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Abstract title: Prenatal brain growth impairments predict neurodevelopmental outcome in infants with congenital heart disease

Background: Infants with complex CHD are at increased risk for brain injury and associated neurodevelopmental impairments. We have previously shown that brain growth is impaired in fetuses and neonates with CHD however its impact on neurodevelopmental outcomes remains unclear

Objective: To determine the relationship between delayed in-utero fetal brain development and 18-month neurodevelopmental outcomes in infants with CHD

Study Design/Methods: Women with normal singleton and CHD-complicated pregnancies prospectively underwent two fetal MRI studies in the late second and third trimesters. All newborns (CHD and controls) underwent a neonatal MRI after birth (CHD preoperatively). A 1mm3 isotropic 3D brain image was utilized for automatic segmentation of the cortical/subcortical gray matter, white matter, lateral ventricles, cerebellum and brainstem. Manual corrections were performed using ITK-SNAP software. Operative measures were extracted from patient medical records. Neurodevelopment was evaluated using Bayley, Vineland and M-CHAT at 18-months of age. Linear regression model and generalized estimating equation were used to measure the associations between prenatal and neonatal brain volumes (and operative measures) and neurodevelopmental outcomes in CHD infants

Results: We performed prospective serial studies in 176 subjects: 122 healthy fetal-neonatal control dyads at a mean gestational age (GA) of wks (fetal 32.48, neonatal 41.64) and 54 fetal-neonatal CHD dyads mean GA wks (fetal 32.88, neonatal 39.27) for a total of 437 fetal and neonatal scans. 20 1V and 32 2V subjects were in CHD cohort for total 137 fetal-neonatal scans. We observed significantly lower language, motor, communication, daily living and socialization skills in CHD versus control infants (all $p < 0.05$). Decreased prenatal cerebellar and subcortical gray matter brain volumes were associated with greater impairments in motor skills, expressive language, and overall language composite skills in CHD infants (all $p < 0.05$). Similarly, lower cerebellar, cortical gray and white matter brain volumes were also associated with expressive communication, motor and language composite skills after birth before cardiac surgery

Conclusions: We report for the first time that impaired in utero regional brain growth impairments in fetuses with CHD is associated with delayed motor and expressive language skills at 18 months of age. These data suggest that altered prenatal brain development predicts long-term neurodevelopmental impairments in survivors of open heart surgery