

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?
 - Are there neurometabolite differences between HIV–infected children that started ART before/after 12 weeks of age?

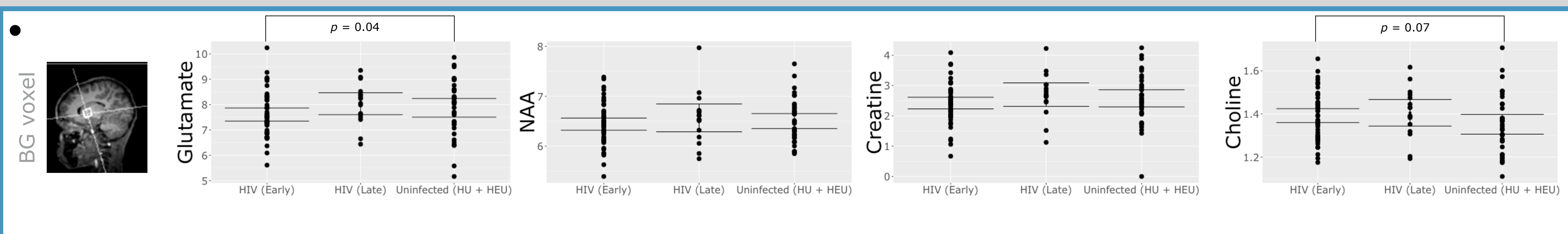
- We find:
- Higher **choline** levels in frontal gray matter in all HIV–infected children.
 - Lower basal ganglia **glutamate** levels only in HIV–infected children starting ART before 12 weeks of age.

STUDY

- **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.

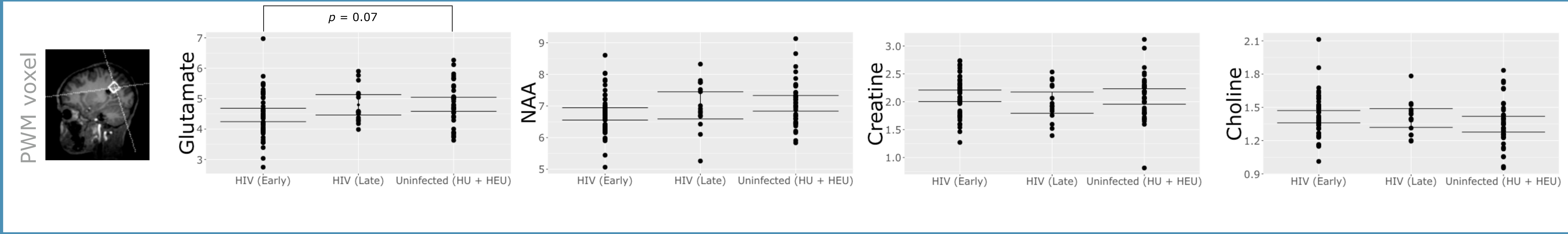
Basal Ganglia (BG):

1 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); $p=0.07$)



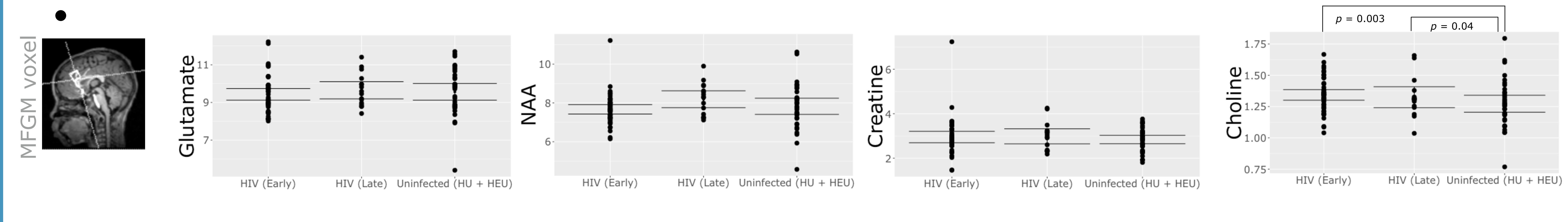
Peritrigonal white matter (PWM):

2 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):

3 HIGHER mean choline levels in HIV–infected children compared to HIV uninfected (HEU +HU) children (Early–ART: $\beta = 0.12$ (s.e. = 0.04); $p = 0.003$. Late–ART: $\beta = 0.11$ (s.e. = 0.05); $p = 0.04$)



FINDINGS