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Mitochondrial Morphology in Orbitofrontal Cortical Neurons During Incubation of Oxycodone Craving

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Relapse is a major challenge in treating opioid addiction, including oxycodone, a commonly abused prescription opioid. In rats, cue-induced oxycodone seeking progressively increases during abstinence. Our previous work demonstrated that orbitofrontal cortex (OFC) plays a critical role in this incubation of oxycodone craving. However, the molecular mechanisms in OFC that contribute to this incubation are unknown. Here, we focus on mitochondrial dynamics in OFC and characterize the mitochondrial morphology in OFC neurons during incubation of oxycodone craving. We used a dual-virus approach to sparsely label mitochondria in OFC neurons by injecting the adeno-associated virus (AAV)-hSyn-GFP together with AAV-CMV-mitoDsRed bilaterally into OFC. Next, we trained male rats to either selfadminister saline (as the control group) or oxycodone (0.1 mg/kg/infusion) for 6 h/day over 10 days. On abstinence day 15, we perfused both groups of animals and processed the brain for confocal microscopy. Our image analysis showed that in the somas of OFC neurons, there was a significant increase in the size-frequency of the smallest mitochondria, accompanied by overall increased mitochondria density, in oxycodone rats compared with saline rats. This finding suggests that mitochondria in OFC neuronal cell bodies enhanced fission after 15-day abstinence from oxycodone self-administration. In contrast, we did not observe the differences in primary dendrites of OFC neurons between the two groups. Studies are underway to examine whether enhanced mitochondrial fission in OFC somas is time-dependent after abstinence and whether there are sex differences in mitochondrial morphology during incubation of oxycodone craving.