Maternal Obesity Negatively Affects Offspring's Brain White Matter Development

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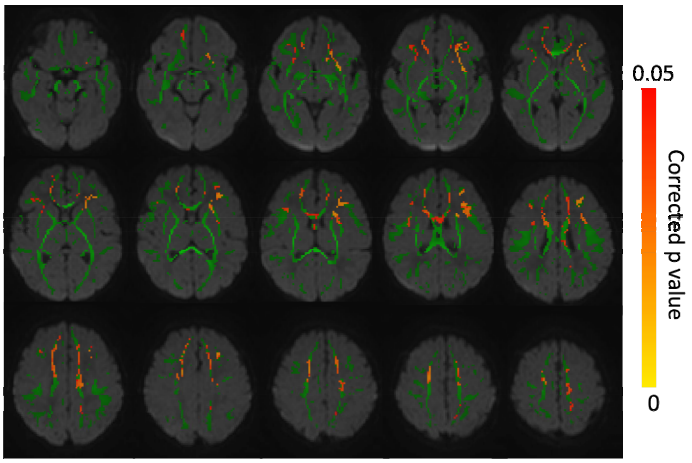
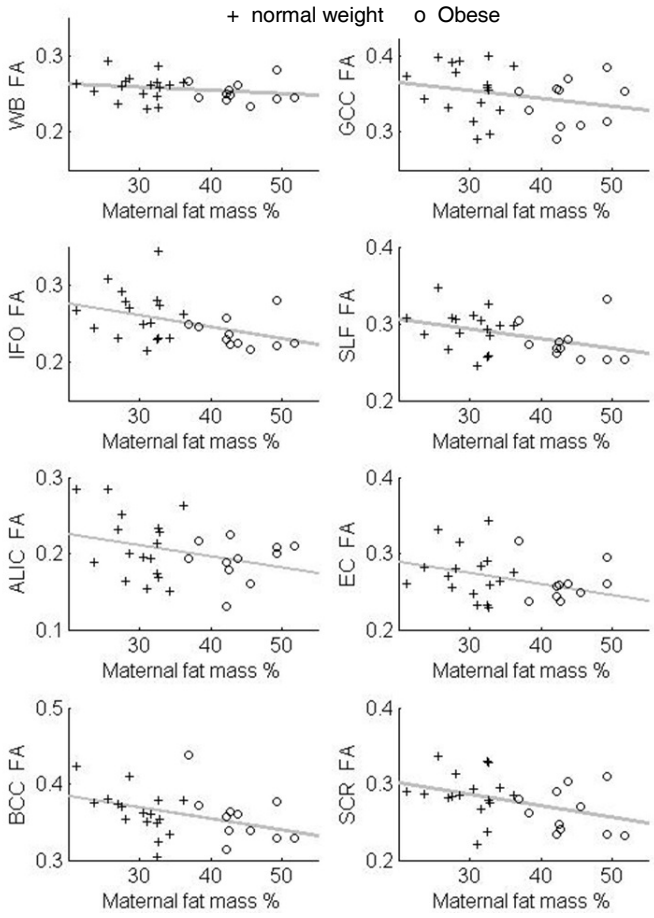
INTRODUCTION: While strong evidence links maternal adiposity with increased risk for childhood obesity and related health concerns, less is known about potential effects of maternal body composition on fetal CNS development. In this study, we employed diffusion tensor imaging (DTI) to examine brain structure in 2-week-old infants born from normal weight and obese mothers.

METHODS: Twenty-eight full-term, appropriate for gestational age infants born to normal weight mothers (BMI<25, N=17) and obese mothers (BMI>30, N=11) who had uncomplicated pregnancies were studied. All mothers were non-smokers, without gestational diabetes mellitus, pre-eclampsia or other pregnancy complications. Maternal body composition was measured using air displacement plethysmography within the first 10 weeks of gestation. Birth weight and length were self-reported. Infant's weight, length and head circumference were measured using standardized methodology at age two weeks and MRI examinations of their brain were performed. The infants were fed, swaddled in warm sheets, and immobilized using a MedVac Infant Immobilizer prior to the MRI. No sedation was used. The MRI examinations were performed on a 1.5 Tesla Philips Achieva MRI scanner with a single shot spin echo planar imaging sequence with acquisition voxel size 2 mm x 2 mm x 3 mm and diffusion weighting gradients (b = 700 s/mm^2) uniformly distributed in 15 directions. The fractional anisotropy (FA) maps for each infant were computed and preprocessed for DTI tract-based spatial statistics (TBSS) analysis by FSL. Specifically, FA data sets were aligned to identify the most representative one that subsequently served as the target, and then nonlinear transforms were performed to register each FA data set to this target. All FA images were merged, averaged, and entered into a skeletonisation program to create a mean FA skeleton in which a threshold of FA ≥0.15 was chosen. Finally, randomization with threshold-free cluster enhancement (TFCE) option and 5000 permutations was used for the voxel-wise comparison of FA values between the maternally normal weight and obese groups. The analyses were corrected for multiple comparisons and adjusted for gestational weight gain, infants' gender, birth weight, length, head circumference, infant diet, and postmenstrual age at MRI, which were included as covariates during the randomization. In addition, correlation between mean FA in the whole brain (and in several white matter regions) and maternal fat mass percentage were evaluated. Spearman's rank partial correlation coefficient was calculated and P<0.05 after controlling for all covariates was regarded significant.

RESULTS:



Left images: Voxel-wise TBSS analysis showed that offspring from normal weight mothers have widespread white matter tracts with higher FA values (P<0.05, corrected) than offspring from obese mothers. The mean skeleton of major white matter tracts (green) for all infants is overlaid on raw DTI images. Orange/yellow color on the skeleton represents regions with significantly higher FA in offspring born of normal weight mothers.



Right plots: Mean FA values in whole brain white matter and in specific white matter regions significantly and negatively correlated with maternal fat mass percentage: whole brain (WB, r=-0.51, P=0.02); genu of corpus callosum (GCC, r=-0.58, P<0.01); inferior frontal-occipital fasciculus (IFO, r=-0.57, P<0.01); superior longitudinal fasciculus (SLF, r=-0.57, P<0.01); anterior limb of internal capsule (ALIC, r=-0.43, P=0.05); external capsule (EC, r=-0.50, P=0.02); body of corpus callosum (BCC, r=-0.71, P<0.01); and superior corona radiata (SCR, r=-0.51, P=0.02).

CONCLUSIONS: Our results demonstrated that term infants from uncomplicated pregnancies of otherwise healthy obese women have lower white matter development (as indicated by lower FA values) than those born of normal weight mothers. White matter development in newborn infants negatively correlated with maternal adiposity. The mechanisms underlying these effects and their consequences are under investigation.

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