IMPACT OF PRETERM BIRTH ON HIPPOCAMPAL STRUCTURE UTILIZING VOLUMETRIC MRI TECHNIQUES

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Introduction: Preterm birth is known to contribute to perinatal morbidity and mortality. Improvements in obstetric and neonatal intensive care have resulted in declining mortality rates; however adverse long-term neurodevelopmental outcomes remain common[1]. It is unclear how perinatal exposures are interacting with preterm brain development in order to cause long-term neurological impairment. Potentially injurious conditions external to the environment in which the preterm brain naturally develops include respiratory illness and subsequent exposure to postnatal steroids, hypoxia, hypotension, sepsis and inflammation, poor nutrition, and noxious sensory stimuli. As a result, preterm infants may face cerebral palsy, mental retardation, and other cognitive or motor impairments. Injury or impaired development in the hippocampus may form the basis for impairments in memory and learning in the preterm infant. Volumetric MRI studies in older preterm infants have shown the hippocampus to be reduced in volume and correlated with memory and cognitive function[2].

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, and other perinatal factors such as white matter injury and immaturity.

Methods: Fifty-eight preterm and 22 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 intracranial volumes (ICV) were calculated. 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[3] (Figure 1). At two years' corrected age, children underwent the Bayley Scales of Infant Development (BSID-II) assessment for cognitive functioning (Mental Developmental Index, MDI) and motor development (Psychomotor Development Index, PDI). Statistical analyses were undertaken using SPSS 12.0.1.

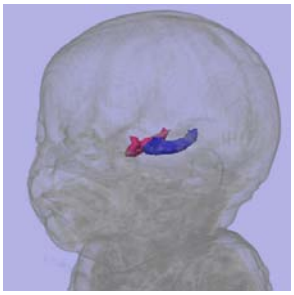

Fig 1. 3D representation of the right and left hippocampi.

Results: Preterm infants had a mean gestational age of 26.4 ± 1.8 weeks and a mean birthweight of 856 ± 206 grams. Full term infants had a mean gestational age of 38.9 ± 1.1 weeks and a mean birthweight of 3342 ± 492 grams. The groups did not differ in terms of gestational age at time of scan, and were equal in gender distribution. There was a striking reduction in hippocampal volume for the preterm infants when compared with full term infants for both hemispheres after controlling for ICV (Table 1).

Table 1. Right and left hippocampal volumes for preterm and full term infants after controlling for ICV

	Mean Volume (SD), ml						
	Preterm	**Full Term**	Mean diff (ml)	95% CI of diff (ml)	F	Sig	Partial Eta^2
Right	1.02 (0.01)	1.19 (0.09)	-0.17	-0.24, -0.11	29.5	p<0.0005	0.28
Left	1.01 (0.15)	1.16 (0.11)	-0.16	-0.23, -0.09	17.0	p<0.0005	0.18

White matter injury was the only perinatal variable associated with hippocampal volume differences within preterm infants, as determined by multiple linear regression (Right: mean diff 0.06ml, p= 0.02; Left: mean diff 0.07ml, p= 0.01). Surprisingly, there was no effect due to postnatal steroids, immaturity, or a range of other perinatal exposures. The mean MDI scores for preterm (PT) infants were significantly lower than for full term (FT) infants (PT: 74 ± 21; FT: 106 ± 13, p<0.0005) as were PDI scores (PT: 80 ± 21; FT 102 ± 10, p<0.0005). Preterm infant hippocampal volumes correlated moderately with MDI scores (Right: r= 0.27, p= 0.05; Left: r= 0.30, p= 0.03, See Figure 2) and to a lesser extent PDI scores (Right: r= 0.25, p= 0.07: Left: r= 0.26, p= 0.06). This trend was diminished once intracranial volume and social risk were corrected for.

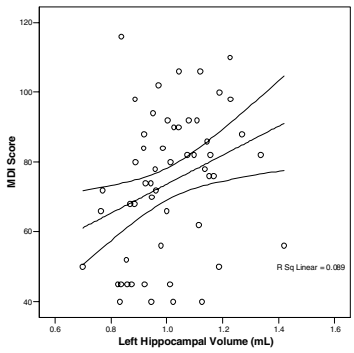

Fig 2. Left hippocampal volume vs. MDI score

Conclusion: Reductions in preterm infant hippocampal volumes at term were associated with reduced cognitive development as assessed at two years' corrected age. There were no defined perinatal factors contributing to reduced hippocampal volumes apart from white matter injury. Hypoxic ischemic injury can contribute to both hippocampal and white matter structural abnormalities, therefore the 'cause and effect' of these factors requires further study. Clearly hippocampal insults are not compensated for during early childhood, as demonstrated by adverse two year outcomes. 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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