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Multimodal neuroimaging differences related to HIV/ART exposure in 7-year-old South African children

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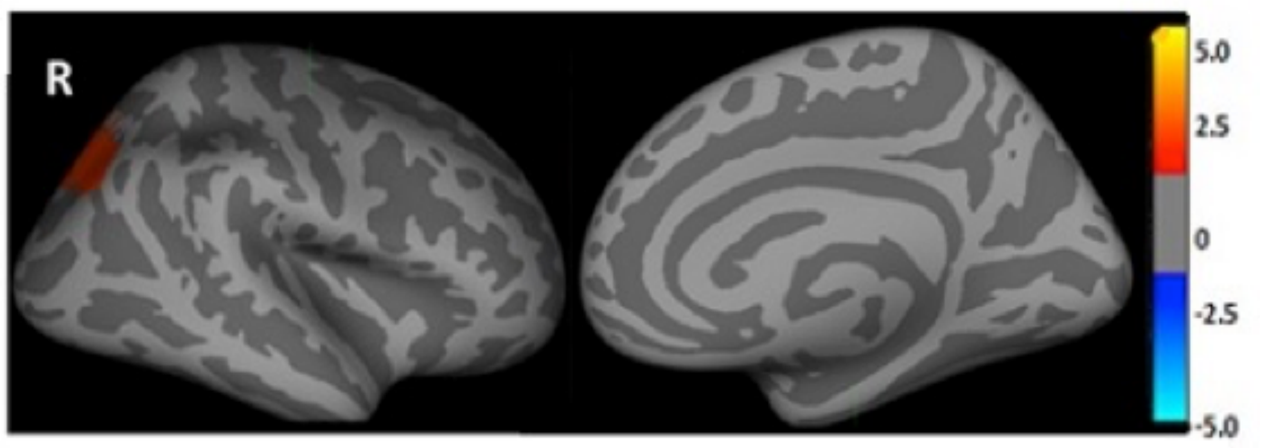
QUESTION: In the 7-year-old brain, are there structural, functional and/or biochemical differences between HEU and HU children?

We found significant differences between HEU and HU children across all neuroimaging modalities at age 7. These results suggest differences in brain maturation related to HIV/ART exposure - involving (1) cortical folding, (2) white matter microstructure, (3) functional networks, and (4) localized metabolism.

STUDY

- Study included both HIV-exposed, uninfected (HEU) and HIV uninfected (HU) children from similar socioeconomic and demographic background. HEU children were exposed to treatment for PMTCT, mostly zidovudine antenatally from 28 to 34 weeks and single dose nevirapine (sd NVP) to the mother and zidovudine for a week and a sd NVP to the infant.
- Fifty one 7-year-old children (23 Female; mean age ± sd: 7.2 ± 0.1; 9 Cape Coloured/42 Xhosa; 23 HEU/28HU) were scanned on a 3 Tesla MRI scanner (Magnetom Allegra, Siemens, Erlangen, Germany) in Cape Town, South Africa from an ongoing longitudinal study.
- The protocol included structural MRI, single voxel ^{1}H magnetic resonance spectroscopy (MRS) in the midfrontal gray matter (MFGM), diffusion tensor imaging (DTI), and resting state functional MRI (RS-FMRI). Statistical analyses included gender and ethnicity as confounders.

1 Structural MRI: measures volume, cortical thickness, and gyrification (cortical folding)

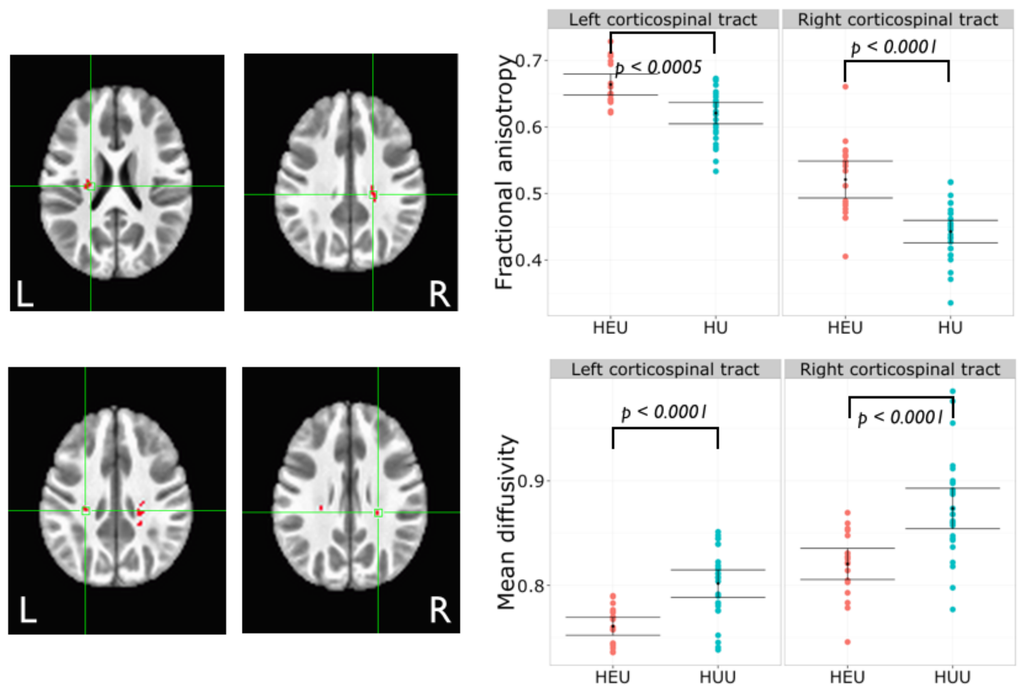


HEU children have HIGHER *local gyrification indices (LGI)* ($p < 0.05$) in right precuneus region.

LGI describes the depth and frequency of gyri.

No differences in volume or cortical thickness were found between groups.

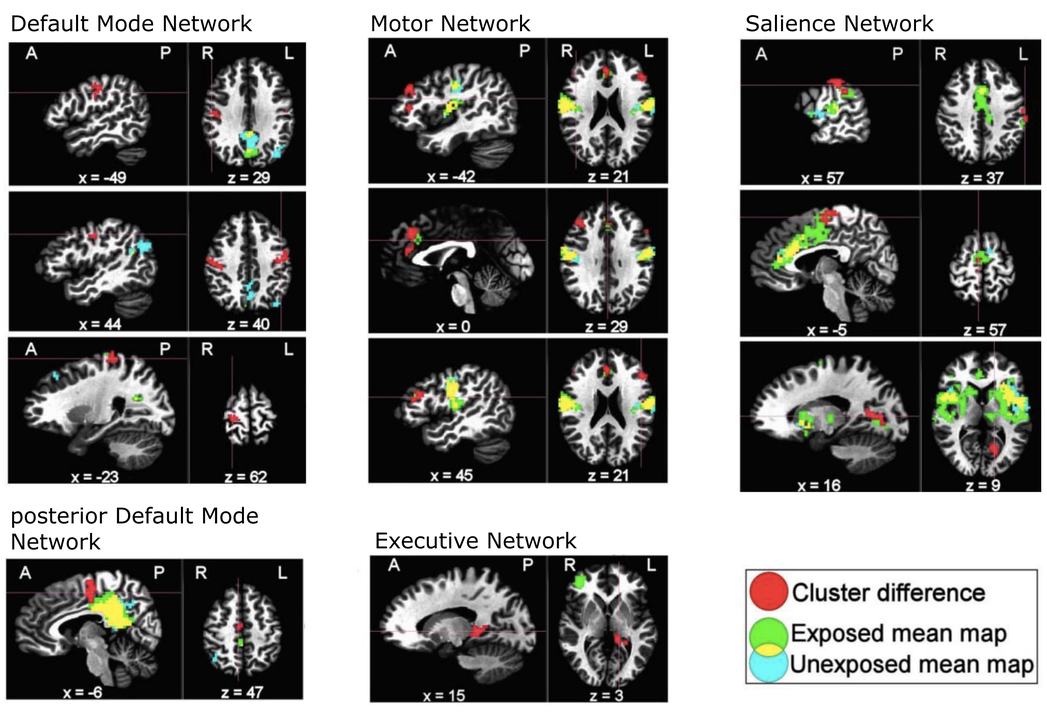
2 DTI: measures of white matter microstructure



HEU children have HIGHER *fractional anisotropy (FA)* and LOWER *mean diffusivity (MD)* ($p < 0.0005$) in bilateral corticospinal tract clusters.

FA is used to describe white matter integrity and MD is a measure of white matter maturation (and decreases with age).

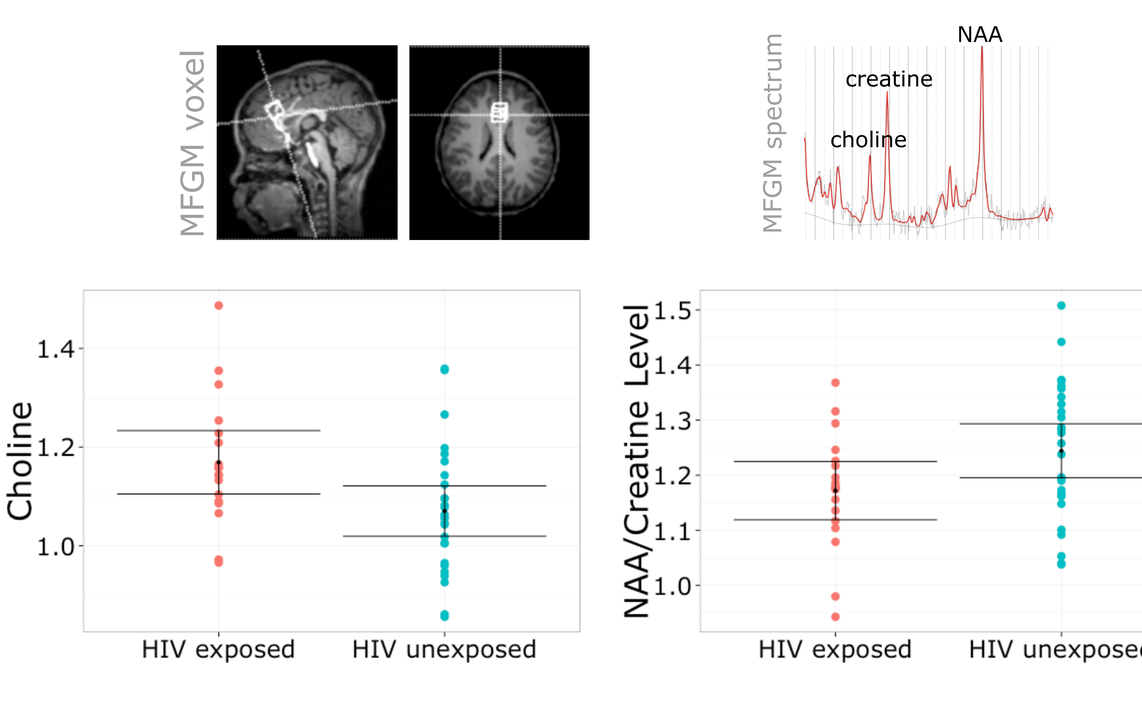
3 RS-FMRI: Describes functional networks



HEU children have HIGHER mean *connectivity* ($p < 0.05$) from seeds in the default mode, executive control, motor, and salience networks.

Connectivity refers to how similar patterns of blood flow are between regions (high connectivity = similar patterns of blood flow)

4 ^{1}H MRS: measures localized metabolite levels related to cellular and neuronal health



HEU children have HIGHER mean *choline* levels ($p = 0.02$) and LOWER mean *NAA/creatine* ratios ($p = 0.05$) in gray matter.

Choline is associated with cellular health, NAA is related to neuronal density/integrity and creatine is involved in energy metabolism.

FINDINGS

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