Maternal prenatal stress programming of fetal neuroconnectivity

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BACKGROUND: Intrauterine exposure to stress is hypothesized to impact fetal brain and emergent function, but evidence in support of this supposition is currently lacking. We examine the hypothesis that the organizational efficiency of neural functional circuitry will be reduced in fetuses of mothers high in cumulative prenatal stress, and that this difference in efficiency will be observable in utero.

METHODS: We examined the effect of maternal prenatal stress on fetal brain functional connectivity using resting-state fMRI in N=47 fetuses. Maternal self-report measures were submitted to exploratory and confirmatory latent factor analyses to produce a robust, representative factor of cumulative stress burden. Fetal fMRI data were submitted to graph theoretical analyses. The association between stress and neural efficiency was tested in a multi-level model that included age, motion, and gender as covariates.

RESULTS: Scales from five questionnaires assessing maternal stress were best represented as single latent factor, showing high loadings and good model fit ($\chi^2=10.23$, df=5, $p=.07$; CFI=.98; TLI=.96; RMSEA=.087, SRMR=.03). Structural equation examination confirmed construct validity of the derived stress factor relative to relevant demographic variables and other indices of poor psychosocial functioning. Maternal stress, represented as a single latent factor was significantly negatively correlated with normalized neural efficiency of fetal brain functional networks.

CONCLUSIONS: For the first time, we report that maternal prenatal stress exerts intrauterine programming of in vivo human neural functional networks. This discovery has implications for transfer of risk via early brain programming, which may be relevant to long-term psychiatric health.

Keywords: fetal, connectivity, MRI, pregnancy, resting-state

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