

Handouts for Diagnosing AIDS Dementia 17.01.2007

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AAN (1991) Criteria for clinical diagnosis in adults and adolescents of HIV-1 associated cognitive/motor complex

All of the following diagnoses require laboratory evidence for systemic HIV-1 infection (ELISA test confirmed by Western blot, polymerase chain reaction, or culture)

I. Sufficient for diagnosis of AIDS

A. HIV-1-associated dementia complex*

Probable (must have *each* of the following):

1. Acquired abnormality in at least *two* of the following cognitive abilities (present for at least 1 month): attention/concentration, speed of processing information, abstraction/reasoning, visuospatial skills, memory/learning, and speech/language. The decline should be verified by reliable history and mental status examination. In all cases, when possible, history should be obtained from an informant, and examination should be supplemented by neuropsychological testing.
Cognitive dysfunction causing impairment of work or activities of daily living** (objectively verifiable or by report of a key informant). This impairment should not be attributable solely to severe systemic illness.
2. At least *one* of the following:
 - a. Acquired abnormality in motor function or performance verified by clinical examination (e.g., slowed rapid movements, abnormal gait, limb incoordination, hyperreflexia, hypertonia, or weakness), neuropsychological tests (e.g., fine motor speed, manual dexterity, perceptual motor skills), or both.
 - b. Decline in motivation or emotional control or change in social behavior. This may be characterized by any of the following: change in personality with apathy, inertia, irritability, emotional lability, or new onset of impaired judgment characterized by socially inappropriate behavior or disinhibition.
3. Absence of clouding of consciousness during a period long enough to establish the presence of #1.
4. Evidence of another etiology, including active CNS opportunistic infection or malignancy, psychiatric disorders (e.g., depressive disorder), active alcohol or substance use, or acute or chronic substance withdrawal, must be sought from history, physical and psychiatric examination, and appropriate laboratory and radiologic investigation (e.g., lumbar puncture, neuroimaging). If another potential etiology (e.g., major depression) is present, it is *not* the cause of the above cognitive, motor, or behavioral symptoms and signs.

2006 NIMH/NINDS Revision of Diagnostic Guidelines

HIV Associated Asymptomatic Neurocognitive Impairment (ANI)[^]

1. Acquired impairment in cognitive functioning, involving at least two ability domains, documented by performance of at least 1.0 standard deviation 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/speeded processing; abstraction/executive; memory (learning; recall); complex perceptual-motor performance; motor skills.
2. The cognitive impairment does not interfere with everyday functioning.
3. The cognitive impairment has been present at least one month.
4. The cognitive impairment does not meet criteria for delirium or dementia.
5. There is no evidence of another preexisting cause for the ANI.*

*If the individual with suspected ANI also satisfies criteria for a major depressive episode or substance dependence, the diagnosis of ANI should be deferred to a subsequent examination conducted at a time when the major depression has remitted or at least 1 month has elapsed following termination of dependent-substance use.

[^]If there is a prior diagnosis of ANI, but currently the individual does not meet criteria, the diagnosis of ANI in remission can be made.

HIV-1 Associated Mild Neurocognitive Disorder (MND)[^]

1. Acquired impairment in cognitive functioning, involving at least two ability domains, documented by performance of at least 1.0 standard deviation 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/speeded processing; abstraction/executive; memory (learning; recall); complex perceptual-motor performance; motor skills. **Typically, this would correspond to an MSK scale score of 0.5 – 1.0**
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 has been present at least one month.
4. The cognitive impairment does not meet criteria for delirium or dementia.
5. There is no evidence of another preexisting cause for the MND.*

*If the individual with suspected MND also satisfies criteria for a major depressive episode or substance dependence, the diagnosis of MND should be deferred to a subsequent examination conducted at a time when the major depression has remitted or at least 1 month has elapsed following termination of dependent-substance use.

[^]If there is a prior diagnosis of MND, but currently the individual does not meet criteria, the diagnosis of MND in remission can be made.

HIV-1 Associated Dementia (HAD)[^]

1. Marked acquired impairment in cognitive functioning, involving at least two ability domains (e.g., memory, attention): typically the impairment is in multiple domains, especially in learning of new information, slowed information processing, and defective attention/concentration. The cognitive impairment can be ascertained by history, mental status examination, or neuropsychological testing. **Typically, this would correspond to an MSK scale score of 2.0 or greater.**
2. The cognitive impairment produces marked interference with day-to-day functioning (work, home life, social activities).
3. The marked cognitive impairment has been present for at least one month.
4. The pattern of cognitive impairment does not meet criteria for delirium (e.g., clouding of consciousness is not a prominent feature); or, if delirium is present, criteria for dementia need to have been met on a prior examination when delirium was not present.
5. There is no evidence of another, preexisting cause for the dementia (e.g., other CNS infection, CNS neoplasm, cerebrovascular disease, preexisting neurological disease, or severe substance abuse compatible with CNS disorder).*

✓ *If the individual with suspected HAD also satisfies criteria for a major depressive episode or substance dependence, the diagnosis of HAD should be deferred to a subsequent examination conducted at a time when the major depression has remitted or at least 1 month has elapsed following termination of dependent-substance use.

[^]If there is a prior diagnosis of HAD, but currently the individual does not meet criteria, the diagnosis of ANI in remission can be made.

CLINICAL STAGING OF THE AIDS DEMENTIA COMPLEX (ADC)

Stage (ADC)	Characteristics
Stage 0 (normal)	Normal mental and motor function.
Stage 0.5 (equivocal/subclinical)	Either minimal or equivocal symptoms of cognitive or motor dysfunction characteristic of ADC, or mild signs (snout response, slowed extremity movements), but without impairment of work or capacity to perform activities of daily living (ADL). Gait and strength are normal.
Stage 1 (mild)	Unequivocal evidence (symptoms, signs, neuropsychological test performance) of functional intellectual or motor impairment characteristic ADC, but able to perform all but the more demanding aspects of work or ADL. Can walk without assistance.
Stage 2 (moderate)	Cannot work or maintain the more demanding aspects of daily life, but able to perform basic activities of self-care. Ambulatory, but may require a single prop.
Stage 3 (severe)	Major intellectual incapacity (cannot follow news or personal events, cannot sustain complex conversation, considerable slowing of all output) or motor disability (cannot walk unassisted, requiring walker or personal support, usually with slowing and clumsiness of arms as well).
Stage 4 (end stage)	Nearly vegetative. Intellectual and social comprehension and output are at a rudimentary level. Nearly or absolutely mute. Paraparetic or paraplegic with double (urinary and bowel) incontinence.

NOTE: Staging definition revised as of 1-27-92. ADL = activities of daily living

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Outline of criteria for classifying HIV-related neurocognitive disorders

Asymptomatic Neurocognitive Impairment (ANI)

Neuropsychological (NP) Testing is available

NP impairment in ≥ 2 cognitive domains that cannot be explained by opportunistic CNS disease, systemic illness, psychiatric illness, substance use disorders, or medications with CNS effects (confounding conditions, see Table 4). No reported or demonstrated functional decline.

NP Testing not available

Mental Status Exam (MSE) impairment involving ≥ 2 cognitive domains, that cannot be explained by opportunistic CNS disease, systemic illness, psychiatric illness, substance use disorders, or medications with CNS effects. (confounding conditions; see Table 4). No reported or demonstrated functional decline.

Mild Neurocognitive Disorder (MND)

At least mild NP impairment (>1 SD below a demographically appropriate normative mean), involving ≥ 2 cognitive domains that cannot be explained by confounding conditions (see Table 4). AND
Reported or demonstrated mild functional decline that cannot be explained by confounding conditions (see Table 4).

At least mild MSE impairment (>1 SD below a demographically appropriate normative mean), involving ≥ 2 cognitive domains, that cannot be explained by confounding conditions (see Table 4) AND
Reported or demonstrated mild functional decline that cannot be explained by confounding conditions (see Table 4).

HIV-Associated Dementia (HAD or ADC)

Note: Severity of NP impairment and functional decline must both meet these standards in order to diagnose the person as having HAD. If either NP impairment or functional decline is mild, the condition should be classified as MND.

\geq Moderate NP impairment (>2 SD below a demographically appropriate normative mean) on ≥ 2 cognitive domains.*
Impairment cannot be explained by confounding conditions (see Table 2). AND
Reported or demonstrated major functional decline that cannot be explained by confounding conditions (see Table 4).

\geq Moderate MSE impairment (>2 SD below a demographically appropriate normative mean), involving ≥ 2 cognitive domains, that cannot be explained by confounding conditions (see Table 4). AND
Reported or demonstrated major functional decline that cannot be explained by confounding conditions (see Table 4).

*Alternatively, one domain could be more severely impaired (>2.5 SD below the mean) and another less severely impaired (>1 SD below the mean) --see Woods et al., 2004.

Examples of NP tests that may be used to document impairments in ability domains.

Fluency

Controlled Oral Word Association Test (FAS) (Benton & Hamsher, 1989; Gladsjo et al., 1999)
Thurstone Word Fluency Test (Thurstone & Thurstone, 1962; Heaton et al., 2004)
Category Fluency (e.g., animals, fruits, and vegetables) (Spree & Strauss, 1998)
Action Fluency (Piatt et al., 1999)
Design Fluency Tests (e.g., Ruff, Light & Evans, 1987; Delis, Kaplan & Kramer, 2001)

Executive Functions

Stroop Color and Word Test (Interference Trial or Ratio Score) (Golden, 1978)
Trailmaking Test – Part B (Reitan & Wolfson, 1985; Heaton et al., 2004)
Color Trails –II (Maj et al., 1993)
Wisconsin Card Sorting Test (Heaton et al., 1993)
Halstead Category Test (Reitan & Wolfson, 1985; Heaton et al., 2004a)
Odd Man Out Test (Frearson & Eysenck, 1986; Marder et al., 2003;
The Dana Consortium on Therapy for HIV Related Cognitive Disorders, 1996)
Tower Tests (Toronto, London, Hanoi, etc.) (Saint Cyr & Taylor, 1992; Shallice, 1982; Goel & Grafman, 1995)
Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan & Kramer, 2001)

Speed of Information Processing

WAIS-III Digit Symbol Subtest (Wechsler, 1997a)
WAIS-III Symbol Search Subtest (Wechsler, 1997a)
Symbol Digit Modalities Test (Smith, 1982)
Trailmaking Test – Part A (Reitan & Wolfson, 1985; Heaton et al., 2004a)
Color Trails – I (Maj et al., 1993)
Digit Vigilance Test (time component) (Lewis, 1995; Heaton et al., 2004a)
Stroop Color Naming (Golden, 1978)
Reaction Time Tests, e.g., California Computerized Assessment Battery (Cal-Cap; Miller et al., 1990)

Attention/Working Memory

WAIS-III Digit Span Subtest (Wechsler, 1997a)
WAIS-III Letter-Number Sequencing Subtest (Wechsler, 1997a)
WMS-III Spatial Span Subtest (Wechsler, 1997b)
Paced Auditory Serial Addition Test (Diehr et al., 1998)
Digit Vigilance Test (error component) (Lewis, 1995; Heaton et al., 2004)

Verbal and Visual Learning/Memory

Verbal:

California Verbal Learning Test (Original and Revised; Total Learning) (Delis et al., 1987, 2000)

Rey Auditory Verbal Learning Test (Total Learning) (Rey, 1964)
Story Memory Test (Learning component) (Heaton et al., 2004a)
Hopkins Verbal Learning Test- Revised (Total Learning) (Benedict et al., 1998)
Buschke Selective Reminding Test (Total Learning, Buschke & Fuld, 1974)
WMS-III Logical Memory I (Wechsler, 1997b)
WMS-III Paired Associates I (Wechsler, 1997b)

Visual:

WMS-III Visual Reproduction-I (Wechsler, 1997b)
WMS-III Family Pictures-I (Wechsler, 1997b)
Brief Visuospatial Memory Test – Revised (Total Learning) (Benedict, 1997)
Figure Memory Test (Learning component) (Heaton et al., 2004a)
Rey-Osterreith Complex Figure Test (Immediate Recall) (Corwin & Bylsma, 1993a, 1993b).

Motor Skills

Grooved Pegboard Test (Klove, 1963; Heaton et al., 2004a)
Purdue Pegboard Test (Tiffin, 1968; Agnew et al., 1988)
Arendt Central Motor Test Battery (Arendt et al., 1990, 1992)
Finger Tapping Test (Heaton et al., 2004a)
Timed Gait (Robertson et al., in press)

NOTE: WAIS-III is Third Edition of the Wechsler Adult Intelligence Scale; WMS-III is the Third Edition of the Wechsler Memory Scale.

International HIV Dementia Scale (IHDS)

Memory-Registration – Give four words to recall (dog, hat, bean, red) – 1 second to say each. Then ask the patient all four words after you have said them. Repeat words if the patient does not recall them all immediately. Tell the patient you will ask for recall of the words again a bit later.

1. Motor Speed: Have the patient tap the first two fingers of the non-dominant hand as widely and as quickly as possible.

4 = 15 in 5 seconds

3 = 11-14 in 5 seconds

2 = 7-10 in 5 seconds

1 = 3-6 in 5 seconds

0 = 0-2 in 5 seconds

2. Psychomotor Speed: Have the patient perform the following movements with the non-dominant hand as quickly as possible: 1) Clench hand in fist on flat surface. 2) Put hand flat on surface with palm down. 3) Put hand perpendicular to flat surface on the side of the 5th digit. Demonstrate and have patient perform twice for practice.

4 = 4 sequences in 10 seconds

3 = 3 sequences in 10 seconds

2 = 2 sequences in 10 seconds

1 = 1 sequence in 10 seconds

0 = unable to perform

3. Memory-Recall: Ask the patient to recall the four words. For words not recalled, prompt with a semantic clue as follows: animal (dog); piece of clothing (hat); vegetable (bean); color (red).

Give 1 point for each word spontaneously recalled.

Give 0.5 points for each correct answer after prompting

Maximum – 4 points.

Total International HIV Dementia Scale Score: This is the sum of the scores on items 1-3. The maximum possible score is 12 points. A patient with a score of ≤ 10 should be evaluated further for possible dementia.

From Sacktor NC, Wong M, Nakasujja N, Skolasky RL, Selnes OA, Musisi S, Robertson K, McArthur JC, Ronald A, Katabira E. The International HIV Dementia Scale: a new rapid screening test for HIV dementia. AIDS. 2005 Sep 2;19(13):1367-74

Antiretroviral CNS Penetration/Efficacy

High	NRTI	ZDV	ABV			
	NNRTI	NVP	DLV			
	PI	ATV-r	APV-r	f-APV-r	IDV-r	LPV-r
Medium	NRTI	3TC	FTC	D4T		
	NNRTI	EFV				
	PI	APV	f-APV	ATV	IDV	
Low	NRTI	TFV	DDI	DDC		
	PI	NFV	SQV	SQV-r	RTV	TPV-r
	FI	T20				

- Notes. High, Medium, Low denote proposed level of penetration/efficacy within the CNS. NRTI-Nucleoside Reverse Transcription Inhibitors, NNRTI- Non-Nucleoside Reverse Transcription Inhibitors, PI-Protease Inhibitors, FI- Fusion Inhibitors. The suffix -r refers to Ritonavir boosting. Adapted from: Robertson, K., Fiscus, S. A., Robertson, W., Meeker, R., and Hall, C. *CSF HIV RNA and CNS Penetrating Antiretroviral Regimens (746-W)*. in *9th Conference on Retroviruses and Opportunistic Infections*. 2002.
- Letendre, S., Capparelli, E., Best, B., Clifford, D., Collier, A., Gelman, B., McArthur, J., McCutchan, J., Simpson, D., Ellis, R., and the CHARTER Group. *Better Antiretroviral Penetration into the Central Nervous System Is Associated with Lower CSF Viral Load*. in *13th Conference on Retroviruses and Opportunistic Infections*. 2006.
- Marra, C., Sinha, S., Evans, S., Letendre, S., Coombs, R., Aweeka, F., Clifford, D., Shriver, S., Li, X., Robertson, K., and ACTG 736 Team. *ACTG 736: CSF HIV-1 and Cognitive Function in Individuals Receiving Potent ART*. in *13th conference on Retroviruses and Opportunistic Infections*. 2006. Denver, CO.

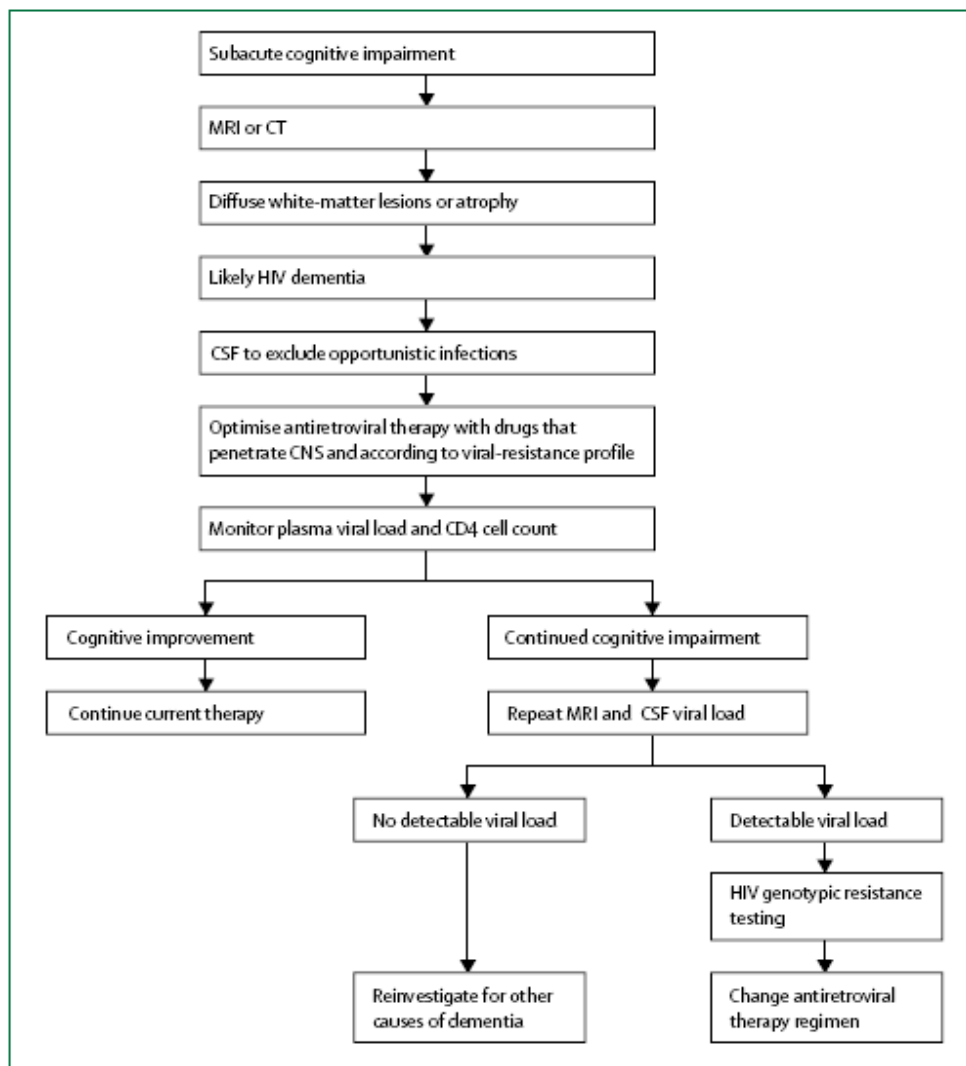


Figure 3: Flow chart of management of subacute or chronic cognitive impairment in HIV AIDS

From McArthur J, Brew B, Nath A. Neurologic Complications of HIV, Lancet Neurol 2005; 4: 543–55