Functional Alterations in Resting State Connectivity in Infant Rats Following Postnatal Morphine Exposure

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Introduction: Opioids, including morphine, remain a mainstream therapy for pain treatment and sedation of newborns. Unfortunately, prolonged administration of opioids leads to rapid development of analgesic tolerance and physical dependence at this early age. Using fMRI in a developing rat model, this project examines immediate and long-term effects of central adaptations to chronic morphine. Our initial preliminary work described spontaneous, intrinsic brain activity in the absence of any stimulation as system-wide, resting state networks in the developing rat brain under light inhalational anesthesia (*2015 SFN Abstract 4569*). Whether patterns of resting state activity are affected by prolonged morphine administration in a developing rat model is unknown.

Methods: We used functional MRI and independent component analysis to map patterns of resting-state activity in 2-week old rat pups following either morphine or saline twice-daily injections for two weeks since postnatal day 1 (N=12/group).

Results: A total of 11 networks were identified, 6 of which displayed significant differences in connectivity between treatment groups. Morphine treated rats showed increased connectivity in the Default Mode Network, Basal Ganglia-Hypothalamic Network, Sensory (Exteroceptive) Network, Interoceptive Network, Auditory network, and Hippocampal Network. In contrast, morphine treated rats showed decreased connectivity in three of these networks: Basal Ganglia-Hypothalamic Network, Sensory (Exteroceptive) Network, and Auditory Network.

Discussion: Presented results show that resting-state networks driven by spontaneous BOLD signal fluctuations under light anesthesia are not only present in the developing rat brain at 2 weeks of age, but are also affected by prolonged morphine administration. Results provide a foundation for future translational research for a novel adjunct therapy to improve age-specific pain treatment and attenuate possible long-term sequelae of prolonged opioid treatment in infant children.

Funding was provided by the NIDA K08 DA035972-01 and Trailblazer Award from Department of Anesthesiology, Perioperative and Pain Medicine, Boston Children's Hospital (D. Bajic), as well as K24 NINDS NS064050 (D. Borsook).