Effects of maternal and early-life anaemia on child brain development: a South African birth cohort study

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Introduction

- Anaemia, indicated by low serum haemoglobin, is a prevalent global health concern affecting approximately 273.2 million people worldwide.[1]
- Women are particularly vulnerable with 29% of women of reproductive age and 38% of pregnant women estimated to be anaemic.[1,2]
- This is largely due to chronic iron deficiency, the most common nutritional deficiency worldwide.[3]
- Antenatal maternal anaemia has consistently been associated with poor developmental and paediatric neurocognitive outcomes in multiple settings, including South Africa.[4]
- However, little is known about the effect of anaemia on child brain structure, and the relative influence of antenatal versus postnatal anaemia.

Objectives

We aimed to examine the associations between antenatal maternal anaemia, postnatal child anaemia, and child brain structure using Magnetic Resonance Imaging (MRI) in children at age 2-3 years.

Method: Study Design

Pregnant women were enrolled into the Drakenstein Child Health Study (DCHS) population-based birth cohort.[5] Mother-child pairs were followed prospectively.

Exposure Variable: Anaemia (Haemoglobin; Hb)
- Antenatal maternal anaemia (Hb<11g/dL): Classifications into mild (10.0–10.9g/dL), moderate (7.0–9.9g/dL), and severe anaemia (<7.0g/dL)
- Child anaemia: WHO and local Hb guidelines

Outcome Variable: Child Brain Structure
- T1-weighted MR images: FreeSurfer cortical reconstruction and volumetric segmentation

Method: Statistical Analyses

Linear regression models: Associations between maternal anaemia status and child anaemia status with child brain volumes, adjusting for child age and sex, intracranial volume, maternal education, and household income.

In each brain region where an association was observed (p<0.05), separate multivariable linear regression models were run using standardised regression coefficients for:
- Categorical maternal anaemia severity
- Continuous maternal haemoglobin concentrations
- Mediation analysis: structural equation modelling

Sensitivity analyses: Adjusted for pregnancy trimester, maternal smoking, alcohol, and HIV.

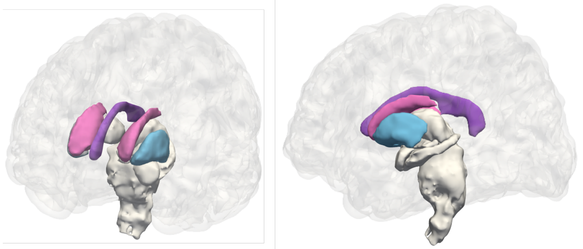
Results

In the neuroimaging sub-group (n=147; mean scan-age 34 months, 56.5% male), 31.3% of mothers were anaemic during pregnancy. Of which:
- 52.2% mild anaemia
- 47.8% moderate anaemia

In the sub-group of children (n=80): 52.5% anaemic

No group differences (p>0.05) in:
- Socio-demographic characteristics
- Maternal smoking, alcohol, and HIV
- Maternal and child anthropometry

Figure 1. Subcortical and corpus callosum volumes associated with maternal anaemia on a cortical surface



*Key: Purple = corpus callosum; pink = caudate nucleus; blue = putamen

Results Continued

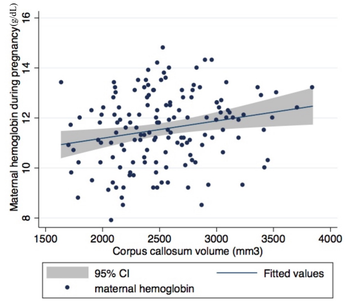
Maternal anaemia was significantly associated with:
- 5.4% volume reduction of the left caudate
- 5.2% volume reduction of the right caudate
- 4.3% volume reduction of the left putamen
- 7.8% volume reduction of the total corpus callosum

Table 1. Adjusted mean differences in child brain volumes by exposure to maternal anaemia in pregnancy

Brain Volumes	Hemisphere / Region	Mean (SD) volume (mm^3) No Maternal Anaemia	Mean (SD) volume (mm^3) Maternal Anaemia	Adjusted Mean Difference (95% CI)	*P*-Value	Effect size Cohen's *d* (95% CI)
Subcortical Regions						
Caudate	L	3302 (533)	3142 (407)	-178.82 (-316.42 to -41.22)	0.011*	-0.35 (-0.70 to -0.00)
Caudate	R	3393 (542)	3241 (406)	-176.76 (-314.11 to -39.41)	0.012*	-0.34 (-0.69 to 0.01)
Putamen	L	4524 (530)	4331 (689)	-195.95 (-380.76 to -11.14)	0.038*	-0.33 (-0.68 to 0.02)
Putamen	R	4558 (528)	4450 (624)	-80.77 (-254.05 to 92.51)	0.358	-0.14 (-0.49 to 0.21)
Corpus Callosum						
Body	NA	1182 (258)	1089 (223)	-96.79 (182.23 to -11.35)	0.027*	-0.38 (-0.73 to -0.03)
Total	NA	2600 (441)	2410 (430)	-201.73 (-345.55 to -57.92)	0.006*	-0.44 (-0.80 to -0.09)

- Results were significant even in mild maternal anaemia.
- Continuous maternal haemoglobin predicted brain volumes (p<0.05).
- Strongest results were evident for the corpus callosum.

Figure 2. Linear regression of total corpus callosum volume by maternal haemoglobin in pregnancy



- No significant relationships between child anaemia and brain volumes (n=80; p>0.05).
- Child anaemia did not mediate the effect of maternal anaemia on child brain structure.

Conclusions

This study provides evidence for the recognition of anaemia in pregnancy as a health priority.

- Maternal anaemia, but not child anaemia, was associated with reduced basal ganglia and corpus callosum volumes in the child brain.
- Maternal anaemia, even when mild, is a significant predictor of child brain volume in these regions.
- Antenatal maternal anaemia may have persistent consequences for the developing brain.
- Findings emphasise the foetal origins of brain health

Implications: Optimising interventions for anaemia during pregnancy may improve child brain outcomes.

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