MANAGEMENT PERSPECTIVE

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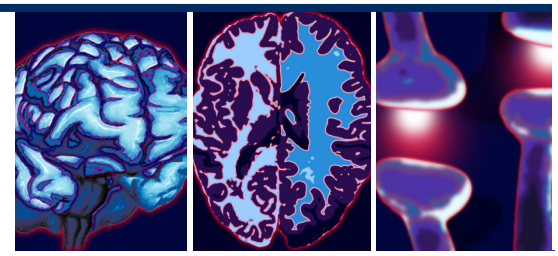

A perspective on the proposal for neurocognitive disorder criteria in DSM-5 as applied to HIV-associated neurocognitive disorders

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Practice points

- Use HIV-specific diagnostic terminology to complement those of the Diagnostic and Statistical Manual of Mental Disorders (DSM) for the diagnosis of HIV-associated neurocognitive disorders (HAND).
- Rely upon formal neuropsychological testing, whenever possible, for documentation of the presence of neurocognitive impairment as a criterion for the diagnoses of HAND.
- Use a quantified cut-off based on neuropsychological testing to generate a standardized designation for the documentation of the presence of HIV-associated neurocognitive impairment.
- Use a minimum of two impaired domains to qualify for the documentation of the presence of HIV-associated neurocognitive impairment.
- Include information processing speed and motor function but exclude social cognition as separate domains to be assessed for the documentation of the presence of HIV-associated neurocognitive impairment.
- Use documentation of any type of changes in activities of daily living (not solely changes involving independence) that are related to HIV-associated neurocognitive impairment as documentation for the functional status decline required for HAND diagnoses.
- Always rule out general medical illnesses, neurological diseases and psychiatric disorders that might confound the diagnoses of HAND prior to making the diagnoses definitive.

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SUMMARY HIV-associated neurocognitive disorders remain common in the current era of effective antiretroviral therapy. However, the severity at presentation of these disorders has been reduced, and the typical manifestations have changed. A revision of the American Academy of Neurology (AAN) criteria has been made on this basis, and a revision of the analogous criteria by the American Psychiatric Association will be forthcoming in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5. This article compares the relevant sets of diagnostic criteria that will be employed. It is concluded that a greater degree of integration of the revised, HIV-specific AAN criteria for HIV-associated neurocognitive disorders with the criteria proposed for the DSM-5 would prove advantageous for research, clinical, educational and administrative purposes.

The current proposal for the criteria to be used for neurocognitive disorders in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 has been published in a draft form [1]. This proposal is intended to include the area of HIV-associated neurocognitive disorders (HAND). However, the proposal is based upon an update of the more general criteria proposed for "Delirium, Dementia, and Amnestic, and Other Cognitive Disorders" published in the DSM-IV [2,3]. The DSM-IV contained no specific criteria for HAND, and the current proposal for these disorders in the DSM-5 would have the same result. Yet such an outcome could lead to a continued lack of utilization by psychiatrists of diagnostic criteria with widely acknowledged specificity for HAND and a lack of integration with the current research on HAND. HAND is not well represented by the criteria developed for Alzheimer's disease (AD), which largely constitute the basis upon which the DSM-IV criteria were defined in the aforementioned cognitive disorders subsection. This remains the case when adding the consideration of the impact of 'minor cognitive impairment', as defined for the general population. This article will systematically present the evidence addressing how the lack of integration of the DSM criteria with the Frascati conference-based revision of the American Academy of Neurology (AAN) criteria for HAND over time detracts from the future utility of the diagnoses of the neurocognitive disorders associated with HIV infection in the DSM-5.

If the currently proposed draft criteria for neurocognitive disorders in the DSM-5 are successfully promulgated, not only will the criteria that will be applied to HAND be improperly depicted in an overly generalized fashion, but it will also remain the case that there will be no specific criteria for HAND at all. First, it should be stated that HAND is significantly different from AD, as HAND is based upon a neuroinfectious process with a predilection for the basal ganglia, periventricular white matter and the hippocampus. HAND may occur at a much younger age and is more likely to be reversible. At least initially, HAND is best represented as a 'subcortical dementia' as opposed to AD, which is best characterized as a 'cortical dementia'. While it can be argued that this differentiation is not definitive, it aids heuristically in depicting how these different types of neurocognitive disorder present. Moreover, the lack of inclusion of any explicitly defined criteria for HAND was not justified in the DSM-IV, just as it remains unjustified today for the DSM-5. When the DSM-IV was published in 1994, specific criteria for HAND had already been published by the AAN for 3 years [4]. Those criteria had explicitly defined the disorders of 'HIV-associated dementia' (HAD) and 'HIV-associated minor cognitive-motor disorder' (MCMD). Yet, the DSM-IV criteria ultimately made no reference to any specific criteria for HAND. While a relevant diagnosis was nominally included in the DSM-IV (as a subtype of "dementia due to a general medical condition" [294.1]), there were no specific criteria assigned to it. Furthermore, there was no analog for the less severe disorder of HIV-associated MCMD in the final, approved version of the DSM-IV [2,3]. Although a 'research diagnosis' analogous to MCMD was designated and listed in research appendix B as 'mild neurocognitive disorder' (MND) in the DSM-IV [2,3], the only approved diagnostic term for this disorder was 'cognitive disorder – not otherwise specified' (294.9).

The current proposal for neurocognitive disorders in the DSM-5 makes no reference to the criteria that have been designated for HAND in neurology. However, 4 years ago, the AAN criteria were revised and published by an expert, international consensus panel. This revision was based upon the need to redefine the criteria for HAND that were originally promulgated in 1991 due to changes in the manifestations of HAND

over the subsequent 16 years, particularly following the introduction of effective antiretroviral therapy (ART). It has been reported that: the spectrum of severity of clinical symptoms has been dampened in the era of effective ART [5]; there are neuropathological correlates for this reduced level of clinical severity (although the prevalence remains high) [6]; and patients with HAD have a longer survival time in the current era [7]. Thus, the DSM-IV criteria identifying HAND only at the level of a dementia had become progressively less sensitive over time. However, the diagnostic criteria currently proposed for the neurocognitive disorders in DSM-5 still make no reference to the revised criteria for HAND adopted in neurology. Thus, the same lack of cross-referencing of these disorders across related fields is likely to occur again.

Currently, the DSM-5 work group is recommending that HAD be subsumed under a new disorder to be termed 'major neurocognitive disorder' **(Table 1)** [1]. For the purposes of discussion, please refer to the revised, HIV-specific AAN criteria for HAD that follow:

- There must be a marked, acquired impairment in neurocognitive performance, involving at least two domains (or areas). In addition, the presence of neurocognitive impairment must be ascertained by neuropsychological (NP) testing with at least two domains demonstrating scores at 2 standard deviations (SDs) or greater below the demographically corrected means. Typically, impairment is observed over multiple domains, especially in the areas of information processing speed, learning of new information, verbal memory and attention/concentration. It is noted that for resource-limited settings where NP testing is not available, a standard neuropsychiatric evaluation and simple bedside mental status examination testing may be substituted for standardized NP testing. Nevertheless, this should be done with standardized assessments of mental status. While the Mini-Mental State Examination with an index for the presence of neurocognitive impairment taken as a score of less than 26 [8] was referenced in the revised AAN criteria [9], this screening device should not be used due to its lack of sensitivity for the predominantly subcortical neurocognitive processes comprising HAND. Other standardized mental status examinations that might be used include the HIV Dementia Scale [10] and the International HIV Dementia Scale [11]. It is preferred that the domains selected for screening do not include the language domain, which is typically preserved in HAND until the late stage of disease. However, a timed test of language performance may be employed with validity.

- The neurocognitive impairment observed must be associated with marked interference in functional status of activities of daily living. It is preferred but not required that functional status be confirmed by standardized measures with established norms. However, standardized measures are required for documentation of impaired neurocognitive performance. Ideally, both self-report and objective functional status measures should be employed, as patients frequently minimize the report of the deficits consistent with a frontostriatal process like HAND. Of note, examples of useful self-report functional status measures are the Sickness Impact Profile [12], the Cognitive Difficulties Scale [13] and the Medical Outcomes Study (MOS)-HIV Cognitive Functional Status Subscale [14,15]. Examples of objective functional status measures are the Direct Assessment of Functional Status [16] and the University of California at San Diego (UCSD) Performance-Based Skills Assessment [17].

- The neurocognitive impairment should not support the diagnosis of delirium. That is, disturbance of consciousness and a short period of evolution of the observed impairment should not be prominent features [2,3]. If delirium is present, then the criteria for dementia must have been met previously.

- There should be no evidence of another, pre-existing cause for the dementia. There are many potentially confounding conditions to be considered that are associated with or are specific to the immunodeficiency associated with HIV that would not be part of a standard work-up for dementia in an immunocompetent patient. These confounding illnesses include neurological conditions dating back to the beginning of the epidemic (e.g., CNS toxoplasmosis, cryptococcal meningitis, cytomegalovirus encephalopathy, primary CNS lymphoma, neurosyphilis and tuberculous meningitis). In addition, several conditions of recently increasing neurological awareness and concern in the HIV infected should be assessed (e.g., cerebrovascular disease, CNS hepatitis C virus infection and immune reconstitution

Table 1. Criteria for neurocognitive disorders proposed for the Diagnostic and Statistical Manual of Mental Disorders 5 and the Frascati conference-based revision of American Academy of Neurology criteria.

DSM-5	Frascati conference-based revision of AAN criteria
Major neurocognitive disorder	**HIV-associated dementia**
A. Evidence of significant cognitive decline from a previous level of performance in one or more of the domains outlined in the text based on: 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 text; and: 2. Clear deficits in objective assessment of the relevant domain (typically >2 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]) 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]) 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 or schizophrenia)	A. Marked acquired impairment in cognitive functioning, involving at least two ability domains; typically the impairment is in multiple domains, especially in the learning of new information, slowed information processing and defective attention/concentration. The cognitive impairment must be ascertained by neuropsychological testing with at least two domains being 2 SD or greater below that of demographically corrected means B. The cognitive impairment produces marked interference with day-to-day functioning (work, home life and social activities) C. The pattern of cognitive impairment does not meet criteria for delirium D. There is no evidence of another, pre-existing cause for the dementia (e.g., other CNS infection, CNS neoplasm, cerebrovascular disease, pre-existing neurologic disease or severe substance abuse compatible with CNS disorder)
Minor neurocognitive disorder	**HIV-associated mild neurocognitive disorder**
A. Evidence of minor cognitive decline from a previous level of performance in one or more of the domains outlined in the text based on: 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 in the text. Typically, these will involve greater difficulty performing these tasks or the use of compensatory strategies; 2. Mild deficits on objective cognitive assessment (typically 1–2 SD below the mean [or in the 2.5–16th 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 patient's own baseline would serve as more definitive evidence of decline 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 or schizophrenia)	1. Acquired impairment in cognitive functioning, involving at least two ability domains, documented by performance of at least 1 SD below the mean for age/education-appropriate norms on standardized neuropsychological tests. The neuropsychological assessment must survey at least the following abilities: verbal/language, attention/working memory, abstraction/executive, memory (learning and recall), speed of information processing, sensory–perceptual and motor skills 2. The cognitive impairment produces at least mild interference in daily functioning (at least one of the following): a) Self-report of reduced mental acuity, inefficiency in work, homemaking or social functioning; b) Observation by knowledgeable others that the individual has undergone at least mild decline in mental acuity with resultant inefficiency in work, homemaking, or social functioning 3. The cognitive impairment does not meet criteria for delirium or dementia 4. There is no evidence of another pre-existing cause for the mild neurocognitive disorder. If the individual with suspected mild neurocognitive disorder also satisfies criteria for a severe episode of major depression with significant functional limitations or psychotic features, or substance dependence, the diagnosis of mild neurocognitive disorder should be deferred to a subsequent examination conducted at a time when the major depression has remitted or at least 1 month after cessation of substance use

In DSM-IV criteria [2,3], there are currently no criteria for a diagnosis analogous to 'mild neurocognitive disorder' of the Frascati conference-based revision of the AAN criteria (with the exception of the research appendix).
AAN: American Academy of Neurology; DSM: Diagnostic and Statistical Manual of Mental Disorders; SD: Standard deviation.

Table 1. Criteria for neurocognitive disorders proposed for the Diagnostic and Statistical Manual of Mental Disorders 5 and the Frascati conference-based revision of American Academy of Neurology criteria (cont.).

DSM-5 (cont.)	Frascati conference-based revision of AAN criteria (cont.)
No equivalent criteria	**HIV-associated asymptomatic neurocognitive impairment**
–	1. Acquired impairment in cognitive functioning, involving at least two ability domains, documented by performance of at least 1 SD below the mean for age/education-appropriate norms on standardized neuropsychological tests. The neuropsychological assessment must survey at least the following abilities: verbal/language, attention/working memory, abstraction/executive, memory (learning and recall); speed of information processing, sensory–perceptual and motor skills 2. The cognitive impairment does not interfere with everyday functioning 3. The cognitive impairment does not meet criteria for delirium or dementia 4. There is no evidence of another pre-existing cause for the asymptomatic neurocognitive impairment

In DSM-IV criteria [2,3], there are currently no criteria for a diagnosis analogous to 'mild neurocognitive disorder' of the Frascati conference-based revision of the AAN criteria (with the exception of the research appendix).
AAN: American Academy of Neurology; DSM: Diagnostic and Statistical Manual of Mental Disorders; SD: Standard deviation.

inflammatory syndrome manifesting with CNS symptoms). Moreover, psychiatric confounding conditions should be excluded (e.g., major depressive disorder and bipolar affective disorder [and associated mania]), as should neuropsychiatric prescribed medication toxicities (e.g., those associated with IFN-α and efavirenz) and intoxication, withdrawal and long-term sequelae associated with psychoactive substance use (e.g., methamphetamine, cocaine and alcohol).

The aforementioned revised criteria were developed at the Frascati conference by an international working group charged by the National Institute of Mental Health (NIMH) and the National Institute of Neurological Disorders and Stroke (NINDS) of the USA to critically review the adequacy and utility of the prior AAN criteria. Those criteria differ significantly from the generalized neurocognitive disorder criteria that have been suggested by the DSM-5 Neurocognitive Disorders Work Group:

- First and foremost, it must be pointed out that the DSM-5 criteria are not specific in terms of etiology. In the case of HAND, the pathogen has been identified and should be specified to be HIV.

- Second, the proposed DSM-5 criteria indicate that the diagnosis must be based upon report by the patient or a knowledgeable informant or by observation by a clinician, together with deficits on standardized NP testing. However, in the revised AAN criteria standardized NP testing is fully relied upon, and it is not required that a report of the patient, a report of a knowledgeable informant or a confirmatory observation by a clinician be documented.

- Third, the proposed DSM-5 neurocognitive domains to be sampled differ from that set forth in the revised AAN criteria. The DSM-5 supports the idea of six domains: complex attention (sustained attention, divided attention, selective attention and information processing speed); executive ability (planning, decision-making, working memory, responding to feedback/error correction, overriding habits and mental flexibility); learning and memory (immediate memory and 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 and behavioral regulation). The revised AAN criteria denote seven domains: verbal/language, attention/working memory, abstraction/executive functioning, memory (learning and recall), speed of information processing, sensory–perceptual, and motor skills. The primary differences are that the DSM-5 criteria include a domain of 'social cognition' not included in the

revised AAN criteria, while the revised AAN criteria denote information processing speed and motor skills as separate domains not included by the DSM-5 criteria. Little to no data exist on the importance of social and emotional cognition in the diagnosis of HAND, and it is likely that the inclusion of this domain would bias against the likelihood of reaching a HAND diagnosis. The revised AAN criteria are based upon the research on HAND demonstrating that information processing speed is considered to be the hallmark of deficits observed in early HAND [18]. In addition, the motor domain is well known to be affected by HIV infection of the brain, manifesting as secondary Parkinsonism [19] related to basal ganglia infection occurring as an early-recognized event [20] and associated with neurocognitive changes [21]. It is unclear how the inclusion of the virtually unstudied domain of social cognition by the DSM-5 could be expected to offset its omissions of the frequently impaired domains of information processing speed and motor function in HAND.

- Fourth, another important difference between these two criteria sets is that the revised AAN criteria set requires that at least two NP domains be impaired, whereas the DSM-5 Neurocognitive Disorder Work Group criteria require only one NP domain to be impaired. The issue with the use of a single domain-based impairment definition is that it is not sufficient to denote the global deterioration of neurocognitive performance required by definition with the use of the term 'dementia' and – analogously – by 'major neurocognitive disorder' as well. In fact, it is not uncommon to find that isolated impairment in the memory domain may particularly occur without any impairment in other domains, and such a condition is better defined as a different syndrome.
- Fifth, the quantified level of deficit required in NP performance differs between the two criteria sets as well. The revised AAN criteria for HAD indicate that impairment must be ascertained by NP testing with at least two domains being 2 SDs or greater below demographically corrected means. Alternatively, the patient could score greater than 2.5 SDs below norms (an operational definition for moderate to severe impairment) on one domain and greater than 1 SD below norms on another. However, the DSM-5 Work Group criteria do not impose a quantified impairment definition and only specify that 'typically' the deficits will be >2 SDs below the mean (or below the 2.5th percentile) of an appropriate reference population. In order to generally standardize diagnoses of HAND, the use of a quantified NP impairment definition would improve reliability and validity, and the revised AAN criteria present a yet more differentiated approach to the level of HAND with respect to MND versus HAD by the application of its differential, quantitative NP cutoffs for these diagnoses.
- Sixth, the DSM-5 Neurocognitive Disorder Work Group criteria require that the neurocognitive deficits be associated specifically with deficits in functional status in activities of daily living involving independence. However, the revised AAN criteria simply require that the neurocognitive impairment produces marked interference with any activities of daily living (e.g., work, home life or social activities – regardless of whether they interfere with independence). The requirement of deficits in independence would likely skew the frequency of these diagnoses toward a more severe level than would otherwise be the case when general activities of daily living are assessed. The rationale for prioritizing independence in HAND diagnoses or for neurocognitive disorder diagnoses more generally is unclear. Another advantage of the revised AAN criteria is that they recommend (but not require) that standardized functional status instruments be used. Of note, the instruments chosen should have norms that are appropriate to the patient population being examined (i.e., for that patient's culture and a comparable sociodemographic group).
- A seventh and final issue with the criteria promoting 'major neurocognitive disorder' (as defined by the DSM-5) versus those promoting 'HAD' (as defined by the revised AAN criteria) are the exclusionary criteria that must be met. The DSM-5 Work Group states that the neurocognitive deficits not be wholly or primarily attributable to another axis I psychiatric disorder (e.g., major depressive disorder or schizophrenia). By contrast, the revised AAN criteria state that there should be no evidence of another, pre-existing cause for the dementia (e.g., other CNS infection, CNS neoplasm, cerebrovascular disease or pre-existing

neurologic disease). Of note, the revised AAN criteria for HAD include ruling out relevant psychiatric disorders as a pre-existing cause as well (e.g., substance dependence compatible with CNS disorder and major depressive disorder), whereas the DSM-5 Neurocognitive Disorder Work Group criteria do not analogously specify exclusion of neurological or general medical conditions of any kind. It would seem that the latter approach should be modified at this time in the development of research on CNS diseases when specific etiologies are generally becoming much more commonly focused upon and are of manifest relevance to the definition of HAD.

Considering the less severe neurocognitive disorder subsumed by the term 'HAND', there are also currently no HIV-specific criteria denoted in the DSM-IV [2,3] for either 'HIV-associated MND' as defined by Antinori *et al.* [9], or for the previously defined AAN diagnosis of HIV-associated minor cognitive-motor disorder [4]. This diagnosis – as alluded to previously – falls under the DSM-IV generic diagnosis of 'cognitive disorder not otherwise specified' (294.9). However, we have previously noted that the MND diagnosis could be mapped to the non-HIV-specific research diagnosis of the same name contained in appendix B of DSM-IV. In that research appendix, the term 'MND' is not related to etiology and is defined as requiring two or more of the following: memory impairment, executive function deficits, attention and information processing speed deficits, perceptual–motor impairment and language impairment. Of note, the functional status criterion of MND in DSM-IV appendix B was that the neurocognitive deficits should cause "marked distress or impairment in social, occupational and other important areas…", which would seem to be inappropriate for this 'mild' disorder.

The current criteria proposed for this neurocognitive disorder in the DSM-5 have changed the DSM-IV research diagnosis nomenclature of 'mild neurocognitive disorder' to 'minor neurocognitive disorder'. As such, this is the opposite of the analogous change in nomenclature between the prior [4] and current [9] sets of AAN neurocognitive disorder criteria. In this case, the prior term was 'HIV-associated minor cognitive-motor disorder' and the current term is 'HIV-associated mild neurocognitive disorder'. Given the DSM-5 Neurocognitive Disorder Work Group's statement about the term 'dementia' having acquired pejorative and stigmatizing connotations, it would seem that the work group might be similarly concerned about the connotations for the public of the term 'minor neurocognitive disorder'. This term could be anticipated to be perceived as diminishing the importance of the functional consequences of this disorder. In fact, the patients so diagnosed may perceive this disorder as anything but 'minor' in terms of its impact in their own lives. Hence, it is unclear why the switch from 'mild neurocognitive disorder' to 'minor neurocognitive disorder' would have been made, and the change seems to be inconsistent with that made by deleting the term 'dementia' in favor of 'major neurocognitive disorder'.

Beyond diagnostic labels, the comparison of the less severe neurocognitive disorder criteria sets themselves are similar to those between 'major neurocognitive disorder' and 'HAD' – with two exceptions. One is that the NP deficits are now defined as mild on NP testing by the DSM-5 Neurocognitive Disorders Work Group (i.e., 'typically' 1–2 SDs below the mean [or in the 2.5–16th percentile] of an appropriate reference population). The other is that the deficits must not be sufficient to interfere with functional status related to the maintenance of independence, although greater effort and compensatory strategies might be required to maintain independence. In terms of the comparison between the mild and more severe disorders as defined by the revised AAN criteria, the criteria for MND are similar to those defined for HAD, with the exceptions that the acquired impairment in neurocognitive performance involves performance on standardized NP tests of at least 1 SD below the mean for appropriate norms (with the same domains defined as those for HAD), and that the neurocognitive impairment is associated with at least mild interference in functional status of activities of daily functioning. It is also suggested that performance-based, standardized functional status tests should also be administered, with patient scores >1 SD below an appropriate normative mean required for the diagnosis. In addition and of specific relevance to MND, language function is typically preserved until late-stage HIV CNS disease. Hence, the proposed DSM-5 Work Group criteria including language as a domain for MND are not as well supported as those proposed for the revised AAN criteria, in which

the comparable domain is defined as 'verbal/language'. The latter domain has a much broader purview by including all verbal functions rather than language functioning alone. Thus, regardless of the prior considerations of the differences between criteria sets on 'major neurocognitive disorder' and 'HAD', it may be concluded that the proposed DSM-5 Neurocognitive Disorder Work Group nomenclature and criteria for 'minor neurocognitive disorder' would require additional revisions.

Finally, consider the mildest neurocognitive condition subsumed by the term 'HAND', 'HIV-associated asymptomatic neurocognitive impairment' (ANI), which has been adopted with the revision of the AAN criteria [9]. There is no analogous diagnostic term in the DSM-IV in either the approved or research criteria sets, nor in the proposed criteria for the DSM-5 currently promoted by the Neurocognitive Disorders Work Group. The revised AAN criteria define ANI as presented earlier for MND – with the exception that the acquired neurocognitive impairment does not interfere with functional status in activities of daily living. It is important to note that this diagnostic entity is more properly classified as a 'condition' rather than a 'disorder', as its presence is not intended to represent an 'illness', which would mandate treatment in order to re-establish normal functioning. Rather, this term represents "a potential predecessor of an illness", which does not currently mandate treatment because functional status in activities of daily living remains normal. It might be suggested that 'subclinical' neurocognitive impairment should be preferred to ANI, as these patients may experience and complain of neurocognitive symptoms but still not qualify by the results of their functional status assessment for the diagnosis of MND.

Conclusion

A significant set of disjunctions has been identified between the proposed DSM-5 Neurocognitive Disorder Work Group's revision of the DSM-IV criteria as applied to HAND [2,3] and the HIV-specific criteria set forth by the Frascati conference-based revision of the prior AAN criteria for HAND [4,9]. Of general importance, the combined prevalence of the conditions subsumed by HAND renders HAND as the most prevalent neuro-AIDS condition today. Within this spectrum, HAD has received more-than-adequate research attention to demonstrate that it is sufficiently unique to warrant being described with its own specific diagnostic criteria in the DSM-5. It is manifest that the neurocognitive disorder diagnoses as applied to HAND should be defined as requiring demonstration of positive HIV serostatus. Regarding other general changes, the attempt to define criteria less directly related to those for AD represents progress in the proposed DSM-5 criteria for the neurocognitive disorders. In addition, the indicated change to create a single categorical heading – neurocognitive disorder (differentiated as 'major' vs 'minor') – might be considered to be an advantage for the proposed DSM-5 criteria over the revised AAN criteria. Moreover, this would be true for the elimination of the term 'dementia' in favor of 'major neurocognitive disorder'. However, it seems that the reverse applies regarding the change from 'mild neurocognitive disorder' in the DSM-IV (and in the currently revised AAN criteria) to 'minor neurocognitive disorder' proposed for the DSM-5. It must also be argued that at least two domains should be required to be impaired to imply the 'global' deterioration of functioning implied by the term 'neurocognitive disorder' (whether major or minor), as is required by the revised AAN criteria for HAD, MND and ANI. Overall, the advantages for the revised AAN criteria set are that neurocognitive deficits are explicitly quantified and functional status deficits are not limited to the specific aspect of 'independence'. By contrast, any type of functional status compromise that is referable to HIV-associated neurocognitive impairment is consistent with the diagnosis of HAND. Finally, the exclusion criteria required for these diagnoses should span both neurologic and psychiatric disorders and should include CNS illnesses specific to the setting of immunodeficiency caused by HIV infection, as noted by both the original AAN criteria and the current Frascati conference-based criteria. The integration of the foregoing considerations into the neurocognitive disorder criteria proposed for the DSM-5 would bring the psychiatric diagnostic criteria to be applied to HAND to the point of addressing the established specificity of neurocognitive disorders (major and minor) in HIV infection and to integrating published research results on the entities comprising HAND.

The clinical implications of these changes are noteworthy, as the specification of the diagnoses subsumed by 'HAND' in the DSM-5 would allow psychiatrists to internationally utilize these

diagnoses more systematically for psychiatric clinical purposes, whether or not local resources allowed for standardized NP testing. Such changes would also contribute to a greater integration of HIV psychiatry within mainstream psychiatry. In addition, they would allow the more ready coordination of clinical care with neurologists using the revised criteria originated by the AAN. Moreover, use of such a coordinated diagnostic system for HAND would allow improved communication and care coordination with the primary care provider (most typically an infectious disease physician specializing in HIV medicine). It should also be pointed out that HAND represents only one type of neurocognitive disorder of a group that might be similarly considered for their own specific diagnostic criteria in the DSM-5, most notably AD [22–25]. While criteria are suggested for AD within the proposal of the DSM-5 Neurocognitive Disorders Work Group, those criteria are presented as a "subtype of major and minor neurocognitive disorder" and as "an example" of how specific etiologies would be coded. No criteria for any other subtype of neurocognitive disorder are offered.

Finally, and most importantly, the delineation of HIV-specific neurocognitive disorder diagnostic criteria in the DSM-5 would allow reimbursement of psychiatrists for clinical interventions aimed at the treatment of both MND and major neurocognitive disorder associated with HIV infection. These interventions include the potential use of CNS-penetrating ART, psychostimulants and other therapies aimed at neurotransmitter manipulation, CNS anti-inflammatory agents, antineurodegenerative agents, neurotrophic agents, nutritional manipulation and a spectrum of cognitive rehabilitative techniques.

Future perspective

Dementia and other cognitive disorders, due to HIV infection, were classified solely at a nominal level by prior versions of the DSM. Therein, they have been referred to as a dementia or a cognitive disorder "due to a general medical condition". This broad rubric has significantly limited the utility of these diagnoses to psychiatrists for both diagnostic and treatment purposes. However, specific criteria for the HIV-associated subset of these disorders have now been in use by neurologists for 20 years. To account for changes that more recent research has documented in these entities since the introduction in 1996 of 'highly active ART' (now referred to as 'combination ART' or simply as 'effective ART'), those criteria were revised based upon an international consensus conference 4 years ago. An opportunity for integration with this diagnostic revision now presents itself with the advent of the DSM-5.

Disclosure

The content is solely the responsibility of the authors and does not necessarily reflect the official views of the National Institute of Mental Health or the National Institute on Neurological Disorders and Stroke.

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No writing assistance was utilized in the production of this manuscript.

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- ▪ of interest
- ▪▪ of considerable interest

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▪▪ **Sets forth the proposed neurocognitive disorder criteria (subsuming HIV-associated neurocognitive disorders [HAND]) to be incorporated into the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5.**

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