Heterogeneity in Maternal Stress Trajectories Relates to Offspring Brain and Behavior

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Maternal prenatal stress (MPS) has been linked to increased risk for development of psychiatric disorders in offspring. Most studies primarily consider the overall level or magnitude of MPS as the risk factor; however, less is known about how the timing and pace of MPS change over pregnancy (i.e., the trajectory) affect brain systems and behavioral phenotypes in infancy. This study examined the relationship of MPS trajectories and magnitudes to perinatal amygdala functional connectivity and negative affect development over the first two years of life.

Methods: Here maternal stress was assessed at each trimester and 1 month of infant age using the Perceived Stress Scale, State Trait Anxiety Inventory, and Center for Epidemiological Studies Depression for 115 maternal-infant dyads. MPS trajectories were created for the pre- and perinatal period using our new algorithm called the Functional Random Forest. Perinatal resting state functional connectivity (rs-FC) MRI of the amygdala-anterior insula (Am-aI) and amygdala-ventromedial prefrontal cortex (Am-vmPFC) were examined relative to MPS trajectories. In addition, infant negative affect was assessed at 3, 6, 9, 12, & 24 months using the Infant Behavior Questionnaire-Revised and compared to MPS trajectories.

Results: Four distinct MPS trajectories were identified with our Functional Random Forest algorithm. In addition, our approach identified a split in MPS by magnitude. The MPS trajectory that was characterized by peak stress during the 3rd trimester predicted increased rs-FC for Am-aI and Am-vmPFC ($p=0.02$). The MPS trajectory characterized by increasing stress across the 3rd trimester predicted increased rs-FC Am-vmPFC as well as a smaller increase in infant negative affect from 3 - 24 months. MPS magnitude predicted higher infant negative affect at 3 months.

Conclusions: Overall, we show that heterogeneity in MPS can be characterized by both magnitude and trajectory over the pre- and perinatal period. This characterization is associated with both perinatal functional connectivity of limbic systems and infant negative affect development over 24 months of age. These data highlight that the trajectory, in addition to the magnitude, of MPS may contribute to offspring brain and affective development. Work is ongoing determining biologic correlates of these findings (e.g., maternal inflammation) in both human and animal models.

Funding: NIH MH105538; OD023349; MH111805