



Imaging in Pediatric 'neuroHIV'

Dr Jackie Hoare
Head of Liaison Psychiatry
Groote Schuur Hospital, UCT

? Spectrum of Neurocognitive disorders

- + The adult literature on HIV related CNS damage supports a spectrum of HAND
- + The criteria have clinical utility
- + allow for the conceptualisation of a range of functional impairment
- + formulation of individual management plans

Why so important?

- + Similar spectrum criteria are needed in pediatric HIV
- + better understand the impact
- + social and educational management needed to support the large number of children in Sub- Saharan Africa with vertically infected HIV
- + HIV and slow progressors
- + Neuroimaging is likely to have a role in defining the spectrum of neurocognitive disorders

Neuroimaging is likely to have a role

- + in defining the spectrum of neurocognitive disorders in HIV positive children and adolescents
- + Conventional neuroimaging currently has two roles in the evaluation of HIV positive children
 1. in the detection of cerebral atrophy and other early signs of encephalopathy
 2. for excluding or investigating secondary CNS complications associated with HIV such as opportunistic infections and tumours
- + In resource limited settings CT is more accessible than MRI
- + However MRI studies are more sensitive and specific in detecting primary HIV related brain changes (Avison et al., 2002).

Review

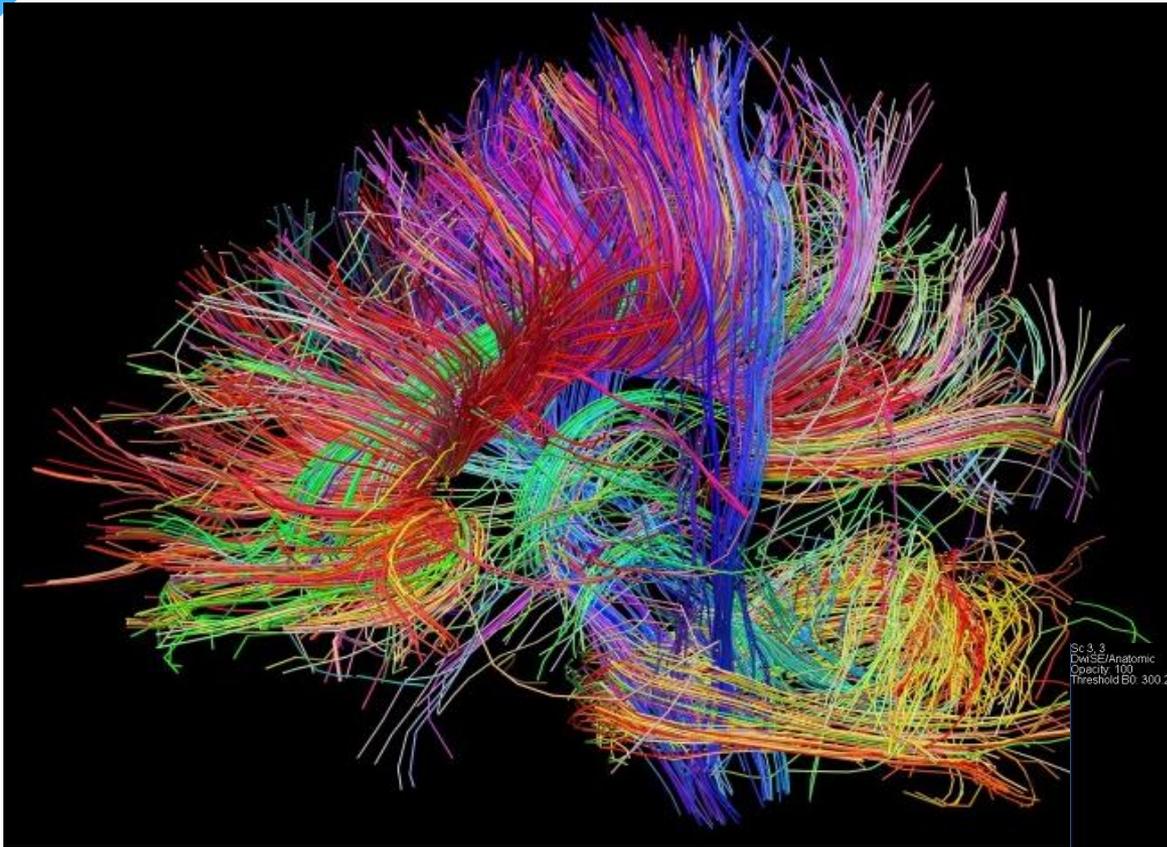
- + Systematic review of neuroimaging studies in vertically transmitted HIV positive children and adolescents. Jacqueline Hoare , Gabrielle L. Ransford, Nicole Phillips, Taryn Amos, Kirsten Donald and Dan J. Stein. Metabolic Brain Disease. 10.1007/s11011-013-9456-5
- + The most frequent brain abnormalities reported in vertically infected HIV across the included studies were
- + ventricular enlargement, cortical and subcortical atrophy, involvement of the basal ganglia, frontal white and frontal grey matter abnormalities, calcifications and damage to the corpus callosum.

Can novel imaging techniques tell us more?

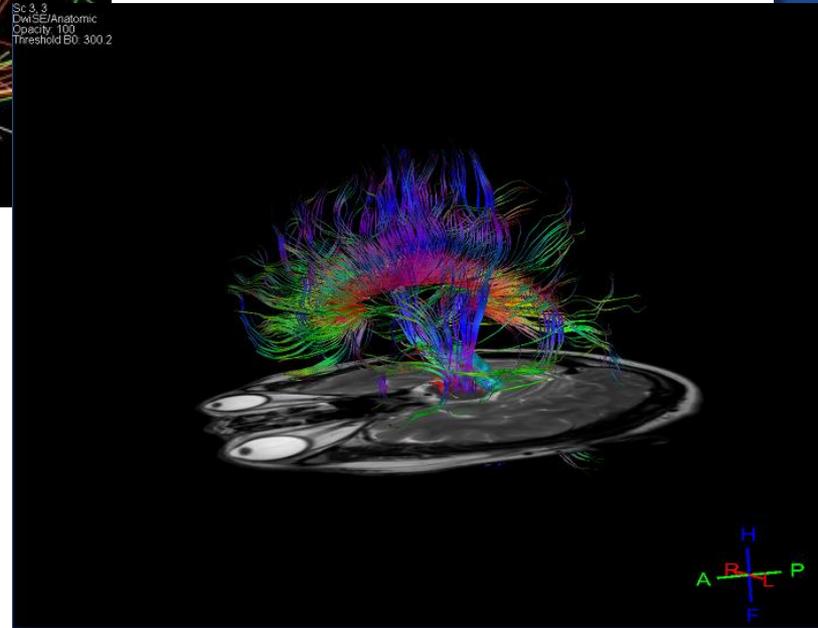
- + Of the 11 studies included in the review, six studies used CT, four used MRI, two used MRS, one used PET and one used DTI
- + PET=Hypometabolism in the temporal and occipital lobes was greater in the symptomatic group and in symptomatic children, hypermetabolism in the caudate and lenticular nuclei.
- + MRS of the encephalopathic children had lower NAA/Cr ratios in the regions of the basal ganglia and white matter compared to non-encephalopathic and control children.
- + significantly increased choline/creatine ratios were observed bilaterally in both the frontal gray and white matter, in the left parietal white matter

Why DTI?

- + Non invasive
- + Quick to collect
- + DTI is able to examine the microstructural integrity and directionality of the white matter
- + capable of providing information on the location of white matter microstructural changes
- + correlated with clinical variables in vertically infected HIV positive children.



Sc 3, 3
DWSE/Anatomic
Opacity: 100
Threshold B0: 300.2



DTI of slow progressors

- + A diffusion tensor imaging and neurocognitive study of HIV-positive children who are HAART-naïve "slow progressors". Hoare J, Fouche JP, Spottiswoode B, Donald K, Philipps N, Bezuidenhout H, Mulligan C, Webster V, Oduro C, Schrieff L, Paul R, Zar H, Thomas K, Stein D. J Neurovirol. 2012 Jun;18(3):205-12.
- + There are few neuropsychological or neuroimaging studies of HIV-positive children with "slow progression".
- + "Slow progressors" are typically defined as children or adolescents who were vertically infected with HIV, but who received no or minimal antiretroviral therapy.
- + 12 asymptomatic HIV-positive children (8 to 12 years) with matched controls on a neuropsychological battery as well as DTI in a ROI focusing on the corpus callosum, internal capsule and superior longitudinal fasciculus.

Cognitive Results

- + The 'slow progressor' group performed significantly worse than controls on the Wechsler Abbreviated Scale of Intelligence Verbal and Performance IQ scales
- + on standardized tests of visuospatial processing, visual memory, and executive functioning.

DTI results

- + “Slow progressors” had lower fractional anisotropy (FA), higher mean diffusivity (MD) and radial diffusivity (RD) in the corpus callosum ($p < 0.05$), and increased MD in the superior longitudinal fasciculus, compared to controls.
- + A correlation was found between poor performance on a test of executive function and a test of attention with corpus callosum FA, and a test of executive function with lowered FA in the superior longitudinal fasciculus.
- + These data suggest that demyelination as reflected by the increase in RD may be a prominent disease process in paediatric HIV infection.

Clinical associations of white matter damage in HAART treated HIV positive children in South Africa

- + A range of factors may contribute to white matter damage in vertically infected HIV positive children;
- + these include combination anti-retroviral treatment (CART) variables, socio-demographic factors, nutritional-hematological status, HIV-relevant clinical variables, and cognitive variables.
- + We explored associations between a number of these factors and diffusion tensor imaging (DTI) measures in 50 CART treated children aged 6 to 15 years.

Methods

- + Fractional anisotropy (FA), mean diffusion (MD), radial (RD) and axial diffusion (AD)
- + were derived from 48 cerebral white matter regions.
- + Significant effects of clinical variables were found with white matter integrity in a number of brain regions.

Results

- + Decreased FA, a measure of neuronal damage, was associated with being on second line CART, low hemoglobin and younger age
- + Children with increased MD, a measure of neuronal damage, were younger, had reduced albumin and hemoglobin and increased total protein and viral load.
- + Decreased AD, a measure of axonal damage, was associated with increased viral load and total protein, decreased albumin and hemoglobin, younger age, poorer frontostriatal cognition and being on second line CART.
- + Increased RD, a measure of myelin loss, was associated with younger age, low current CD₄ count, low albumin and hemoglobin and higher viral load and total protein.

Conclusions

- + The current findings underline the possible association of first line treatment failure with white matter brain dysfunction in pediatric neuroHIV,
- + and the importance of examining the effects of HIV disease in the context of treatable clinical variables such as anemia and nutritional status.

Future

- + 100 DTI scans and cognitive assessments of HIV positive children
- + Groups: Controls, slow progressors, HAART treated and HIV
- + Clade and tat sequencing
- + CTAAC longitudinal RO1 grant for 3 years

Thanks

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