Quantitative volumetric analysis of the premature neonatal brain following IVH by using 3T MRI

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Synopsis:
A prospective case control study was conducted to test our hypothesis that uncomplicated intraventricular hemorrhage (IVH) in very low birth weight (VLBW) premature infants, results in a reduction of cortical gray matter (CGM) volume. Volumes of brain regions were measured using three dimensional (3D) magnetic resonance images acquired using a specialized neonatal 3 T IMRIS system. Volumes of cortical gray matter at 34.6-37.1 postmenstrual weeks were found to be significantly reduced in the IVH group compared to controls ($p = 0.03$).

Introduction:
IVH is the most common brain injury in premature infants, the incidence of which still ranges from 20% to 30% of VLBW infants in most neonatal intensive care units. The majority of these cases represent uncomplicated germinal matrix-intraventricular hemorrhage with no parenchymal involvement or posthemorrhagic hydrocephalus. Studies have shown a correlation of these uncomplicated IVH cases to impaired neuro-developmental outcome [1]. It is believed that IVH causes the destruction of the germinal matrix, leading to the destruction of glial progenitor cells. Theoretically, this may result in a disturbance of cortical development [2,3] , which could be manifested as reduced CGM volume. The objectives of our study were (i) to determine whether uncomplicated IVH results in reduced CGM volume in VLBW infants and (ii) to reveal any changes in the volumes of sub-cortical gray matter (SCGM) and white matter (WM).

Design and Methods: Prospective case controlled study.
Patients: Infants with birth weight less than 1501 grams entered the study at 34 to 37 weeks postmenstrual age (PMA) after written parental consent was obtained. Infants with birth weight > 2 standard deviations (SD) below the mean for gestational age, were not included. Infants with congenital infections or brain malformations, hypoxia-ischemia, cystic periventricular leukomalacia, seizures, ongoing sepsis, metabolic diseases, intraventricular hemorrhage with parenchymal involvement and posthemorrhagic hydrocephalus were also excluded. The infants had the MRI scan after routine cerebral ultrasound scans. Infants with no brain abnormality detected in the cerebral ultrasound scans were assigned to the control group and those with evidence of intraventricular hemorrhage were assigned to the IVH group.

Table 1: Patients	Controls(n=3)	IVH(n=4)	p
Gest. Age (wks)	27.4 ± 2.4	27.3 ± 3.5	0.97
Birth Wt (grams)	1096 ± 288	947 ± 420	0.62
Birth HC (cm)	25.1 ± 1.6	24.1 ± 3.2	0.64
PMA at MRI (wks)	35.8 ± 1.1	36.1 ± 0.9	0.67

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Procedure & Image Acquisition: Imaging studies were performed with our dedicated neonatal 3 T MRI system (IMRIS Winnipeg, Canada). A nurse and a neonatologist remained with the infant throughout the procedure. Heart rate and oxygen saturation were monitored and earplugs were used. Also, the image sequences were optimized for low acoustic noise exposure (< 85dB). A single oral dose of Chloral Hydrate 50mg/kg was administered for sedation when necessary. Three dimensional images were acquired in 6.5 min with a centre-out acquisition MP-RAGE sequence [4]. Imaging parameters included TRseg = 5200 ms, TI = 2250 ms, TR = 10 ms, TE = 5 ms, BW = 33.3 kHz, flip angle = 10 degrees, matrix size = 120 x 120 x 75, and FOV = 160 x 160 x 100 mm giving an isotropic resolution of 1.3 mm.

Image Analysis: Analyze 4.0 software[5] was used for image analysis. Segmentation of the CGM from WM was performed manually and segmentation of the SCGM from WM was performed with the auto-trace function of Analyze 4. The analyst was blinded to the subjects analysed. The SD of the intra-observer variability was <3%, as determined by 10 repeated measurements of a single slice.

Results:
The quantitative volumetric analysis of the CGM, SCGM, WM (cerebellum and brainstem not included in the analysis) are presented in table 2. The two groups were compared with one-tailed t test for CGM volume (hypothesis) and two-tailed t test for the other regions. The results show a significant reduction (18%) in the mean volume of cortical gray matter in the IVH group ($p = 0.03$). There was no significant reduction in the relative CGM volume (% of cerebral volume) and there was no difference in the white and sub-cortical gray matter volumes.

Table 2: Results	Controls(n=3)	IVH(n=4)	p
Cortical GM (mls)	136 ± 14.1	111 ± 12.8	**0.03**
CGM % of cerebrum	48.7 ± 4.3	44.4 ± 3.0	0.18
SCGM (mls)	13.6 ± 1.1	12.7 ± 1.2	0.40
WM (mls)	114 ± 15.6	114 ± 5.7	0.93

Discussion:
Using a MP-RAGE sequence we were able to segment and make volumetric measurements of the premature neonatal brain. The volumes in the control group are consistent with previous studies in the literature [6]. Additional subjects and follow-up imaging at later age will provide further significant data to this important question for the brain development after intraventricular hemorrhage.

Conclusion:
The results support our hypothesis that the CGM volume is reduced in the IVH group while the SCGM and WM volumes are unchanged.

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