

Neurocognitive Aspects of HIV Infection in Children

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1. Increasing importance of
neurocognitive (NC) functioning
of HIV+ children as they live longer
owing to antiretroviral therapy (ART)

2. HIV infection in children typically

co-occurs with one or more other

major risk factors each detrimental to

children's neurocognitive development,

such as:

- prenatal drug exposure to, e.g.,
 opioids, cocaine, alcohol, nicotine
- prematurity
- low birthweight
- malnourishment
- deficiency of micronutrients, e.g., iodine, zinc
- hemophilia
- cerebral malaria
- other infections
- parental illness and death

3. Estimation of neurocognitive functioning

- Comparison to own kind vs. to test norms
- Qualitative judgments of what counts as “within normal/average range”

4. Neurocognitive functioning of HIV+ children without antiretroviral therapy (ART)

- Natural history of HIV effects on NC
- Cases prior to ART or Untreated
- Still relevant data for resource-poor areas

Findings:

- Static-to-progressive encephalopathy
- Early onset and rapid progression during infancy, often to death

Progressive Encephalopathy

- Decline in test scores > 1 S.D.
- Plateau or Loss of developmental milestones
- Acquired microcephaly
- Spasticity

Static Encephalopathy

- Continue to develop and grow
 - but along a lower growth curve for age
 - (acquire skills at slower rate for age)
- Seen into school age in Class C children

Specificity of effects by HIV

Some evidence that more particularly in

spatial, visual-motor integration,

expressive language, and

executive function domains,

but predominantly **global NC deficits**

Brain findings include:

CT—calcification of basal ganglia

MRI—lesions in white matter

MRS—changes in cortical metabolites,
such as lower N-acetylaspartate (NAA)

- But—puzzlingly—neurocognitive

performance of some Untreated

children only moderately affected for

many years

5. Timing of initial HIV infection and severity of effects on neurocognitive functioning

- Gestation — severe, early onset
- Labor/delivery — when most infections occur and could be reduced
- Infancy — e.g., from breast milk
- Later years — e.g., hemophilia; as older, more like adults

6. Neurocognitive functioning of HIV+ children with antiretroviral therapy (ART)

Limitations of results from studies:

- Few studies with large number of Ss
- Pool data of varied ART regimens
- Variability in age of initiation of ART regimens and ages for follow up

Findings--mixed

- **Small-scale case studies**

Some recovery in NC skills after decline,
but not all the way to baseline.

Increase in cerebral metabolite

N-acetylaspartate [NAA])

associated with better NC performance.

- **Large-scale controlled comparisons of cohorts pre- and post-availability of HAART**

Trend—increase in neurocognitive scores

but

- **Large-scale controlled medication trials of ART regimens over time**

Generally minimal or no improvements

in neurocognitive scores from ART

(while major decrease in viral load)

So ART, particularly HAART, can achieve improvements in viral load and CD4s

without significant improvements in neurocognitive scores.

- Differences between virus in plasma vs CSF
- Insufficient penetration into CNS?
- Insufficient concentration in CSF?

7. Recommendations

Need neurocognitive testing

- To include neurocognitive testing/monitoring as an integral part of comprehensive care

Need to start testing early

- To test for early signs or precursors of neurocognitive deterioration so could initiate, intensify, or change ART regimens

Need useable neurocognitive tests

- To develop/modify neurocognitive

measures appropriate and economical

for culture and language

Need to deliver antiretroviral drugs

- To expand delivery of antiretroviral drugs

appropriate for children

and then to help sustain adherence

to ART regimens

Need drugs that work on brain

- To design, investigate, and administer
antiretroviral (or other anti-neuroAIDS)
medications

with good CNS penetration

and high CSF concentration

Need to stop HIV in children

...and most important of all,

- To help **prevent HIV** infection of children
in the first place!

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