NORTHERN HEALTH RESEARCH CONFERENCE

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Effect of Prenatal Glucocorticoid Exposure on Circadian Rhythm Gene Expression in the Brains of Adult Rat Offspring

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ABSTRACT:
Circadian clocks developed in organisms as a way of estimating time of day. In mammals, the circadian clock is based on molecular oscillators that operate through transcriptional-translational feedback loops. Normal circadian signaling relies on a 'master clock', in the suprachiasmatic nucleus (SCN), to synchronize peripheral oscillators to environmental light. Glucocorticoid receptor (GR) signaling, however, has the ability to reset peripheral clocks. GR is responsive to cortisol and is central to the regulation of genes involved in stress response, immune regulation and metabolism. Phase shifts allow peripheral clocks to become uncoupled from the master clock. The SCN does not express GR and this ensures it stays tied to the light-dark cycle. It has been shown that maternal exposure to glucocorticoids (GCs) can lead to modification of hypothalamic-pituitary-adrenal (HPA) function and impact stress-related behaviours via GR activation. While exploring the effects of prenatal GC exposure on rat offspring, our lab previously demonstrated altered circadian rhythm signaling in the adrenal glands using whole transcriptomic profiling. Pregnant WKY rats were given daily subcutaneous injections of 0.1 mg/kg/day DEX (Dexamethasone, a synthetic GC), or a saline vehicle throughout the third semester, and offspring sacrificed at 18 weeks of age. Brain regions were isolated through a micropunch technique and RNA extracted. Results from the current study show prenatal GC exposure affects circadian rhythm gene expression in molecular oscillators of the amygdala, hippocampus, prefrontal cortex, paraventricular nucleus as well as the main oscillator in the SCN. Transcripts of circadian rhythm genes in these tissues were measured through RT-qPCR and demonstrated both sex and tissue specific alteration in expression of circadian genes. This widespread dysregulation of the circadian rhythm system points to a mechanism whereby the dysfunction in the adrenal gland arises from a programmed dysregulation of the entire circadian system beginning with the master clock.