Sex-Specific Epigenetic and Behavioral Outcomes of Prenatal Stress in Parvalbumin-Expressing Interneurons

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The prenatal period is a critical time for development, and prenatal stressors can significantly alter later-life outcomes[1]. Both human and animal studies have shown that prenatal stress (PNS) has molecular and behavioral effects on later life outcomes[2,3]. This research project aims to elucidate how PNS leads to sex-dependent behavioral and molecular changes in a preclinical rat model.

Broadly, the Honeycutt RAT Lab aims to identify the impact of early life stress on anxiety-like behaviors that may develop later in life; my project furthers this goal by examining the effects of PNS—a novel paradigm in the lab—and its impact on the fetal development and later life outcomes of rats.

To invoke mild chronic stress in the pregnant Sprague-Dawley rat mothers (dams), a restraint stress paradigm was used during a specific gestational period, corresponding to the second trimester. For the restraint stress, 4 pregnant dams were placed into rigid plastic restraint tubes for 3 40-minute sessions, daily for a week. The goal of this stress procedure is to activate the hypothalamic-pituitary-adrenal (HPA) axis, which is responsible for releasing corticosterone during times of stress.

Literature shows that corticosterone release can impair the development of parvalbumin-expressing interneurons (PV^+ cells)[2,4]. These cells are of particular interest because they are involved in the regulation of brain circuitry, preventing overexcitation of brain regions that are involved in anxiety response[3]. Disruption in the development of PV^+ cells and thus decreased expression is a key mechanism in early life adversity-induced stress.

To effectively test behavioral outcomes in the different cohorts, I used the open field test (OFT) with ultrasonic vocalization (USV;22 kHz) playback. The USV playback mimics distress calls from other rats, invoking anxiety in the rat being tested. This assay allows me to see displays of anxiety-like behavior which are aggregated by condition (control or PNS) and sex (male or female).

For molecular testing, the brains of the rats were perfused and collected post-sacrifice of the rats. The brains were sliced into thin sections, displaying key brain regions associated with PV+ cell circuitry in anxiety (prefrontal cortex, basolateral amygdala, e.g.). In a future project, these brain slices will be stained and imaged using immunohistochemistry to study the localization of PV^+ cells and correlate these findings with the behavioral data.

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