Diminished neural connectivity in fetuses that will subsequently be born preterm

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Background: While it is known that infants and adults born preterm manifest diminished connectivity in functional brain circuitry and more frequent incidence of neurodevelopmental impairment, data collected postnatally cannot resolve the origin of these differences. Examinations of human brain networks at or after preterm birth are confounded by potential insults conferred both by the absence of neuroprotective elements and addition of neurotoxic influences, which are inherent conditions of early delivery. The recent development of resting-state fMRI (rs-fMRI) methodology for the human fetus offers the first opportunity to investigate altered functional connectivity prior to birth, to determine whether neurological challenges associated with preterm birth have intrauterine origins.

Methods: Thirty-two women, mean age 25.3 years, SD, 5.6, participated in a fetal brain functional MRI study between their 22nd and 36th week of pregnancy. Neural functional connectivity was compared between term-born (N=18) and preterm-born (N=14) fetuses. After movement censoring and preprocessing, functional connectivity of each voxel was measured using intrinsic connectivity distribution (ICD). Areas of group ICD difference were followed up using seed-based connectivity analyses.

Results: Strength of connectivity was greater in term-born fetuses in a substantial area of the left hemisphere, proximal to what will later become Broca’s area. In contrast, there were no areas in which connectivity was greater in those later born preterm. We found that diminished functional connectivity was also linked to individual differences in the preterm group, suggesting that maturation of brain circuitry may be associated with the circumstances of an individual pregnancy.

Conclusions: Results demonstrated that neurological connectivity differences associated with human preterm birth begin in utero, prior to the potentially injurious experiences of early delivery. These constitute the first human data to suggest that disabilities frequently accompanying extreme prematurity, such as autism and ADHD, may derive from pre-existing intrauterine neurological conditions, especially given that these disorders have neuroconnectional bases.