Resting State Functional MRI in Neonates with Prenatal Opioid Exposure: Analysis of Thalamocortical Functional Connectivity

Zoe Guckien[1], Jonathan Dietrich[1], Ramana Vishnubhotla[2,3], MaKayla Picklesimer[2], Christina Sparks[4], David Haas[5], Senthilkumar Sadhasivam[4], Rupa Radhakrishnan[2,3]

[1]Indiana University School of Medicine; [2]Indiana University School of Medicine, Department of Radiology and Imaging Sciences; [3]Riley Hospital for Children at Indiana University Health, Department of Radiology and Imaging Sciences; [4]Indiana University School of Medicine, Department of Anesthesia; [5]Indiana University School of Medicine, Department of Obstetrics and Gynecology;

Background/Objective: Prenatal opioid exposure (POE) is a growing public health issue that can result in premature birth, Neonatal Abstinence Syndrome (NAS), and adverse neurodevelopmental outcomes. However, the neural basis for these findings remains relatively unknown. In this study, we aimed to investigate the neural correlates of POE based on neonatal thalamocortical functional connectivity using resting state functional magnetic resonance imaging (rs-fMRI).

Methods: In this prospective, IRB-approved study, nineteen neonates with POE and twenty opioid naive (ON) controls underwent non-invasive MRI during natural sleep at mean post-menstrual age (PMA) of 44.7 ± 2.6 and 44.6 ± 2.6 weeks respectively. MR imaging included anatomic T2-weighted images and rs-fMRI. General Linear Model (GLM) seed-based whole brain functional connectivity analysis was performed for each subject, with the right and left thalamus as distinct seed regions. Unpaired mixed-effects group analyses between POE and ON groups were conducted for each seed region corrected for PMA and sex.

Results: Thalamic connectivity to cortical and subcortical structures differed in the POE group compared to the ON control group. The POE group exhibited higher functional connectivity to deep gray structures, frontal, medial prefrontal, parietal, occipital, and anterior temporal cortices compared to controls. The POE group exhibited lower connectivity to the nuclei accumbentes, bilateral caudate nuclei, posterior cingulate gyri, superior frontal gyri, insular, and dorsolateral prefrontal cortices.

Conclusion and Potential Impact: Overall, these novel results suggest the presence of opioid exposure-related alterations in thalamic functional connectivity. Given that the thalamus plays a crucial role in early brain development, the described alterations in thalamocortical and thalamic-subcortical connectivity may have implications in stratifying risk and informing treatment for the adverse neurodevelopmental outcomes associated with POE. Future studies should explore the relationship between POE-associated disruptions in thalamic connectivity and developmental outcomes.