ISUOG 2020 Abstract: maximum of 2000 characters

Title:

Assessment of Brain Development using Super-Resolution MRI Following Fetal Surgery for Spina Bifida

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Objectives:

To analyse changes in brain development following open spina bifida (OSB) repair, using advanced Magnetic Resonance Imaging (MRI) quantification of volume, surface area, shape, and gyrification of cerebral structures.

Methods:

MRI images of 29 OSB fetuses before fetal surgery (<26 weeks), one week and six weeks post-surgery, were compared to 36 age-matched controls (21-36+6 weeks). Automated super-resolution reconstruction provided 3D isotropic brain volumes. White matter, cerebellum and ventricles were automatically segmented and manually refined; cerebral and cerebellar volume growth/week, surface area, and volume/surface area ratio change per week, were quantified. Shape parameter, an indication of brain complexity, was defined as volume/surface area. In order to quantify the change in gyrification of the brain surface, the change in shape index (SI), was calculated pre, one week, and six-weeks post-surgery. These parameters were further assessed according to lesion type (e.g. myeloschisis (MS) vs Myelomeningocele (MMC)), persistent hindbrain herniation (HH) post-surgery, and presence of additional supratentorial anomalies (e.g. partial agenesis or abnormal corpus callosum (CC), and heterotopia).

Results:

Cerebellar volume growth increased in both groups when imaged <26 weeks. The change was less in MMC fetuses scanned before and one week after surgery compared to controls (median: 419, IQR:188-588 mm^3/week vs 748,IQR:565-838 mm^3/week,$p<0.001$). Six weeks after fetal surgery, MMC cerebellar volume growth was not significantly different to control fetuses. MMC ventricular volume growth and shape parameter change per week were higher at six weeks after surgery compared to control fetuses; (median:3400;IQR:1666-3604 mm^3/week,vs 708;IQR: 435-966 mm^3/week,$p<0.001$), and (median:0.075;IQR:0.047-0.112 mm/week vs 0.022;IQR: 0.009-0.042 mm/week,$p<0.001$). Cases with severe ventriculomegaly and CC abnormalities had persistently higher ventricular volume growth (p=<0.001-0.02) and shape parameter change per week (p=<0.001-0.003) in the six weeks after fetal surgery in comparison to those without these anomalies when compared with controls. In that time period, MMC white matter volume growth increased (median:11446; IQR:10342-11891 mm^3/week, vs 10304;IQR: 8254-11192 mm^3/week, $p=0.048$), whilst shape parameter change per week decreased compared to controls, (median:0.074;IQR:0.058-0.096 mm/week vs 0.1;IQR:0.085-0.140 mm/week, $p= 0.01$). Cases with persistent HH ($p=0.035$), MS ($p=0.024$), and heterotopia ($p=0.027$) had persistently decreased white matter shape parameter change per week compared to those without these abnormalities when compared with controls. There was no detectable cerebral change in SI per week post operatively vs controls, which promotes further work to calculate gyrification for each brain lobe in both hemispheres.

Conclusion:

Six weeks following fetal OSB repair, cerebellar volume growth normalises, whilst ventricular growth, and ventricular and white matter shape parameter change per week remains different compared to controls; particularly in those with additional brain anomalies. These findings suggest that fetal surgery for MMC causes changes in brain development that are in addition to the effects on CSF circulation. These observations may have implications for neurocognitive prognosis.