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Integrated systems analysis of mixed neuroglial cultures proteome post oxycodone exposure: Implications for altered synaptogenesis

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In recent years, opioid abuse has become a major public health crisis that affects millions of individuals across the globe. This widespread abuse of prescription opioids and dramatic increase in the availability of illicit opioids have created what is known as the opioid epidemic. Pregnant women are a particularly vulnerable group since they are prescribed opioids such as morphine, buprenorphine, and methadone, all of which have been shown to cross the placenta potentially impacting the developing fetus. However, till date, there is very limited information on the effect of oxy on inducing alterations at the synapse. To fill this knowledge gap, we employed an integrated systems approach to identify proteomic signatures and pathways impacted on postnatal day 14 (P14) mixed neuroglial cultures (majorly consisting of neurons and astrocytes) exposed to oxy for 24h. Differentially expressed proteins were then mapped onto global canonical pathways using Ingenuity Pathway Analysis (IPA) that identified pathways associated with ephrin and semaphorin signaling, synaptic long-term depression, and endocannabinoid and opioid signaling to be significantly enriched. Further analysis by clueGO identified the dominant category of differentially expressed protein functions was associated with GDP binding. Since opioid receptors are G-protein coupled receptors (GPCR's), these preliminary data indicate that oxy exposure perturbs key pathways associated with synaptic function. Current ongoing studies are focused on validating key protein hits identified from our proteomics screen including their subsequent validation *in vivo*.