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Fibroblast Growth Factor 21 Attenuates Morphine-induced Preference, Tolerance, and Dependence Without Affecting Analgesia

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Fibroblast growth factor 21 (FGF21) is a member of the endocrine family of growth factors, which cross the blood-brain barrier and exert many effects on the central nervous system. FGF21 transgenic (FGF21-Tg) mice were bred and were found to have a 2400-fold higher FGF21 protein serum level than wildtype littermates. FGF21-Tg mice had a 60% reduction in the preference for 10 mg/kg morphine in the conditioned place preference assay in comparison to wildtype littermates. A similar decrease in the preference for 3 mg/kg morphine was observed. FGF21-Tg mice had the same ED₅₀ values as wildtype littermates for morphine-induced antinociception in both the 55 °C hot-plate and tail withdrawal assays. However, FGF21-Tg mice had a greatly attenuated development of morphine-induced antinociceptive tolerance compared to wildtype littermates in both analgesic assays. Also, FGF21-Tg mice had a 65% reduction in naloxone-induced withdrawal jumping in comparison to wildtype littermates. These findings suggest that FGF21 affects the development of antinociceptive tolerance and dependence without affecting the ability of morphine to produce analgesia. We are interested in understanding genetic changes induced by FGF21 that affect the development of opioid tolerance and dependence.