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 alone1. 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 gestation2, however intrauterine assessment of fetal brain and cerebellar volume using MRI has been limited by difficulties assessing this in the presence of fetal motion.

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: 003/6375 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 intra-uterine 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 reconstruction3. 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.

RESULTS The SVR reconstruction was successful in all cases examined. There was an increase in whole brain volume (range: 27200 - 271000 mm3) and cerebellum volume (range: 756.6 - 17500 mm3) in both groups with increasing gestation. There was no significant correlation in whole brain volume growth restricted and normally grown fetuses (p = 0.93 and 0.38 respectively) and only when the latter is severe. The sample size in our study is relatively small, and a larger study is planned to confirm this finding. Results 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.

REFERENCES