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Transcriptomic adaptations in emotional and sensory brain nuclei in perinatal fentanyl exposed rodents

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Since the early 2000s, there has been an increase in opioid consumption within the US, including among pregnant women. Use of the synthetic opioid fentanyl has increased ~300% within the last decade. However, little is known about the molecular mechanisms underlying fentanyl use particularly during brain development. Using a rodent model of perinatal fentanyl exposure, we previously demonstrated a lasting emotional and sensory deficit at adolescent and adult ages, consistent with human findings. In the present study, our aim is to understand the neurobiological mechanisms occurring with developmental fentanyl exposure. We use a Multi-omic sequencing approach to investigate the transcriptional programs dysregulated in fentanyl use in a brain tissue specific manner. Fentanyl was administered in drinking water of pregnant dams from embryonic day 0 through gestational periods until weaning at P21. Tissue punches were collected from 5 brain areas from juvenile aged mice (~P35) and processed for RNA-sequencing. Brain regions analyzed include emotional/reward brain regions: nucleus accumbens (NAc), ventral tegmental area (VTA), prelimbic (PrL) region of the prefrontal cortex and sensory brain regions: primary somatosensory cortex (S1) and ventrobasal (VB) thalamus. These experiments were performed in both sexes as we had observed sex differences in some of the lasting behaviors. We identified differentially expressed gene sets, and performed enrichment analysis, weighted gene coexpression network analysis (WGCNA), and upstream transcription factor analysis. We observed sex driven differences in differentially expressed gene sets within all brain regions analyzed. We identified upstream transcriptional programs and hub genes that could mediate the lasting behavioral changes in fentanyl use. Collectively, our studies are identifying unique gene expression adaptations across multiple brain regions relevant for lasting behaviors observed in perinatal fentanyl exposed mice.