

R01 DK137899 (PI: Shan Luo) 8/1/2024-7/31/2029

NIMH

Effects of Maternal Diabetes on Early Brain Development

Role: site-PI

Total Award Amount: \$3,053,040

Collaboration with USC

Abstract: One in every five youth are living with obesity, placing them at increased risk for developing diabetes and cardiovascular disease. Identifying risk factors contributing to obesity is extremely critical so that prevention strategies can be taken early to mitigate the obesity risk. Maternal diabetes in pregnancy is a strong risk factor for offspring obesity. Multimodal neuroimaging has the potential to reveal important mechanistic insights into the link between prenatal exposure to maternal diabetes and offspring obesity, but most existing studies possess major flaws including: 1) cross-sectional design evaluating later developmental periods, introducing uncertainty around the influence of other perinatal exposures; 2) poor accounting for the effects of maternal obesity; 3) low statistical power and overly homogeneous populations; and 4) use of a single imaging modality, limiting our ability to understand the complexity and full scale of brain abnormality associated with exposure to maternal diabetes. By integrating noninvasive structural and functional magnetic resonance imaging (MRI) with developmental neuroscience techniques and targeting the critical period of development, the first 1000 days of life, we aim to test the hypothesis that prenatal exposure to maternal diabetes will be independently associated with altered brain development during very early childhood, and that maternal obesity will further exacerbate these effects. We further hypothesize that these brain alterations will contribute to a higher risk of obesity early in life. To explore this hypothesis, the applicant, and her team plan to leverage longitudinal brain and body weight and length data during the first ~1000 days of life from 8 existing cohorts that participated in NIH-funded The Organization for Imaging Genomics in Infancy (ORIGINs) consortium, part of the Enhancing Neuroimaging Genetics through Meta-analysis (ENIGMA). We aim to examine effects of maternal diabetes exposure either separately or together with maternal obesity on brain metrics at birth (Aim 1) and brain developmental trajectories from birth to 2-3 years of age (Aim 2). Furthermore, we will discriminate exposed vs. un-exposed offspring (Aim 3) with replication by using innovative machine learning algorithms and identify multi-modal imaging markers that predict obesity by age 2-3. This will be the largest and most highly powered neuroimaging study to identify robust multi-modal brain signatures of prenatal exposure to maternal diabetes, thereby enhancing our understanding of etiologic/causal pathways of obesity development.

Dr. Zhu specializes in multi-modal imaging and deep learning methods. She developed the Latent Variables Visualization Toolbox, which will be used to interpret learned latent features. Additionally, her expertise in deep learning is crucial for multi-modal data fusion, enabling the discrimination of exposure status and the prediction of offspring obesity.

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