Effects of HIV exposure on metabolite levels in midfrontal gray matter in children: at 5 and 7 years

Introduction
Magnetic resonance spectroscopy (MRS) is a non-invasive neuroimaging technique used to investigate neurological development in children. Many childhood neurological processes include metabolite changes that may correlate with age [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 evidence suggesting possible long-term neurological effects 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].

MRS measures metabolite levels in a small region of interest in the brain. Our study focused on two metabolites - NAA (N-acetylaspartate) and choline (glycerophosphocholine (GPC) + phosphorylcholine (PCh)). NAA is associated with neuronal density and integrity, and increases with age in childhood [1,2]. Choline is related to cellular density and glial integrity, and remains constant throughout childhood [2].

We investigate the possible effects of HIV exposure on metabolite levels in midfrontal gray matter in healthy children at ages 5 and 7.

Study
Single voxel spectroscopy 1H-MRS data were acquired in the midfrontal gray matter (MFGM) in twenty-one 5-year-old (median age (range)): 5 years 4 months (5 years 1 month - 6 years 5 months); 15 Xhosa/6 Cape Coloured; 13 HEU/8 HIV-unexposed, uninfected (HUU)) and thirty-one 7-year-old children (7 years 3 months (7 years 7 years 8 months); 24 Xhosa/7 Cape Coloured; 9 HEU/22 HUU) on a Siemens 3T Scanner (Siemens, Erlangen, Germany) in Cape Town, South Africa. Nine children imaged at both ages.

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.

Results

Absolute metabolite levels calculated with LCModel. R was used for statistical analysis. A mixed effect linear regression model was used for repeated measures.

S U M M A R Y
1. In the MFGM, we observe higher choline levels in HEU children only at age 7.
2. In the MFGM, we observe increasing NAA levels across all children from age 5 to 7, driven by HUU children.

References

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