Neurodevelopmental Criteria for Classification of HIV-Related CNS Disease in Children

Probable HIV-Related Encephalopathy

(One or more of the following criteria must be met):

- loss of previously-acquired skills and/or behaviors;
- significant drop in cognitive test scores, generally to the delayed/borderline range with functional deficits;
- cognitive test scores are in the delayed/borderline range with functional deficits;
- significantly abnormal neurologic exam with functional deficits (i.e. significant tone, reflex, cerebellar, gait, and movement abnormalities);
- significant improvement in cognitive test scores over approximately a six-month period associated with a new treatment when baseline scores are in the borderline to delayed range (no history of previous testing) with or without significant brain imaging or neurologic abnormalities (retrospective classification)

3 Subtypes of HIV Encephalopathy:

• **Progressive:**
  -- **Subacute**--children exhibit a loss of previously acquired skills, resulting in a significant decline in raw and standard score on psychometric tests, and new neurologic abnormalities.

  -- **Plateau**--children either do not gain further skills or exhibit a slowed rate of development compared to their previous rate of development, resulting in a significant drop in standard scores on psychometric tests.

• **Static:** children exhibit consistent but slower than normal development in the delayed range or their neuropsychological functioning remains stable for least one year after a significant decline (IQ scores remain below average and without significant decline for at least one year).
Possible HIV-Related CNS Compromise

(One or more of the following criteria must be met):

- significant drop in cognitive test scores, but generally still above the delayed range, with or without mild brain imaging abnormalities, with no loss of previously-acquired skills and no apparent functional deficits (adaptive behavior and school performance stable); or

- cognitive test scores in the borderline range with no significant functional deficits;

- cognitive test scores within normal limits (low average range or above) with no significant functional deficits and moderate to severe brain imaging abnormalities consistent with HIV-related changes;

- abnormal neurologic findings but not significantly affecting function;

- significant improvement in cognitive test scores over approximately a six month period associated with a new treatment when baseline scores are in the low average to average range (no history of previous testing) and no neurologic or brain imaging abnormalities (retrospective classification)

Considerations for classification of HIV Encephalopathy or CNS Compromise:

- If no other factors can reasonably explain the drop in cognitive test scores, compromised/delayed cognitive functioning, and/or abnormal neurologic exam (such as myopathy, neuropathy, cord lesions, CNS opportunistic infections, neoplasms, or vascular diseases, non-HIV-related developmental or learning disabilities, behavioral problems, or psychosocial/environmental circumstances), and the impairments are considered most likely due to HIV, classify as either HIV-related encephalopathy or CNS compromise (depending on the criteria met).

- If other factors (i.e. behavioral, environmental, acute illness, other infection, etc.) may possibly explain the drop in scores or low cognitive functioning, do not classify as HIV-related CNS compromise or encephalopathy and re-evaluate at a later time.

Non-HIV-Related CNS Impairment

- overall cognitive scores or selective areas of deficits below the Low Average range, but careful review of medical and family history suggests factors other than HIV disease most likely explain the low scores.

Apparently Not Affected

- cognitive test scores within or above normal limits with no significant functional deficits or decline in scores, a normal neurologic exam, and no significant brain imaging abnormalities.
Definitions:

Significant decline in cognitive function:

For infants from birth to 42 months (on the Bayley Scales)*
- a decline of 2 standard deviations (30 points) in the Mental Developmental Index (MDI) on the Bayley Scales, or
- a decline of 1 standard deviation (15 points) in the MDI to the mildly delayed range or below on the Bayley Scales (< 85), maintained over 2 assessments (separated by at least 1 month), or
- a loss of raw score over any period greater/equal to 2 months.

For children > 30 months (on IQ tests)*
- a loss of ≥ 1 standard deviation in McCarthy GCI (16 points) or Wechsler (WPPSI-R, WISC-III & WAIS-R) Full Scale IQ (15 points) and at least 15%, or
- a loss of ≥ 20 IQ points in either the Verbal or Performance IQ,

*the significant drop in scores occurs within approximately 1 year.
*cannot attribute the decline in cognitive functioning to other factors (such as change in test, behavioral/emotional factors, lack of appropriate schooling, acute illness, medication effects, other diseases of the CNS, etc.)

Significant improvement in cognitive function:

For infants from birth to 42 months (on the Bayley Scales)#
- an increase of 1 to 2 standard deviations in the MDI (15 to 30 points) maintained over at least 2 assessments, dependent in part on the age of the child.

For children > 30 months (on IQ tests)#
- the same degree of change as with a significant decline, except test scores increase rather than decrease.

#occurs within approximately 6 months of starting a new antiretroviral treatment.
#cannot be attributed to other factors, such as a change in environment of caregivers, effect of other medications, improvement in test behavior, etc.

Ranges:

<table>
<thead>
<tr>
<th>Cognitive Functioning</th>
<th>Brain Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average range</td>
<td>--degree of cortical atrophy (mild = 1, moderate = 2, severe = 3)</td>
</tr>
<tr>
<td>Low Average range</td>
<td>--absence = 0/presence = 1 of basal ganglia calcifications</td>
</tr>
<tr>
<td>Borderline range</td>
<td></td>
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<tr>
<td>Delayed range</td>
<td>Rating of severity:</td>
</tr>
<tr>
<td></td>
<td>Mild = 1</td>
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<tr>
<td></td>
<td>Moderate = 2</td>
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<tr>
<td></td>
<td>Severe = 3 +</td>
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</tbody>
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Criteria developed by Pam Wolters, Pim Brouwers, and Lucy Civitello, HIV and AIDS Malignancy Branch, NCI