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Fibroblast Growth Factor 21 Attenuates the Preference for Morphine in a Conditioned Place Preference Assay

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Fibroblast growth factor 21 (FGF21) is a member of the endocrine family of fibroblast growth factors. FGF21 crosses the blood-brain barrier and exerts many effects on the central nervous system. A previous study using mice showed that FGF21 reduced sweet and alcohol preference in a 2-bottle choice assay and after two weeks of administration of FGF21 by an osmotic mini-pump, dopamine levels in the nucleus accumbens were decreased (Talukdar et al., 2016). Initially, we investigated whether there was epigenetic regulation of FGF21 synthesis in C6 glioma cells. Both HDAC and GSK-3 β inhibitors increased FGF21 mRNA in a time- and concentration-dependent manner. FGF21 transgenic (FGF21-Tg) mice, obtained from Jackson Laboratories, had a 2400-fold higher FGF21 protein level in serum than wildtype littermates. FGF21-Tg mice were found to have approximately a 50% reduction in the preference for 10 mg/kg morphine in the conditioned place preference assay in comparison to wildtype littermates. At a dose of 3 mg/kg morphine, wildtype mice still had a preference for morphine, while the FGF21-Tg mice did not exhibit any preference for morphine. FGF21-Tg male and female mice had a similar reduction in their preference for morphine. These results suggest that FGF21 may be a novel target for treating opioid use disorder. (This study was partially funded by NIDA CEBRA R21 DA044766 award.)