REDUCED BASAL GANGLIA AND TOTAL GREY MATTER VOLUME IN HIV-EXPOSED UNINFECTED NEONATES

0798

Catherine J Wedderburn,[1,2] Nynke A Groenewold,[2] Annerine Roos,[3] Shunmay Yeung,[1] Jean-Paul Fouche,[2] Andrea M Rehman,[1] Diana M Gibb,[4] Katherine L Narr,[5] Heather J Zar,[2] Dan J Stein,[2] Kirsten A Donald[2]

[1]London School of Hygiene & Tropical Medicine, London, UK; [2]University of Cape Town, Cape Town, South Africa; [3]Stellenbosch University, Stellenbosch, South Africa;

[4]MRC Clinical Trials Unit at University College London, UK; [5]University of California Los Angeles, California, USA

BACKGROUND

Evidence suggests HIV-exposed uninfected (HEU) children have impaired early growth and development compared to HIV-unexposed (HU) children. However, little is known about the neurobiological mechanisms underlying adverse developmental outcomes in this population. We examined the effects of *in utero* exposure to HIV and ART on the neuroanatomy of uninfected neonates in a South African birth cohort.

METHODS

The Drakenstein Child Health Study (DCHS) is a population-based birth cohort in the Western Cape, South Africa.[1] A subgroup of neonates in the DCHS, born after 36 weeks' gestation, without medical comorbidities or neonatal intensive care admission, had magnetic resonance imaging (MRI) at the Cape Universities Brain Imaging Centre, South Africa.[2] Mother-child pairs received HIV testing and ART.



Figure 1. Children from the DCHS (left); Infant in MRI scanner (right). Photos printed with permission.

Acquired structural T2-weighted images were processed using statistical parametric mapping software. Subcortical regions-of-interest were defined using the automated anatomical labelling atlas and volumes were extracted from grey matter segmented images bilaterally. Volumes were compared between groups using multivariable linear regression adjusting for intracranial volume, infant age and sex.

In utero exposure to HIV and ART was associated with abnormal grey matter development in infancy

RESULTS

183 infants in the DCHS had multimodal MRI between October 2012 and September 2015. Following quality control, 146 structural images were included (HEU n=40; HU n=106) (median age 21 days, 51% male). All HEU infants were exposed to ART (88% to maternal triple ART). HEU infants had smaller caudate volumes bilaterally compared to HU (left hemisphere p=0.012, adjusted Cohen's d effect size -0.45 [95% CI -0.82 to -0.09]; right hemisphere p<0.001, adjusted Cohen's d -0.63 [-1.00 to -0.26]). There were no group differences in other subcortical volumes (all p>0.1).

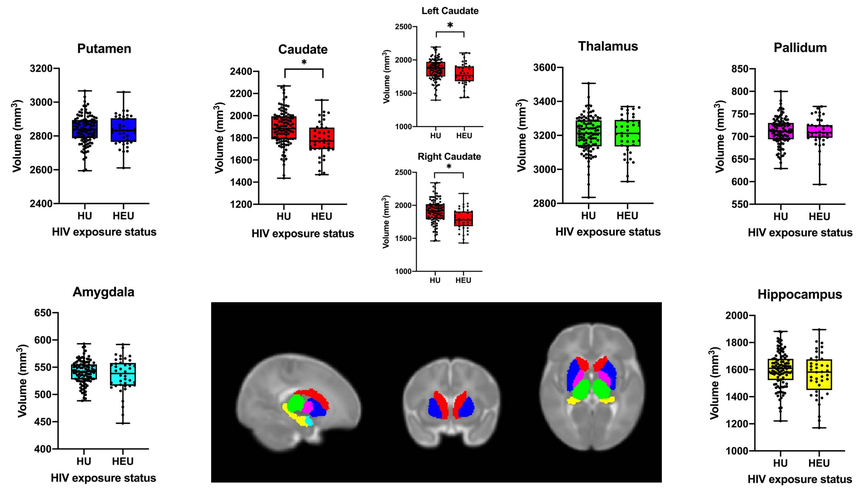


Figure 2. Comparison of subcortical volumes between HEU and HU infants with associated map of brain regions. * p<0.05

RESULTS

Total grey matter volume was also reduced in HEU infants (p=0.035, adjusted Cohen's d -0.33 [-0.69 to 0.04]). The associations remained after further adjusting for maternal age and education, household income, and prenatal alcohol exposure**.** Maternal immunological status was associated with decreased neuroanatomical volumes.

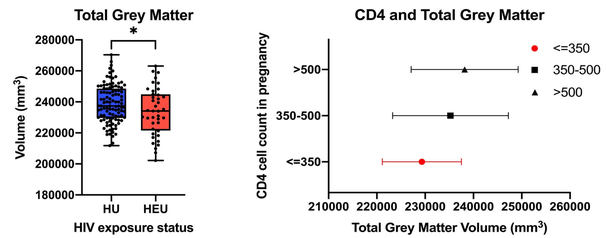


Figure 3. Comparison of total grey matter volume between HEU and HU infants (left); * p<0.05 Association of maternal CD4 cell count with total grey matter volume in HEU infants (right).

CONCLUSIONS

- *In utero* exposure to HIV and ART without infection was associated with smaller basal ganglia and total grey matter volumes in early infancy.
- These findings are consistent with brain regions reported to be affected in HIV-infected children.
- The results suggest that antenatal HIV/ART exposure may impact early brain structural development and maturation.
- This has important implications for understanding the risk of long-term developmental impairment in this population and indicates better antenatal maternal HIV management may improve HEU child neurodevelopmental outcomes.
- Further research will investigate the effects of HIV/ART exposure at older ages.

ACKNOWLEDGEMENTS: DCHS families, children and staff.

ETHICS: University of Cape Town (525/2012; 044/2017) and LSHTM (11903).

REFERENCES: 1. Zar HJ et al. Investigating the early-life determinants of illness in Africa: the Drakenstein Child Health study. Thorax. 2014; 2. Donald KA et al. Drakenstein Child Health Study (DCHS): investigating determinants of early child development and cognition. BMJ Paediatrics Open. 2018. 13;2(1)