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 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 1H-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 (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.

Results

1. Purdue Pegboard Test scores correlate with choline levels in HEU children

Purdue Pegboard Test scores correlate with choline levels in HEU children only (slope = 9.0, p = 0.04).

Interpretation: Higher HPT 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.

2. HEU children have HIGHER mean creatine levels

Hand Motor scores and creatine levels: boys (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.

3. Hand Movement scores correlate with creatine levels across all children

Result: We found HEU children have significantly higher mean creatine levels ((HEU) 5.6 ± 0.3 vs (HUU) 5.3 ± 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.

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