

# VOLUMETRIC MRI PREDICTS STRUCTURAL CHANGES IN PRETERM INFANT HIPPOCAMPI DUE TO WHITE MATTER INJURY AND STEROID EXPOSURE

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**Introduction:** Preterm birth is known to contribute to perinatal morbidity and mortality with significant risks for adverse long-term neurodevelopment<sup>1</sup>. The impact of perinatal exposures on preterm brain development in relation to long-term neurological impairment remains unclear. Potentially negative factors increasing the risk of injury and/or altered brain development in the preterm brain include respiratory illness and subsequent exposure to postnatal steroids, hypoxia, hypotension, sepsis, inflammation, poor nutrition, and noxious sensory stimuli. Injury or impaired development in the hippocampus may form the basis for impairments in memory and learning in the preterm infant<sup>2</sup>.

**Aims:** This study utilized 3D MR imaging to quantitate and compare hippocampal volumes between term and preterm infants at term equivalent. This research aimed to determine the association between preterm hippocampal volumes and perinatal risk factors as well as neurodevelopmental outcomes at two years' corrected age. We hypothesized that hippocampal volumes would be reduced in preterm infants and that this reduction would be associated with postnatal steroid exposure, white matter injury and immaturity.

**Methods:** Two hundred and two preterm and 36 full term control infants were included in the study. All infants were scanned at term equivalent in a 1.5T GE scanner with two imaging modalities: 3-D T1 spoiled gradient recalled (SPGR) (1.2mm coronal slices; flip angle 45°; Repetition Time (TR) 35ms; Echo Time (TE) 9ms; Field of View (FOV) 21 x 15cm; matrix 256 x 192) and T2 dual echo fast recovery fast spin echo sequences with interleaved acquisition (2mm coronal; TR 4000msec; TE 60 / 160msec; FOV 22 x 16cm; matrix 256 x 192, interpolated 512 x 512). White matter injury was assessed qualitatively and total tissue volumes were calculated from an automated segmentation algorithm<sup>3</sup>. Hippocampal segmentation was performed on coronal slices of a combined t2w and pdw image. Tracing proceeded from the hippocampal tail to the head, according to previously defined anatomical criteria<sup>4</sup> (Figure 1). At two years' corrected age, children underwent the Bayley Scales of Infant Development (BSID-II) assessment for cognitive (Mental Developmental Index, MDI) and motor development (Psychomotor Development Index, PDI). Statistical analyses utilized SPSS 12.0.1.

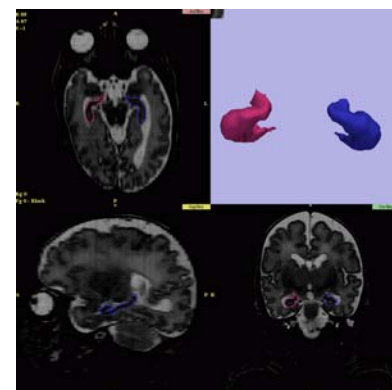


Fig 1. Axial, sagittal, and coronal boundaries of the hippocampi.

**Results:** Preterm infants had a mean gestational age of 27.6 ± 2.0 weeks and birthweight of 965 ± 239 g. Full term infants had a mean gestational age of 38.6 ± 1.5 weeks and birthweight of 3224 ± 546g. The groups did not differ in terms of gestational age at time of scan, and were equal in gender distribution. The hippocampal volume for preterm infants was reduced when compared with full term infants for both hemispheres (Table 1).

Table 1: Right and left hippocampal volumes for preterm and full term infants after controlling for total tissue

	Mean Volume (SD), ml		Mean diff (ml)	95% CI of diff (ml)	Sig
	Preterm	Full Term			
Right	1.13 (0.17)	1.19 (0.14)	-0.06	-0.12, 0.00	P=0.05
Left	1.11 (0.18)	1.14 (0.15)	-0.04	-0.04, 0.03	P=0.2

Moderate or severe white matter injury was associated with reduced hippocampal volume within preterm infants, as determined by multiple linear regression (Right: mean diff -0.17 ml, p<0.0005; Left: mean diff -0.17 ml, p<0.0005). There was also a reduction in preterm hippocampal volume due to postnatal steroid exposure (Right: mean diff -0.16 ml, p= 0.008; Left: mean diff -0.14 ml, p= 0.04), whilst antenatal steroid use increased the volume of the left preterm hippocampi (mean diff 0.10 ml, p= 0.03). Surprisingly, there was no effect due to immaturity, intrauterine growth restriction, or a range of other perinatal exposures within the preterm group. The mean MDI scores for preterm (PT) infants were significantly lower than for full term (FT) infants (PT: 82 ± 19; FT: 101 ± 16, p<0.0005) as were PDI scores (PT: 86 ± 17; FT 100 ± 9, p<0.0005). Preterm infant hippocampal volumes correlated moderately with MDI scores (Right: r= 0.28, p<0.0005; Left: r= 0.27, p<0.0005, See Figure 2) and PDI scores (Right: r= 0.26, p<0.0005; Left: r= 0.25, p= 0.001).

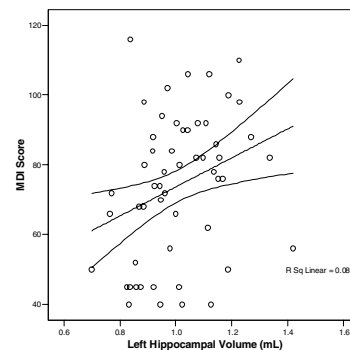


Fig 2. Left hippocampal volume vs. MDI score

**Conclusion:** Preterm infant hippocampal volumes at term were reduced compared with full term infants. Perinatal factors contributing to reduced hippocampal volumes included white matter injury and postnatal steroid exposure. Antenatal steroids tended to accelerate growth of the left hippocampi in preterm infants. Adverse two year outcomes demonstrate that hippocampal insults are not compensated for during early childhood. These findings highlight the need for further investigation of possible intervention strategies to improve hippocampal growth and long-term cognitive performance.

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<sup>2</sup> Isaacs EB, Lucas A, Chong WK, et al. Hippocampal volume and everyday memory in children of very low birth weight. *Pediatric Research*. Jun 2000;47(6):713-720.

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