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Does antiretroviral therapy before 12 weeks of age preserve neurometabolite levels at 9 years in HIV-infected children? - Evidence from the CHER trial

QUESTIONS:

• In the 9-year-old brain, are there biochemical differences between HIV-infected and uninfected children in gray matter, white matter or basal ganglia?

We find:

- Higher **choline** levels in frontal gray matter in all HIVinfected children.
- Lower basal ganglia glutamate levels only in HIV-
- Are there neurometabolite differences between HIV-infected children that started ART before/after 12 weeks of age?

- Subjects 62 HIV-infected and 33 HIV-uninfected 9-year old children (31 girls). HIV-infected children (mean age 9.3 ± 0.2 years) were stratified into those starting ART before (Early-ART, n=46) or after 12 weeks (Late-ART, n=16). The control group (mean age 9.7 ± 0.5) comprised HIV-uninfected (HU, n=18) and HIV-exposed, uninfected children (HEU, n=15).
- Neuroimaging. High-resolution T1-weighted acquisition and single voxel 1H-MRS in basal ganglia (BG), mid frontal gray matter (MFGM), and peritrigonal white matter (PWM) was performed on a 3T Skyra MRI Scanner (Siemens, Erlangen, Germany) in Cape Town, South Africa. Absolute metabolite levels were calculated with LCModel.
- Statistics: A linear regression model in R was used to examine group differences in metabolite levels, with age at scan, gender and ethnicity as confounders.

<u>Basal Ganglia (BG)</u>: LOWER glutamate levels in Early-ART than uninfected (HU + HEU) children ($\beta = -0.48$ (s.e. = 0.23); p = 0.04) HIGHER choline levels in Early-ART compared to uninfected children ($\beta = 0.05$ (s.e = 0.03); p=0.07)

<i>p</i> =	0.04	
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<u>Peritrigonal white matter (PWM)</u>:

LOWER glutamate levels in Early-ART compared to HIV uninfected children ($\beta = -0.31$ (s.e. = 0.17); p = 0.07)



Midfrontal gray matter (MFGM):

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$(\text{Early}-\text{ART}; \beta = 0.12 \text{ (s.e.} = 0.04); p = 0.003. \text{ Late}-\text{ART}; \beta = 0.11 \text{ (s.e.} = 0.05); p = 0.04)$

HIGHER mean choline levels in HIV-infected children compared to HIV uninfected (HEU +HU) children



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