3D fetal brain volumetry in intrauterine growth restriction

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INTRODUCTION Intrauterine fetal growth restriction secondary to placental insufficiency often results in iatrogenic preterm delivery, and a complicated neonatal period. Although in the intrauterine period these fetuses demonstrate the brain sparing effect where head growth tends to be maintained at the expense of other organs; in the longer term, these children may have neurodevelopmental delay and behavioural disorders indicating compromised brain development that cannot be explained by the complications of premature delivery alone[1]. The cerebellum is increasingly recognised to play an important role in cognitive and behavioural functions and one fetal 3D ultrasound study found a reduction total brain and regional brain growth in intrauterine growth restriction from as early as 24 weeks gestation[2], however intrauterine assessment of fetal brain and cerebellar volume using MRI has been limited by difficulties assessing this in the presence of fetal motion.

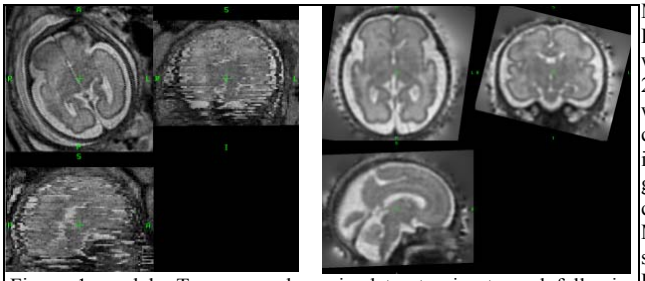

Figure 1a and b: Transverse dynamic dataset prior to and following reconstruction.

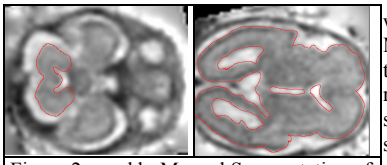

Figure 2 a and b: Manual Segmentation of the cerebellum and Whole brain

METHODS Two groups of women were recruited from Queen Charlotte's and Chelsea Hospital between June 2007 and July 2009. Ethical approval for in utero fetal MR imaging was obtained from the Hammersmith Hospital Research Ethics Committee (Rec No: 2003/6375 and 07/H0707/105). Fetal growth restriction was defined as an estimated fetal weight below the 5th centile in the presence of ultrasound Doppler abnormalities. Exclusion criteria were (1) multiple pregnancy, (2) aneuploidy, (3) fetal growth restriction secondary to in-utero infection, (4) the presence of additional structural abnormalities, and (5) suspected genetic syndromes. We conducted 3-dimensional reconstruction of the fetal brain and calculated total cerebral and cerebellar volumes using a technique described previously as MR snapshot volumetric reconstruction[3]. Data was acquired using dynamic T2 weighted single shot turbo spin echo sequences (TE: 110, TR: 1 500, NSA: 1, matrix: 256 × 272, FOV: 430 × 353 × 88, slice thickness: 2.5mm, slice gap: -1.25mm, acquisition slices: 4 minutes, slices: 64 – 80). 4 loops of transverse data each with full brain coverage, 2 in the sagittal plane, and 2 in the coronal plane were acquired and in each case, all dataset loops were used in the reconstruction process. The 3D reconstruction algorithm was implemented using Matlab software (The Mathworks Inc.) and the registration utilities in ITK software (Department of Computing, Imperial College London). Fetal total brain volume and cerebellar volumes was assessed by manually drawing the region of interest on each slice of the reconstructed brain using MRIcro software. The observers (MD and PP) were blinded to the patient's identity, gestation at scan, and patient group. Total brain volume included white matter, cortical grey matter and deep grey matter. Ventricular space and extracerebral space were excluded from the region of interest. Cerebellar volume included both cerebellar lobes and the vermis. Intra and inter observer variability in calculating fetal brain was between ± 0.1 and 1.3% and between ± 1.3 and 5.9% respectively. Figure 1a and 1b shows the dynamic dataset acquired in a 29 week fetus prior to and following reconstruction. Figure 2a and b show the manual segmentation of the cerebellum and whole brain in a 26.5 week fetus.

SUBJECTS A total of 21 fetuses with growth restriction were imaged using fetal MR. All women delivered fetuses below the 5th centile on customised birthweight charts. The severity of fetal growth restriction was graded in order of increasing severity (1) a pulsatility index (PI) above the 95th centile in the Umbilical Artery (UA) (2) a PI below the 5th centile in the Middle Cerebral Artery as well as a PI above the 95th centile in the UA (cerebral redistribution) (3) absent end diastolic flow in the UA (4) reversed end diastolic flow in the UA and (5) absent or reversed 'a' wave in the Ductus Venosus and/or pulsatility in the Umbilical Vein. One woman had fetal growth restriction severity grade 1, six women grade 2, eight women grade 3, two women grade 4, and four women grade 5.19 women with structurally normal fetuses were scanned once using MR during their pregnancy. All infants were born with a birthweight in the normal range for gestational age (between the 5th and the 95th centile). The gestational age at the time of scan was 26.9 ± 4.3 weeks vs. 29.3 ± 2.6 weeks in the growth restricted and normally grown groups. The gestational age at delivery was 29.9 ± 4.5 weeks vs. 38.6 ± 2.3 weeks. Among the growth restricted pregnancies, 2 patients underwent a termination of pregnancy, 6 patients had an intrauterine fetal death, 12 patients had a livebirth, and 1 patient had a neonatal death. All patients with a normally grown fetus had a livebirth with no neonatal complications.

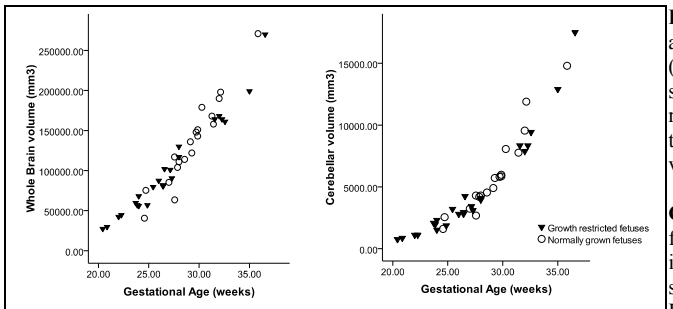

Figure 3a and b: Whole brain and cerebellar volumes against gestational age in growth restricted and normally grown fetuses

RESULTS The SVR reconstruction was successful in all cases examined. There was an increase in whole brain volume (range: 27200 -271000 mm^3) and cerebellar volume (range: 756.6 - 17500 mm^3) in both groups with increasing gestation. There was no significant difference in whole brain volume or cerebellar volume between the growth restricted and normally grown fetuses ($p = 0.93$ and 0.38 respectively after correcting for the effect of gestation). Figures 3a and b demonstrate the whole brain and cerebellar volume across gestation in both groups.

CONCLUSION In this novel study acquiring volumetric MR data from the mobile fetus, we showed that there is no early reduction in either total brain or cerebellar volume in fetuses with intrauterine growth restriction even when the latter is severe. The sample size in our study is relatively small, and a larger study is planned to confirm this finding. Longer term postnatal studies will be needed to determine the natural history of cerebellar development and link to later developmental finding. Serial imaging data can then be compared to results of neurodevelopmental assessment in the surviving infants.

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