

Early Adversity, Neonatal Amygdala and Striatal Connectivity, and Early Childhood Psychopathology

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Early life adversity including exposure to stressors during the perinatal period can alter early brain development. Brain regions underlying emotion regulation and reward processing, commonly linked to risk of later substance use, are vulnerable to this early adversity. Prior work has demonstrated that alterations in functional and structural brain connectivity can be reliably detected in the neonatal brain.^{1,2} Further, variability in neonatal brain connectivity can predict early impairment in social-emotional domains that can place one on a trajectory for later substance use behaviors. This presentation will detail the pattern of amygdala-medial prefrontal cortex and fronto-striatal connectivity at birth in an infant sample enriched for early life adversity. Additionally, neonatal connectivity will be linked to later dimensional measures of childhood externalizing and internalizing symptoms known risk factors for later substance use.

Methods: Preterm and full-term infants from a longitudinal cohort study underwent MRI on a 3T scanner at term-equivalent age (36-42 weeks post menstrual age) with diffusion MRI and resting state fMRI sequences acquired. Structural connectivity was measured using diffusion tractography and whole brain functional connectivity analyses were conducted with seeds placed bilaterally in the amygdala and striatum. Children returned at age 2 years and at age 5 years for assessment of their social-emotional development and symptoms of psychiatric disorders as well as behavioral assessments. Measures of early life adversity including socioeconomic status and maternal psychosocial functioning were obtained during the perinatal period ant at ages 2 and 5 years.

Results: Amygdala and striatal functional connectivity detected in neonates followed connectivity patterns similar to those in older children and adults including functional connections with the medial prefrontal cortex, anterior cingulate, and insula. Functional connections between the amygdala and striatum and these cortical regions predicted internalizing and externalizing symptoms during early childhood. Neonatal structural connectivity of white matter tracts connecting these regions including the cingulum, uncinata, and anterior limb of the internal capsule were also related to variability in these symptoms. Measures of early life adversity appeared to mediate some of these relationships

Conclusions: These analyses suggest that functional connectivity of circuits relevant to substance use disorders are detectable near birth. The connectivity of these brain circuits during the neonatal period relates to early emergence of impairments in developmental domains that increase risk of substance use in later childhood and adulthood with some variability linked to early life adversity.

References: 1. Rogers CE, Smyser T, Smyser CD, Shimony J, Inder TE, Neil JJ. *Pediatr Res.* 2016;79(1-1):87-95. doi:10.1038/pr.2015.172; Sylvester CM, Smyser CD, Smyser T, Kenley, J, Ackerman, JJ, Shimony, JS, Petersen SE, and Rogers, CE. Cortical Functional Connectivity Evident After Birth and Behavioral Inhibition at Age 2. *Am J Psychiatry.* 2018;175(2):180-187.

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