

# HIV exposure effects on the relationship between neuropsychological measures and metabolite levels in the basal ganglia at 7 years

## Introduction

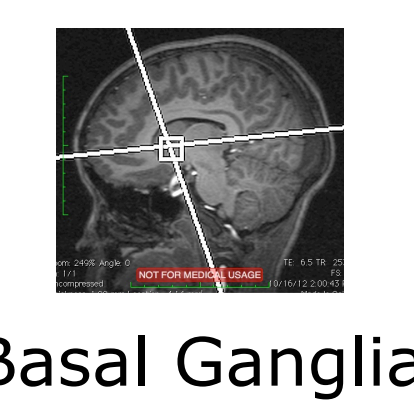
Magnetic resonance spectroscopy (MRS) is a non-invasive neuroimaging technique used to investigate neurological development in children. MRS measures brain metabolite levels, which have been shown to correlate with neuropsychological measures [1,2]. This study is motivated by the burgeoning population of HIV-exposed, uninfected (HEU) children in South Africa - 95% of HIV-positive pregnant women and 68% of HIV-exposed infants have been receiving antiretroviral therapy (ART) [3,4] - and the literature suggesting possible long-term neurological effects observed in HEU children, such as an increased risk of cognitive delay and motor abnormalities [5-8]. The increased risks may involve exposure to HIV antibodies, antiretroviral (ARV) drugs and environmental factors [9].

We examined the metabolites choline (glycerophosphocholine (GPC) and phosphorylcholine (PCh)), and creatine (creatine (Cr) and phosphocreatine (PCr)) in the right basal ganglia (BG). Choline is a marker of cellular density [10]. Creatine is found in neurons and glia, and is associated with energy metabolism [10].

**We explored the relationship between metabolite levels in the BG and neuropsychological measures at age 7, focusing on the potential effects of gender and HIV exposure.**

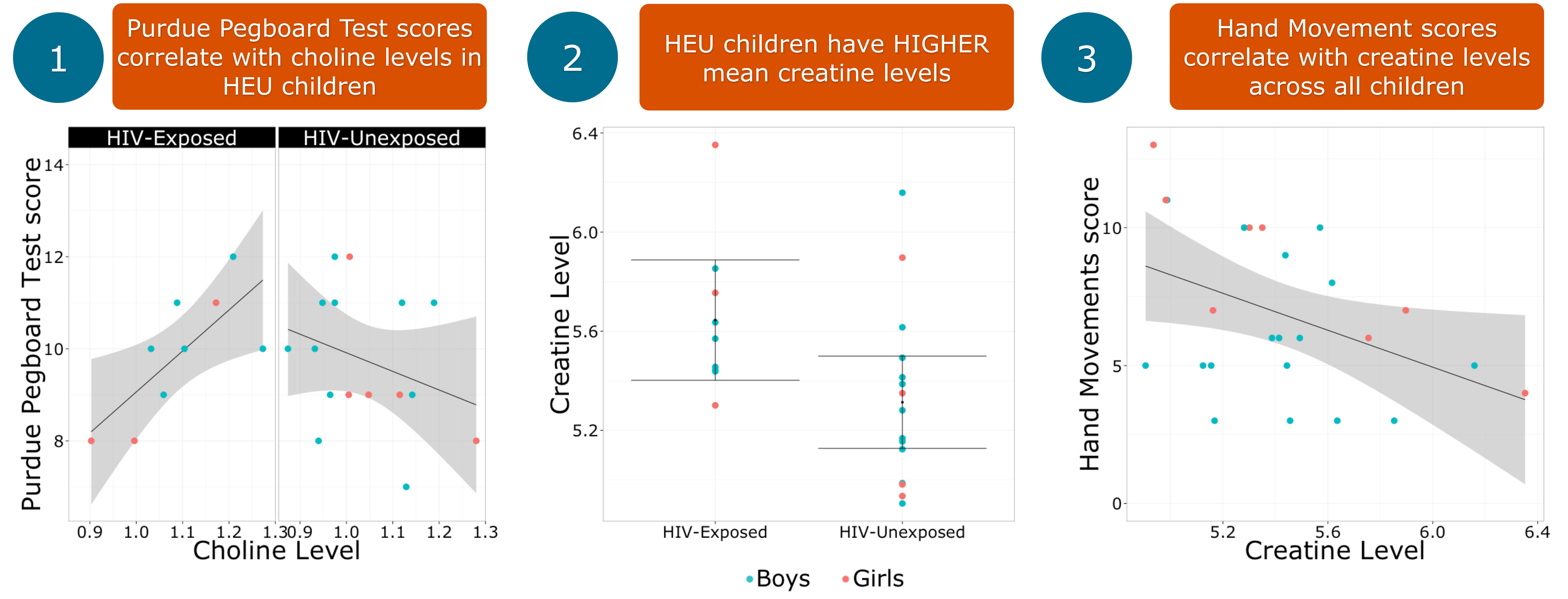
## Study

Single voxel spectroscopy <sup>1</sup>H-MRS data were acquired in the right BG in twenty-five 7-year old HIV-uninfected children, 16 HIV-unexposed (HUU) and 9 HEU, (8 girls; median age (age range): 7 years 3 months (7 years - 7 years 8 months); 6 Cape Coloured/19 Xhosa) were analysed. All HEU children were exposed to treatment for prevention of mother-to-child transmission, 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.



Absolute metabolite levels calculated with LCModel. R was used for statistical analysis. The Purdue Pegboard Test and the Kaufmann Assessment Battery for children 2<sup>nd</sup> edition (KABC-II) [11] was performed (KABC-II subtests standard scores and global Non Verbal Index (NVI) calculated using USA norms). Regression analyses of metabolites done with select KABC-II scales/subtests (Sequential Processing, Learning Ability, Simultaneous Processing, and Hand Movements).

## Results



**Result:** We found a positive relationship between Purdue Pegboard Test (PPT) scores (preferred hand) and choline levels in HEU children only (slope = 9.0,  $p = 0.04$ ).

**Interpretation:** Higher PPT scores (motor dexterity in preferred hand) correlate with higher choline levels *only* among HEU children. Previous studies [12,13] implicate basal ganglia (BG) in poor PPT ability. Choline is associated with cellular density; our result suggests PPT scores are associated with cellular density in BG.

**Result:** We found HEU children have significantly higher mean creatine levels ((HEU)  $5.6 \pm 0.3$  vs (HUU)  $5.3 \pm 0.3$ ;  $p = 0.03$ ). Bars represent confidence intervals.

**Interpretation:** Increased creatine levels among HEU children suggest abnormal energy metabolism in the BG, and may indicate a possible compensatory mechanism.

**Result:** We found an inverse relationship between Hand Movements (HM) scores and creatine levels (slope = -3.4,  $p = 0.04$ ) in all children, driven by girls (slope = -5.2,  $p = 0.01$ ).

**Interpretation:** The relationship between HM scores (visual spatial memory or motor function) and creatine levels is driven by girls. Creatine is expected to be constant across populations, and is rarely examined in relation to pathology, demographics, or cognitive measures.

## SUMMARY

1. Purdue Pegboard Test (preferred hand) scores correlate positively with choline levels in HEU children *only*.
2. HEU children have significantly higher mean creatine levels than HUU children at age 7.
3. Hand Movement scores correlate negatively with creatine levels across all children, driven by girls.

## References

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