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Oprm1 deficiency in nucleus accumbens astrocytes increases sensitivity to heroin and reward consumption

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Mu opioid receptors (MORs) are expressed in astrocytes within the NAc, but the role of these receptors remains poorly understood. We recently reported that astrocytes isolated from the brains of *Oprm1* inducible conditional knockout mice had unchanged levels of glycolysis, but elevated oxidative phosphorylation (increased oxygen consumption rate). Here, we evaluated the effects of astrocyte-restricted knockout of MOR in NAc on sensitivity to the locomotor stimulating effects of heroin and state-dependent reward (sucrose) consumption. Specifically, utilizing AAV8-GFAP-mCh-Cre, in *Oprm1*$^{fl/fl}$ mice, the *Oprm1* gene encoding MOR was selectively deleted from NAc astrocytes. Astrocytic deletion of MOR in NAc did not alter baseline locomotor activity, anxiety, exploratory, or social behaviors. In contrast, *Oprm1* KO mice displayed increased locomotor activity in response to acute subcutaneous heroin administration (5 mg/kg) when compared to controls. We next determined whether MORs in NAc astrocytes are important for state-dependent reward consumption. We used a voluntary sucrose consumption paradigm in which mice were tested for sucrose intake either during ad libitum food availability or following 24h food deprivation. *Oprm1* KO mice did not differ in sucrose intake when food was available but had an increased sucrose pellet consumption in the food-deprived condition, suggesting that deletion of MORs in NAc astrocytes accounts for increased motivation to natural reward during the stress (food-deprived) condition. We hypothesize that altered NAc astrocytic energy metabolism may result in increased excitability of NAc neurons, leading to an enhancement of both sensitivity to heroin and the consumption of natural rewards such as sucrose.