

# Does antiretroviral therapy before 12 weeks of age preserve neurometabolite levels at 7 years in HIV-infected children? - Evidence from the CHER trial

## QUESTIONS:

- In the 7-year-old brain, are there biochemical differences between HIV-infected and uninfected children in gray matter, white matter or basal ganglia?
- Are there neurometabolite differences between HIV-infected children that started ART before/after 12 weeks of age?

## We find:

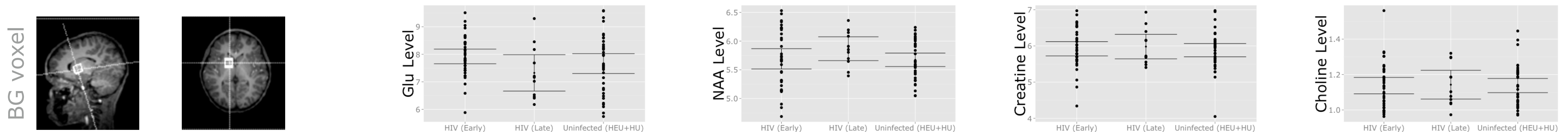
- No group differences in the basal ganglia.
- Lower mean glutamate levels in HIV-infected children in gray matter, driven by children starting ART before 12 weeks of age.
- Higher choline levels in gray matter in HIV-infected children compared to HIV uninfected children.

## STUDY

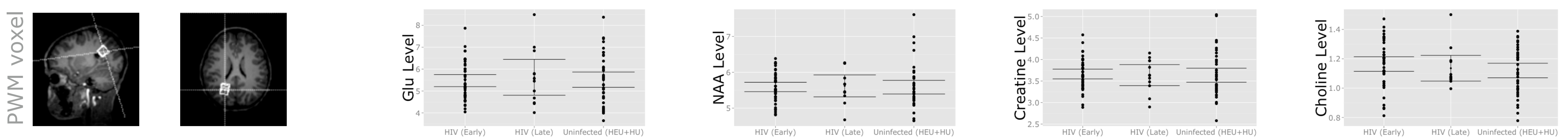
- **Subjects.** Participants included HIV-infected and HIV uninfected 7-year old children. HIV-infected children were stratified into those starting ART at or before 12 weeks of age (Early-ART) or after 12 weeks (Late-ART). The control group comprised matched HIV uninfected (HU) and HIV-exposed, uninfected (HEU) children.
- **Neuroimaging.** The protocol included a high-resolution T1-weighted acquisition and single voxel <sup>1</sup>H-MRS in three brain regions - basal ganglia (BG), mid frontal gray matter (MFGM), and peritrigonal white matter (PWM) - performed on a 3T Allegra MRI Scanner (Siemens, Erlangen, Germany) in Cape Town, South Africa. Absolute metabolite levels calculated with LCModel.
- **Statistics.** The R-programming language was used to examine group differences. We used a linear regression model with age at scan, gender, ethnicity, metabolite standard deviation and signal-to-noise ratio as confounders.

**Subjects.** Fifty-six HIV-infected (13 Late-ART/43 Early-ART; 31 girls; mean age in years  $\pm$  standard deviation:  $7.2 \pm 0.1$ ; 7 Cape Coloured/49 Xhosa) and 45 HIV-uninfected children (27 HU/18 HEU; 20 girls;  $7.2 \pm 0.1$ ; 9 Cape Coloured/36 Xhosa) were analyzed.

## 1 Basal Ganglia: No significant group differences observed.

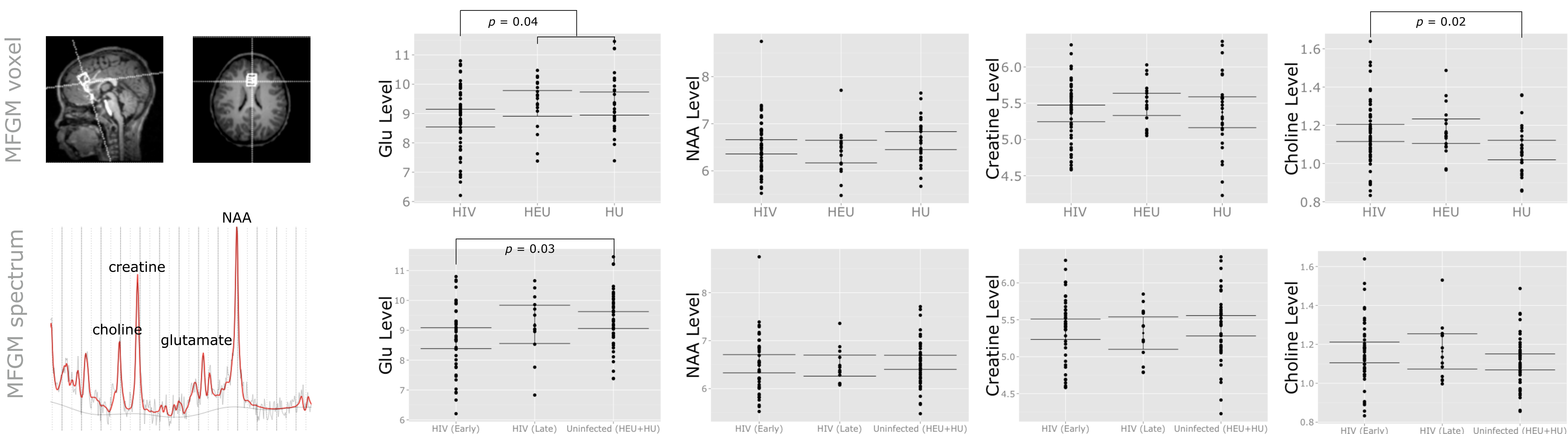


## 2 Peritrigonal white matter: Mean glutamate levels were LOWER in Early-ART group compared to HIV uninfected children ( $\beta = -0.26$ (s.e. = 0.14); $p = 0.07$ ).



## 3 Midfrontal gray matter:

- Mean glutamate levels were LOWER in HIV-infected compared to HIV uninfected (HEU + HU) children ( $\beta = -0.32$  (standard error (s.e.) = 0.15);  $p = 0.04$ ). The main contributor for the difference was in the Early-ART group ( $\beta = -0.37$  (s.e. = 0.16);  $p = 0.03$ ).
- Mean choline levels are HIGHER in HIV-infected compared to HU children ( $\beta = -0.09$  (s.e. = 0.16);  $p = 0.02$ ).



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