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Omega 3- fatty acid: Potential for mitigation of neurodevelopmental outcomes from in utero opioid exposure in a chronic stress rat model

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In recent years, opioid abuse has become a major public health crisis affecting 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. However, in recent years, oxycodone (oxy) prescribed for multiple types of pain is gaining momentum as a potential pain reliever in pregnant women. Whilst successful in inducing analgesic, oxy easily passes through the placenta and can significantly impact the overall development of the fetus. Adding another layer of complexity are associated social stressors (cf. low socioeconomic status, harsh living conditions, lack of proper nutrition etc) in pregnant women dependent on oxy that further impact the overall development of the offspring. Currently, mechanisms that lead to injury and impairment in these exposed offspring inlcuding identification of biomarkers are not well described making the development of effective interventions less likely. This current study is a step forward in filling an important knowledge gap. In this current study, employing a robust preclinical rodent model system, we tested the therapeutic efficacy of omega (n)-3 fatty acids (OFA) in attenuating neurodevelopmental deficits in offspring exposed to chronic stress and oxy *in utero*. Our central hypothesis is supplementation with OFA rescues neurodevelopmental deficits in offspring exposed to oxycodone and social stress in utero. A 2X2 paradigm was employed: Saline - OFA+Stress, Saline+OFA+Stress, Oxy-OFA+Stress and Oxy+OFA+Stress. Offpsring from the different treatment groups were further characterized for phenotypic, biochemical, molecular and behavioral endpoints at different stages. OFA supplementation rescued phenotypic, biochemical, molecular and to certain extent behavioral endpoints in Oxy+OFA+Stress animals. Notably, employing state of the art omics technologies, our studies also have identified distinct key synaptic signatures including functional pathways impacted in the different treatment groups and a step forward to close an important knowledge gap pertinent to maternal-fetal health. Supplementation with OFA rescues neurodevelopmental deficits in offspring exposed to oxycodone and social stress in utero lends significant translational and therapeutic potential.

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