pressing a button every time a tone is heard. Selective attention: maintenance of attention despite competing stimuli and/or distractors—hearing numbers and letters read and asked to count number of *letters only* at end of task. Divided attention: attending to two tasks within the same time period--- rapidly tapping while learning a story being read. Processing speed can be quantified on any task by timing it---time to put together a design of blocks, time to match symbols with numbers.
Executive ability (planning, decision-making, working memory, responding to feedback/error correction, overriding habits, mental flexibility)	Major: Abandons complex projects. Needs to focus on one task at a time. Needs to rely on others to plan appointments or make decisions. Minor: Increased effort required to complete multi-stage projects. Increased difficulty multi-tasking, or difficulty resuming a task interrupted by a visitor or phone call. May complain of increased fatigue from the extra effort required to organize, plan and make decisions. May report that large social gatherings are more taxing or less enjoyable due to increased effort required to follow shifting conversations.	Planning: finding the exit to a maze, Decision-making: simulated gambling. Working memory: the ability to hold and manipulate a group of items --adding up a list of numbers or repeating a span of numbers or words backwards. Feedback/Error correction: rules of a task are determined by whether responses are correct or incorrect—correct to shape for 5 items changes to correct by placement in next 5 items. Overriding habits: choosing a more complex and effortful solution to be correct e.g., looking away from the direction indicated by an arrow, naming ink colors of words, Mental flexibility: ability to shift between two tasks or response rules, e.g., from verbal to key-press response, from adding numbers to ordering numbers, from ordering by size to ordering by color.
Learning and memory (immediate memory, recent memory [including free recall, cued recall, and recognition memory])	Major: Repeats self in conversation, often within the same conversation, can't keep track of short list of items when shopping or plans for the day. Requires frequent reminders to orient to task at hand. Minor: Difficulty recalling recent events, and increased reliance on list-making or calendar. Needs occasional reminders or re-reading to keep track of characters in a movie or novel. Occasionally may repeat self over a few weeks to the same person, loses track of whether bills have already been paid.	Immediate memory span—repeat a list of words or digits. Recent memory: Following a delay, assess Free Recall--ask the subject to name as many words as possible (or present a story, and ask the subject to recall as many elements as possible). For Cued Recall, provide semantic cues like “list all the food items on the list” or “name all of the children from the story” For Recognition Memory, ask about specific items—e.g., was ‘apple’ on the list? or “was the man in the story named Bill?”
Language (expressive	Major: Significant difficulties with expressive or receptive	Expressive language: Confrontational Naming: identification of

language [including naming, fluency, grammar and syntax] and receptive language)	language. Often uses general use terms such as "that thing" and "you know what I mean," and prefers general pronouns, rather than names. With severe impairment, even names of closer friends and family may not be recalled. Idiosyncratic word usage, grammatical errors, spontaneity of output and economy of utterances occur. Stereotypy of speech occurs, echolalia and automatic speech typically precede mutism. Minor: Noticeable word-finding difficulty. May substitute general for specific terms. May avoid use of specific names of acquaintances. Grammatical errors involve subtle omission or incorrect use of articles, preposition, auxiliary verbs, etc. Press of speech is subtle and may involve fewer pauses than socially appropriate.	objects or pictures (note: naming common objects is insufficient to detect Minor impairments). Fluency: name as many items as possible in a semantic (e.g., animals) or phonemic (e.g., starting with f) category in 1 minute. Grammar and Syntax ; omission or incorrect use of articles, prepositions, auxiliary verbs, etc.--errors observed during naming and fluency tests are compared with norms to assess frequency of errors and compare with normal slips of the tongue. Receptive language: comprehension--word definition and object-pointing tasks involving animate and inanimate stimuli.
Visuoconstructional-perceptual ability (construction, visual perception)	Major: Significant difficulties using tools, navigating in familiar environments; often more confused at dusk when shadows and lowering levels of light change perceptions. Minor: May need to rely more on maps or others for directions. Uses notes and follows others to get to a new place. May find self lost or turned around when not concentrating on task. Less precision in parking. Greater effort required for spatial tasks such as carpentry, assembly, sewing or knitting	Construction: assembly of items requiring hand-eye coordination). Visual perception: line bisection tasks for basic visual defect or attentional neglect. Motor-free perceptual tasks (including facial recognition) require the identification and/or matching of figures--best tasks cannot be verbally mediated and are not objects--some require the decision of whether a figure can be "real" or not based on dimensionality.
Social cognition (recognition of emotions, theory of mind, behavioral regulation)	Major: Behavior clearly out of acceptable social range; insensitivity to social standards of modesty in dress, political, religious, or sexual topics of conversation, excessive focus on a topic despite group's disinterest or direct feedback, behavioral intention without regard to family or friends, decision-making without regard to safety (inappropriate clothing for weather or social setting). Typically there is little insight into these changes Minor: Subtle changes in behavior or attitude, often described as a change in personality, such as less ability to recognize social cues or read facial expressions, decreased empathy, an increase in extraversion or introversion, decreased inhibition, or subtle or episodic apathy or restlessness.	Recognition of emotions: identification of emotion in images of faces representing a variety of both positive and negative emotions. Theory of Mind: the ability to consider another person's state of mind or experience—story cards with questions to elicit information about the mental state of the individuals' portrayed such as "where will the girl look for the lost bag?" or "why is the boy sad?" Behavioral Regulation—use tests above, plus measures of disinhibition and impulsivity (e.g., instructed to key press to "H t" in a string of letters whereas key presses to"H x" may indicate disinhibition.

Rationale for Change in Name of Group:

The term in DSM-IV was “Delirium, Dementia, and Amnestic and Other Cognitive Disorders, which the committee felt was unwieldy and did not represent a conceptual whole. The new term is simpler and encompasses a range of disorders in which the primary/principal manifestation is an acquired loss of cognitive ability attributable to known or assumed brain damage/disease. The disorders span all age groups, as long as there is a decline from a previously higher level of cognition (unlike autism or mental retardation). As currently envisioned, they do not include disorders in which acquired cognitive impairment/decline is present but is not the primary/principal manifestation (e.g. schizophrenia, major depression).

Note re Domains:
**In addition to the role of domains in identifying etiologic subtypes of Major and Minor Neurocognitive Disorders, the group is still working on a way to specify which domains are impaired within these criteria.*

DELIRIUM

Delirium is a disturbance in level of awareness or attention, marked by the acute or subacute onset of cognitive changes attributable to a general medical condition; it tends to have a fluctuating course. The condition must *not be solely attributable* to another cognitive disorder, although Delirium is common in the setting of Major Neurocognitive Disorder. Major changes from DSM-IV are to clarify the primary symptom to a disturbance in level of awareness and attention (rather than consciousness), and to add well-documented supportive features and subtypes

Recommended Revised Criteria	DSM-IV Criteria	Brief rationale for proposed change/ Comments	References
GENERAL DIAGNOSTIC CRITERIA 293.0			
A. Disturbance in level of awareness and reduced ability to direct, focus, sustain, and shift attention.	A. Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.	Consciousness is too nebulous a term to describe the symptoms of delirium. Awareness captures the essence of delirium much better	Inouye, 2006; Meagher and Trzepacz 2009
B. A change in cognition, (such as deficits in orientation, executive ability, language, visuoperception, learning and memory) -Cannot be assessed in face of severely reduced level of awareness -Should not be better accounted for by a preexisting neurocognitive disorder	B. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a preexisting, established, or evolving dementia.	Visuospatial impairment and impairment in executive function are key symptoms of delirium; we have also added a clarification that a preexisting neurocognitive disorder does not account for the cognitive changes	Inouye, 2006; Meagher and Trzepacz, 2009
C. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiologic consequences of a general medical condition.	D. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiologic consequences of a general medical condition.	Simply a reversal in the order of criteria so that duration is placed at the end of the criteria	
D. The disturbance develops over a short period of time (usually hours to a few days) and tends to fluctuate *in severity* during the course of a day.	C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.	We have added "in severity" to improve clarity of this criterion.	

Note : The following supportive features are commonly present in delirium but are not key diagnostic features: sleep-wake cycle disturbance, psychomotor disturbance, perceptual disturbances (e.g., hallucinations, illusions), emotional disturbances, delusions, labile affect, dysarthria and EEG abnormalities (generalized slowing of background activity)		Nothing is mentioned in the current criteria about accompanying symptoms. Though not necessary or sufficient in themselves to make the diagnosis, they should be recognized as frequent symptoms of delirium	Inouye, 2006; Meagher and Trzepacz, 2009
Coding note: If delirium is superimposed on a pre-existing Neurocognitive Disorder, indicate the delirium as follows: _____ Coding note: Include the name of the general medical condition on Axis I e.g. 293.0 Delirium Due to Hepatic Encephalopathy	Coding note: If delirium is superimposed on a pre-existing Vascular Dementia, indicate the delirium by coding 290.41 Vascular Dementia, with Delirium Coding note: Include the name of the general medical condition on Axis I e.g. 293.0 Delirium Due to Hepatic Encephalopathy	Coding of Delirium in the setting of Major Neurocognitive Disorder TBD	
If the full criteria are currently met for delirium, specify its current clinical status and/or features: Hyperactive, hypoactive or mixed Short term vs. persistent duration		Evidence is quite good that delirium can be subcategorized into hyperactive/hypoactive/mixed varieties. Evidence is questionable for a subcategory for chronic delirium ***NOTE****: The Committee is still discussing whether to add subsyndromal delirium in parallel with minor neurocognitive disorder, and welcomes input on this issue.*	Camus, 2000; Han, 2009; Marcantonio, 2002 Kiely, 2004; Cole, 2007; 2008

MAJOR NEUROCOGNITIVE DISORDER

Major Neurocognitive Disorder (including what was formerly known as Dementia) is a disorder with greater cognitive deficits in at least one (typically two or more) of the following domains: Complex attention (planning, decision-making, working memory, responding to feedback/error correction, over-riding habits, mental flexibility), Executive ability (planning, decision-making, working memory, responding to feedback/error correction, overriding habits, mental flexibility), Learning and memory(immediate memory, recent memory [including free recall, cued recall, and recognition memory]), Language(expressive language [including naming, fluency, grammar and syntax] and receptive language), Visuoconstructional-perceptual ability (construction and visual perception), and Social cognition (recognition of emotions, theory of mind, behavioral regulation). The cognitive deficits must be sufficient to interfere with functional independence. Important changes from the DSM-IV criteria include: change in nomenclature (MNCD or Dementia), not necessarily requiring memory to be one of the impaired domains, allowing cognitive deficit limited to one domain. In the introductory text, we offer a table that offers more details about the assessment of each domain in the form of specific symptoms of decline that can be elicited or observed and assessment procedures that can be used to document the cognitive impairment and quantify its severity.

Recommended Revised Criteria	DSM-IV Criteria	Brief rationale for proposed change/Comments	References
MAJOR NEUROCOGNITIVE DISORDER	(Based on Criteria Common to Multiple Dementia Diagnoses in DSM-IV)	The term "dementia" is replaced by Major Neurocognitive Disorder, which is conceptualized as including what was formerly known as dementia as well as entities like amnestic disorder. "Dementia" is an accepted term for older adults (e.g., with Alzheimer's disease)—although even in this setting it has acquired a pejorative/ stigmatizing connotation, it is less well accepted among younger adults with deficits related to e.g., HIV or head injury.	Kurz and Lautenschlager2010
A. Evidence of significant cognitive *decline from a previous level of performance* in one or more of the domains outlined above based on:	A. The development of multiple cognitive deficits manifested by both	This rewording focuses on *decline* (rather than deficit—consistent w/ the requirement in the basic definition of an *acquired* disorder) from a previous level of performance.	
	(1) memory impairment (impaired ability to learn new information or to recall previously learned information) (2) one (or more) of the following cognitive disturbances: (a) aphasia (language disturbance) (b) apraxia (impaired ability to carry out motor activities despite intact motor function) (c) agnosia (failure to recognize or identify objects despite intact sensory function) (d) disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)	The previous criteria for dementia used Alzheimer's disease as their prototype and thus required memory impairment as a criterion for all dementias. There is growing recognition that, in other neurocognitive disorders (e.g., HIV-related cognitive decline, cerebrovascular disease, frontotemporal degeneration, traumatic brain injury, etc.), other domains such as language or executive functions may be impaired first, or exclusively, depending on the part of the brain affected and the natural history of the disease. In addition, the terminology for the cognitive domains has been updated to reflect current usage in neuropsychology and neurology.	Royall 2003; Roman et al 1993; Chui et al 2000; Morehouse&Rockwood 2008; Neary et al 2008; McKeith, Galasko, Kosaka et al, 1996; Serby & Samuels 2004

1. Reports by the patient or a knowledgeable informant, or observation by the clinician, of clear decline in specific abilities as outlined for specific domains in the table above. --AND-- 2. Clear deficits in objective assessment of the relevant domain (typically > 2.0 SD below the mean [or below the 2.5th percentile] of an appropriate reference population [i.e., age, gender, education, premorbid intellect, and culturally adjusted])		The new definition, consistent with DSM-wide changes, focuses first on performance rather than disability. In the introductory table, we provide for each domain examples of specific symptoms or observations consistent with the Major level of decline and objective assessments. This encourages the use of objective measures, including formal neuropsychological testing where feasible with lesser exclusive reliance on individual judgment. The presence of both symptoms/observations and objective assessment is included to ensure specificity. This is a larger issue for Minor NCD, but included here for parallel structure of the criteria. ***NOTE**: The committee is in the process of refining these criteria to achieve a balance between preferred formal neuropsychological assessment and what may feasible in some clinical settings. We welcome input on this issue.*	
B. The cognitive deficits are sufficient to interfere with independence (e.g., at a minimum requiring assistance with instrumental activities of daily living, i.e., more complex tasks such as finances or managing medications)	The cognitive deficits in Criteria A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.	The new language preserves the traditional function-based threshold for dementia, but tries to operationalize it more clearly as a loss of independence.	REF IADL
C. The cognitive deficits do not occur exclusively in the context of a delirium.	The deficits do not occur exclusively during the course of a delirium.		
D. The cognitive deficits are not wholly or primarily attributable to another Axis I disorder (e.g., Major Depressive Disorder, Schizophrenia)	The disturbance is not better accounted for by another Axis I disorder (e.g., Major Depressive Disorder, Schizophrenia).	***NOTE**: The committee is still refining this criterion, and discussing to what extent Major Neurocognitive Disorder should be diagnosed in the setting of disorders like schizophrenia and depression. (although this concern applies primarily to Minor Neurocognitive Disorder). We also realize that issues of this nature are being addressed at the DSM-wide level, and are awaiting input of these larger discussions, as well as public input on this issue.*	

MINOR NEUROCOGNITIVE DISORDER

Minor Neurocognitive Disorder has been added to recognize the substantial clinical needs of individuals who have mild cognitive deficits in one or more of the same domains but can function independently (i.e., have intact instrumental activities of daily living), often through increased effort or compensatory strategies. This syndrome, known in many settings as Mild Cognitive Impairment may be particularly critical, as it may be a focus of early intervention. Early intervention efforts may enable the use of treatments that are not effective at more severe levels of impairment and/or neuronal damage, and, in the case of neurodegenerative disease, may enable a clinical trial to prevent or slow progression.

Recommended Revised Criteria	DSM-IV Criteria	Brief rationale for proposed change/Comments	References
MINOR NEUROCOGNITIVE DISORDER	Not previously listed (although a specific option in the NOS section). Includes entities widely referred to in neurodegenerative literature as Mild Cognitive Impairment (MCI) and Cognitive Impairment, No Dementia (CIND) and Age-related cognitive decline (ARCD), Does not include entities representing normal aging, e.g. Age-Associated Memory Impairment (AAMI)	Minor Neurocognitive Disorder is added to account for individuals with minor levels of cognitive impairment who may require assessment and treatment, but are not sufficiently impaired the Major diagnosis. To some extent, this entity will take care of individuals currently coded as Cognitive Disorder NOS without specific criteria. This change is driven by the need of such individuals for care, and by clinical; epidemiological; and radiological, pathological, and biomarker research data suggesting that such a syndrome is a valid clinical entity with prognostic and potentially therapeutic implications. Prime examples are the prevalent neurocognitive disorders associated with various neuromedical conditions such as traumatic brain injury, HIV, substance-use-related brain disorders, diabetes, and early/mild stages of neurodegenerative disorders like Alzheimer's disease and of cerebrovascular disease. As these conditions are increasingly seen in clinical practice, clinicians have a pressing need for reliable and valid diagnostic criteria in order to assess them and provide services including treatment of associated mood symptoms, further investigation of brain function, identification of treatable causes, and, for progressive disorders, appropriate early interventions.	Woods, Moore, Weber, & Grant, 2009; Grant, 2008; Antinori, Arendt, Becker et al, 2007; Grant, Reed, & Adams, 1987; Velin & Grant, 1990; Flicker et al 1991; Petersen, AAN Work Group 2001; Hachinski et al, 2006; Hachinksi, 2008; Gorelick 2007
A. Evidence of minor cognitive *decline from a previous level of performance* in one or more of the domains outlined above based on:		We are aware that the specific term "minor" can be challenged on the grounds that it implies lack of need for services, and are open to alternative suggestions. We chose "minor" rather than "mild" to be parallel with "major" and to be able to maintain the mild, moderate, and severe distinction within	

		Major NCD.	
1. Reports by the patient or a knowledgeable informant, or observation by the clinician, of minor levels of decline in specific abilities as outlined for the specific domains above. Typically these will involve greater difficulty performing these tasks, or the use of compensatory strategies. --AND-- 2. Mild deficits on objective cognitive assessment (typically 1 to 2.0 SD below the mean [or in the 2.5th to 16th percentile] of an appropriate reference population (i.e., age, gender, education, premorbid intellect, and culturally adjusted). When serial measurements are available, a significant (e.g., 0.5 SD) decline from the patients's own baseline would serve as more definitive evidence of decline.		The combination of symptoms/observations and objective assessment is critical in Minor Neurocognitive Disorder to maintain specificity: a report of a *change* in abilities protects against overcalling the disorder in those with lifelong poor performance (since *decline* can only be *inferred* from a single observation), and objective assessment protects against overcalling the disorder in "the worried well." ***NOTE**: The committee is in the process of refining these criteria to achieve a balance between preferred formal neuropsychological assessment and what may be feasible in some clinical settings. The issue is particularly difficult for Minor Neurocognitive Disorder because at lesser levels of cognitive impairment symptom reports may be unavailable or unreliable, observation may be less informative, the interpretation of objective assessments is complicated by variable premorbid abilities, and simpler assessments are likely to be insensitive. We welcome input on this issue.*	
B. The cognitive deficits are not sufficient to interfere with independence (Instrumental Activities of Daily Living are preserved), but greater effort and compensatory strategies may be required to maintain independence.			
C. The cognitive deficits do not occur exclusively in the context of a delirium			
D. The cognitive deficits are not wholly or primarily attributable to another Axis I disorder (e.g., Major Depressive Disorder, Schizophrenia)		***NOTE**: The committee is still refining this criterion, and discussing to what extent Minor Neurocognitive Disorder should be diagnosed in the setting of disorders like schizophrenia and depression. We also realize that issues of this nature are being addressed at the DSM-wide level, and are awaiting input of these larger discussions, as well as input on this issue.*	

ALZHEIMER'S DISEASE SUBTYPE OF MAJOR OR MINOR NEUROCOGNITIVE DISORDER

{*Criteria for the Alzheimer's disease subtype of Major or Minor Neurocognitive Disorder are offered as a sample of how specific etiologies would be coded*.}

Alzheimer's disease is a neurodegenerative disorder, typically seen in late life, but can occur earlier. It is marked by insidious onset, gradual decline, and typically an early prominent memory loss. For Major Neurocognitive Disorder this typical clinical picture has excellent predictive value for the Alzheimer subtype, and is all that is required for a diagnosis of the Alzheimer subtype, although additional evidence adds to the certainty of diagnosis. For less typical clinical profiles such as posterior coritical atrophy or visual variant of AD, additional supportive evidence such as typical neuroimaging patterns of atrophy is required. For Minor Neurocognitive Disorder, because of the modest predictive value of the clinical picture alone, and the significant social consequences of an Alzheimer diagnosis, the Alzheimer's disease subtype is not commonly diagnosed. However, such a diagnosis is possible if there is sufficient information available (e.g., a positive genetic test for dominantly inherited AD, or as the field develops, evidence that certain imaging markers, atrophy of medial temporal lobe structures on MRI, temporoparietal hypometabolism on FDG PET, amyloid deposition on PET scanning or markers for tau and abeta in the CSF are sufficiently predictive of an underlying AD pathology).

Recommended Revised Criteria	DSM-IV Criteria	Brief rationale for proposed change/Comments	References
A. Major: Meets criteria for Major Neurocognitive Disorder, with memory being one of the impaired domains. A. Minor: Meets criteria for Minor Neurocognitive Disorder with memory impairment AND there is clear supporting evidence for the Alzheimer etiology (e.g., a positive test for a known mutation in an Alzheimer's disease associated gene), or with evolving research, documentation based on biomarkers or imaging.	**294.1x Dementia of the Alzheimer's Type** A. The development of multiple cognitive deficits manifested by both: (1) Memory impairment (impaired ability to learn new information or to recall previously learned information)	While patients in memory disorders clinics who meet current research criteria for Mild Cognitive Impairment (similar to minor NCD with impaired memory) progress to dementia of the Alzheimer type at the rate of 12-15% per year, and have neuropathological evidence of both neurodegeneration and cerebrovascular disease, population-based studies show a much lower rate of progression, with some individuals improving. Research is ongoing into what specific features of MCI might reliably indicate the presence of prodromal Alzheimer's disease. Until those features can be identified, we do not feel that the predictive value of minor NCD with memory impairment is sufficient for a diagnosis of Alzheimer's disease. However, such a diagnosis might be made in an individual with an autosomal dominant family history or positive test for a mutation in an autosomal dominant "AD gene", or, after further research, with clearly predictive biomarkers or imaging studies. This is an area in which knowledge is evolving rapidly; The procedures described above are increasingly used in clinical practice at tertiary care centers and outside the US; it is possible some of them will enter standard use in the near future.	Winblad et al 2004, Petersen et al 2009, 2006; Bennett et al, 2005; Morris 2006; Mitchell & Shiri-Feski 2009; Bruscoli & Lovestone 2004 Dubois et al, 2007; Jack et al, 2000; Duara et al, 2008; Klunk et al 2004; Forsberg et al 2008; Kamboh, 2008; Galasko, Chang, Motter et al, 1998

B. Early and prominent impairment in the Memory domain (rarely, other domains such as visuoconstructive perceptual domain may be prominently affected, but Alzheimer's disease would not be diagnosed without clear supporting imaging, biomarker or genetic evidence). Major: Deficits are observed in at least one other domain, often Executive Ability, and as the disease progresses, in additional domains. Minor: Only Memory may be affected, but deficits in Executive Abilities are common.	(2) One (or more) of the following cognitive disturbances: a. Aphasia (language disturbance) b. Apraxia (impaired ability to carry out motor activities despite intact motor function) c. Agnosia (failure to recognize or identify objects despite intact sensory function) d. Disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)		
	B. The cognitive deficits in criteria a1 and a2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.	This requirement is handled through the criteria for Major NCD.	
C. The course is characterized by gradual onset and continuing cognitive decline	C. The course is characterized by gradual onset and continuing cognitive decline.		
D. Evidence from history, examination, and investigations that deficits are not wholly or primarily attributable to other disorders. However, other such disorders may coexist.	D. The cognitive deficits in Criteria A1 and A2 are not due to any of the following: (1) other central nervous system conditions that cause progressive deficits in memory and cognition (e.g., cerebrovascular disease, Parkinson's disease, Huntington's disease, subdural hematoma, normal-pressure hydrocephalus, brain tumor) (2) systemic conditions that are known to cause dementia (e.g., hypothyroidism, vitamin B12 or folic acid deficiency,	Revise previous terminology to recognize the clinical and pathological evidence that comorbidity is the norm in the population at large, and that having cerebrovascular disease does not preclude also having Alzheimer's disease and vice versa, and in the presence of both it is not useful to arbitrarily assign causality to one or the other.	[Schneider, Arvanitakis, Bang, & Bennett, 2007; Launer et al 2008

	niacin deficiency, hypercalcemia, neurosyphilis, HIV infection) (3) substance-induced conditions E. The deficits do not occur exclusively during the course of a delirium. F. The disturbance is not better accounted for by another Axis I disorder (e.g., Major Depressive Disorder, Schizophrenia).		
	Specify subtype: **With Early Onset:** if onset is at age 65 years or below **With Late Onset:** if onset is after age 65 years	There is little scientific rationale for retaining the distinction between early and late onset, as the underlying pathology is the same, and the threshold of age 65 is arbitrary at best.	Hyman and Tanzi, 1995
	Code based on presence or absence of a clinically significant behavioral disturbance: **294.10 Without Behavioral Disturbance:** if the cognitive disturbance is not accompanied by any clinically significant behavioral disturbance. **294.11 With Behavioral Disturbance:** if the cognitive disturbance is accompanied by a clinically significant behavioral disturbance (e.g., wandering, agitation). **Coding note:** Also code 331.0 Alzheimer's disease on Axis III. Indicate other prominent clinical features related to the Alzheimer's disease on Axis I (e.g., 293.83 Mood Disorder Due to Alzheimer's Disease, With Depressive Features, and 310.1 Personality Change Due to Alzheimer's Disease, Aggressive Type).	***NOTE****: Alzheimer's disease is often associated with psychotic features including delusions and visual and auditory hallucinations, with depression, and with other behavioral disturbances. Criteria have been proposed for Psychosis and for Depression of Alzheimer's Disease (see Appendix). There is ongoing discussion of how psychosis, depression, and other behavioral disturbances in Alzheimer's disease (and more broadly in other Neurocogntive Disorders) will be coded. One option is to use fifth digit specifiers for presence or absence of specific behavioral symptoms across Major and Minor Neurocognitive Disorders – i.e., psychosis, depression, agitation, aggression, apathy, wandering,etc). Another is to tailor them to specific disorders. It has also been proposed that separate criteria be provided for Psychosis and Depression of AD along the lines of those in the Appendix., Comments regarding this issue are welcome.*	

REFERENCES

American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR. 4th ed., text revision ed. 2000, Washington, D.C.: American Psychiatric Association.

Antinori A, Arendt G, Becker JT. Updated research nosology for HIV-associated neurocognitive disorders, Neurology 2007, 69: 1789-1799.

Bennett, D.A., et al., Mild cognitive impairment is related to Alzheimer disease pathology and cerebral infarctions. Neurology 2005. 64(5): p. 834-41.

Bruscoli, B. and S. Lovestone. Is MCI really just early dementia? A systematic review of conversion studies. International Psychogeriatrics 2004. 16: p. 129-140.

Camus V, Burtin B, Simeone I, et al: Factor analysis supports evidence of existing hyperactive and hypoactive subtypes of delirium. Int J Geriatr Psychiatry 115:313ÿÿ316, 2000a

Chui HC, Mack W, Jackson JE, Mungas D et al. Clinical criteria for the diagnosis of vascular dementia : a multicenter study of comparability and interrater reliability. Arch Neurol 2000; 57: 191-6

Cole MG 2008, You Y, McCusker J, Ciampi A, Belzile E. The 6 and 12 month outcomes of older medical inpatients who recover from delirium. Int J Geriatr Psychiatry. 2008 Mar;23(3):301-7.

Duara, R., et al., Medial temporal lobe atrophy on MRI scans and the diagnosis of Alzheimer disease. Neurology 2008. 71(24): p. 1986-1992.

Dubois B, Feldman H, Jacova C, DeKosky ST, Barberger-Gateau P, Cummings J, Delacourte A, Galasko D, Gauthier S, Jicha G. Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS–ADRDA criteria The Lancet Neurology, 2007; 6: 734-746

Flicker C, Ferris S, Reisberg B: Mild cognitive impairment in the elderly: predictors of dementia. Neurology 1991;41:1006-1009

Forsberg, A., et al., PET imaging of amyloid deposition in patients with mild cognitive impairment. Neurobiology of Aging, 2008. 29(10): p. 1456-65.

Galasko D, Chang L, Motter R, Clark CM, Kaye J, Knopman D, Thomas R, Kholodenko D, Schenk D, Lieberburg I, Miller B, Green R, Basherad R, Kertiles L, Boss MA, Seubert P. High Cerebrospinal Fluid Tau and Low Amyloid 42 Levels in the Clinical Diagnosis of Alzheimer Disease and Relation to Apolipoprotein E Genotype . Arch Neurol. 1998 ;55:937-945.

Gorelick, P.B., Vascular cognitive impairment: new insights into diagnosis and prevention. Brain and Cognition, 2007. 63(2): p. 193-193.

Grant I, Heaton RK, Marcotte TD. Evaluating the neurocognitive complications of SLE. Lessons from HIV Disease. Annals of the New York Academy of Sciences 1997, vol?? 18 – 43

Grant I, Prigatano GP, Heaton RK, McSweeny AJ, Wright EC, Adams KM. Progressive neuropsychological impairment and hypoxemia: relationship in chronic obstructive pulmonary disease. Arch Gen Psychiatry 1987; 44: 999-1106.

Grant I, Reed R, Adams KM. Diagnosis of intermediate-duration and subacute organic mental disorders in abstinent alcoholics. J. Clin. Psychiatry 1987, 48: 319323.

Grant I. Neurocognitive disturbances in HIV. International Review of Psychiatry 2008; 20: 33-47

Hachinski V. Shifts in tninking about dementia. JAMA 2008; 300(18):2172-2173

Hachinski, V., et al., National Institute of Neurological Disorders and Stroke-Canadian Stroke Network vascular cognitive impairment harmonization standards. Stroke, 2006. 37(9): p. 2220-41.

Hachinski, V., Vascular behavioral and cognitive disorders. Stroke, 2003. 34(12): p. 2775.

Han JH, Zimmerman EE, Cutler N, Schnelle J, Morandi A, Dittus RS, Storrow AB, Ely EW. Delirium in older emergency department patients: recognition, risk factors, and psychomotor subtypes. Acad Emerg Med. 2009 Mar;16(3):193-200. Epub 2009 Jan 20.

Hwang TJ, Masterman DL, Ortiz F, Fairbanks LA, Cummings JL. Mild cognitive impairment is associated with characteristic neuropsychiatric symptoms. Alzheimer Dis Assoc Disord. 2004 18: 17-21.

Hyman BT, Tanzi R. Molecular epidemiology of Alzheimer's disease. New Engl J Med. 1995 Nov 9;333(19):1283-4.

Inouye SK, Zhang Y, Han L, Leo-Summers L, Jones R, Marcantonio E. Recoverable cognitive dysfunction at hospital admission in older persons during acute illness. J Gen Intern Med. 2006 Dec;21(12):1276-81

Jack CR et al., Rates of hippocampal atrophy correlate with change in clinical status in aging and AD. Neurology, 2000. 55(4): p. 484-89.

Kamboh, MI, Molecular genetics of late-onset Alzheimer's disease. Annals of Human Genetics, 2004. 68(Pt 4): p. 381-404.

Kiely DK, Bergmann MA, Jones RN, Murphy KM, Orav EJ, Marcantonio ER. Characteristics associated with delirium persistence among newly admitted post-acute facility patients. J Gerontol A Biol Sci Med Sci. 2004 Apr;59(4):344-9.

Klunk, W.E., et al., Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. Annals of Neurology, 2004. 55(3): p. 306-19.

Kurz AF, Lautenschlager NT. The concept of dementia: retain, reframe, rename or replace? International Psychogeriatrics 2010. 22: 37-42

Launer, L.J., et al., AD brain pathology: vascular origins? Results from the HAAS autopsy study. Neurobiology of Aging, 2008. 29:. 1587-90.

Lyketsos CG, Lopez OL, Jones B, Fitzpatrick AL, Breitner J, DeKosky ST. Prevalence of Neuropsychiatric Symptoms in Dementia and Mild Cognitive Impairment .Results From the Cardiovascular Health Study . JAMA. 2002;288:1475-1483.

Marcantonio E 2002, Ta T, Duthie E, Resnick NM. Delirium severity and psychomotor types: their relationship with outcomes after hip fracture repair. J Am Geriatr Soc. 2002 May;50(5):850-7.

McKeith IG, Galasko D, Kosaka K, et al: Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB). Neurology 1996; 47:1113–1124

Meagher D, Trzepacz PT. Phenomenological distinctions needed in DSM-V: delirium, subsyndromal delirium, and dementias. Phenomenological distinctions needed in DSM-V: delirium, subsyndromal delirium, and dementias. J Neuropsychiatry Clin Neurosci. 2007 Fall;19(4):468-70.

Mitchell AJ, Shiri-Feshki M. Rate of progression of mild cognitive impairment to dementia – meta-analysis of 41 robust inception cohort studies. Acta Psychiatr Scand 2009: 119: 252-65.

Moorhouse P, Rockwood K. Vascular cognitive impairment: current concepts and clinical developments. Lancet Neurology 2008, 7: 246-55

Morris JC. Mild cognitive impairment is early-stage Alzheimer's disease. Time to revise diagnostic criteria. Arch Neurol 2006; 63: 15-16.

Munro CA, Saxton JA, Butters MA. The Neuropsychological Consequences of Abstinence Among Older Alcoholics: A Cross-Sectional Study. Alcoholism: Clinical and Experimental Research, 2006, 24: 1510-1516

Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, Freedman M, Kertesz A, Robert PH, Albert M, Boone K, Miller BL, Cummings J, Benson DF. Frontotemporal lobar degeneration.A consensus on clinical diagnostic criteria. Neurology 1998;51: 1546-1554

Petersen RC, Roberts RO, Knopman DS, et al. Mild cognitive impairment: ten years later. Archives of Neurology.2009; 66: 1447-55.

Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review) Report of the Quality Standards Subcommittee of the American Academy of Neurology . Neurology 2001;56:1133-1142.

Petersen RC. Mild cognitive impairment clinical trials Nature Reviews Drug Discovery 2003; 2: 646-653.

Petersen, R.C., et al., Neuropathologic features of amnestic mild cognitive impairment. Archives of Neurology, 2006. 63: p. 665-672.

Rockwood, K., H. Chertkow, and H.H. Feldman, Is mild cognitive impairment a valid target of therapy. Canadian Journal of Neurological Sciences, 2007. 34 Suppl 1: p. S90-6.

Román GC, Tatemichi TK, Erkinjuntti T, Cummings JL, Masdeu JC, Garcia JH, et al. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. javascript:AL_get(this, 'jour', 'Neurology.'); Neurology 1993, 43(:250-60

Royall, D.R., The 'Alzheimerization' of dementia research. J Am Geriatr Soc, 2003. 51: p. 277-278.

Schneider JA, Arvanitakis Z, Bang W, Bennett DA. Mixed brain pathologies account for most dementia cases in community-dwelling older persons. Neurology. 2007 69(24):2197-204

Serby M, Samuels SC. Diagnostic Criteria for Dementia With Lewy Bodies Reconsidered. Focus, American Psychiatric Association 2004, 2: 309-313 http://focus.psychiatryonline.org/cgi/content/full/2/2/309

Velin RA, Grant I. Neuropsychological correlates of multiple sclerosis. Current Opinion in Neurology and Neurosurgery 1990: 3: 204-207.

Winblad B, Palmer K, Kivipelto M, et al. Mild cognitive impairment--beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. J Intern Med. 2004 256(3):240-6.

Woods SP, Moore DJ, Weber E, Grant I. Cognitive neuropsychology of HIV-associated neurocognitive disorders. Neuropsychology Review 2009, 19: 152-168

APPENDIX

Criteria for Psychosis of AD:
A. Characteristics sx's: Delusions or Auditory or visual hallucinations
B. Primary diagnosis: AD: Chronology of onset of symptoms of dementia prior to onset of psychotic symptoms
C. Duration: >1 month, although the delusions and hallucinations may be intermittent; Symptoms cause clinically significant distress or functional disruption
D. Symptoms not exclusively during delirium
E. Symptoms not due to direct physiological effects of a substance and cannot be better accounted for schizophrenia or other psychotic disorder

Rationale
(1) Public health importance: High prevalence & incidence
(2) Associated with: More agitation, aggression, More rapid cognitive decline, Greater caregiver distress, Earlier institutionalization, and Higher cost of care
(3) Persistence or recurrence common
(4) Aggregates in families
(5) Clinical differences between AD + Psychosis and both AD without psychosis and Psychosis without AD
(6) Specific treatment considerations

Criteria for Depression of AD:
A. 3 (or more) of 10 listed symptoms under Major Depressive Disorder
B. Primary diagnosis: AD
C. Duration: > 2 weeks; Symptoms cause clinically significant distress or functional disruption
D. Symptoms not exclusively during delirium
E. Symptoms not due to direct physiological effects of a substance and cannot be better accounted for by another disorder

Rationale
(1) Public health importance: High prevalence and incidence
(2) Associated with: Higher mortality and Higher cost of care
(3) Persistence or recurrence common
(4) Clinical differences between AD + depression and both AD without depression and Depression without AD
(5) Specific treatment considerations

References :
(1) Bacanu S-A et al., Am J Geriat Psychiatry 2005
(2) Devanand D, et al., Arch Gen Psychiatry 1997
(3) Jeste and Finkel, Am J Geriat Psychiat 2000
(4) Olin et al., Am J Geriat Psychiatry, 2002
(5) Paulsen et al, N*eurology*. 2000;54:1965 (6) Ropacki S, et al, Am J Psychiatry 2005
(7) Sweet R, et al., Brain, 2009
(8) Watson LC, et al., Am J Geriat Psychiatry, 2009