### Title

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# P142. Impact of Unpredictable Maternal Sensory Signals During Early Development on Adolescent Functional Connectivity of the Paraventricular Nucleus of the Thalamus

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**Background:** Emotional circuit maturation is shaped by sensory signals in the environment during early life. For example, unpredictable parental and environmental sensory signals (high entropy) during early life result in increased hippocampal synaptic pruning and enduring changes in emotional circuitry in rodents. In humans, exposure to such high entropy during infancy is associated with deficits in memory and executive control during childhood and adolescence. Maturation of emotional circuitry is dependent on the integration of numerous processes in several circuits, all involving the paraventricular nucleus of the thalamus (PVT). Indeed, there is growing evidence that the PVT contributes to storing memories of salient experiences over long durations, such as memories of early life adversity. However, PVT connectivity in humans has not yet been evaluated prior to adulthood, and the impact of early life entropy on the development of PVT connectivity to key nodes of emotional circuitry during childhood and adolescence is largely unknown.
**Methods:** Maternal sensory signals during mother-child interaction were video-recorded and coded at 6 and 12 months age. The predictability of these signals during the interaction was characterized by calculating state transition probabilities (likelihood the mother would change from one sensory signal to another), computing the entropy associated with the transition probabilities, and averaging between the two sessions (as previously described). Two fMRI imaging sessions were conducted during childhood and early adolescence (n = 37, 16 females, 21 males, 9-13.7 years). Six bilateral regions of interest were selected a priori based on the PVT circuitry in rodent literature, including: the anterior cingulate cortex (ACC), amygdala, bed nucleus of the stria terminalis (BNST), hippocampus, locus coeruleus, lateral hypothalamus (LH), and nucleus accumbens (NAc). Measures of functional connectivity between these regions and the PVT were considered in six independent mixed effects models testing for a main effect of entropy adjusted for age at scan and sex.
**Results:** There was a negative association of entropy with the functional connectivity between the PVT and bilateral LH (T-stat = -2.71, p-uncorrected = 0.0089) and BNST (T-stat = -2.22, p-uncorrected = 0.0308). Functional connectivity between the PVT and NAc (T-stat = 2.65, p-uncorrected = 0.0105) and between the PVT and ACC (T-stat = 2.62, p-uncorrected = 0.0114) was higher in females compared to males of the same age.
**Conclusions:** Unpredictable maternal signals during infancy, reflected here as high entropy, may contribute to the development of PVT functional connectivity to the LH and BNST. In rodents, the lateral hypothalamus to PVT projection plays a role in arousal and reward learning, while the BNST to PVT connections may contribute to anxiety behaviors. The sex effects observed here may be due to sex-differences in pubertal timing during adolescence. Future work will employ large, publicly available datasets to further characterize the development of PVT circuitry and its putative role in mediating the effects of diverse early-life factors in the development of mental illness.
**Keywords:** Paraventricular Nucleus of the Thalamus, Entropy, Unpredictability, Resting State Functional Connectivity, Early-Life Experience
**Disclosure:** Nothing to disclose.