The neuroinflammation biomarker, translocator protein (TSPO), plays a role in sucrose overconsumption in mice

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Australia Sugar overconsumption is a major cause of obesity. Existing pharmacotherapeutics for obesity have failed to stop the growing prevalence of this disease. Emerging research suggests that neuroinflammation mediates the pathogenesis of diet-induced obesity. Neuroinflammation has been implicated in many neuropathologies by measuring the expression of a neuroinflammatory biomarker – the translocator protein (TSPO). Etifoxine, a TSPO partial agonist and FDA approved anxiolytic, is one of the few antipsychotic medications that does not cause weight gain. Given the proposed role of TSPO in anorexia and obesity, we hypothesized that etifoxine may have therapeutic potential in the treatment of sugar overconsumption. In this study, C57/BL6 mice consumed a 25% sucrose solution for 12 weeks starting at 6 weeks of age following common a common addiction consumption paradigm. After 6 and 12 weeks of sucrose consumption, two groups of 12 mice were treated with either intraperitoneal injections of etifoxine (20 mg/kg or 50 mg/kg) or the TSPO specific antagonist PK11195 (1mg/kg or 10 mg/kg). A single injection of 50 mg/kg etifoxine reduced sucrose consumption both 30 mins and 2 hrs into the drinking session, after 4 and 12 weeks of sucrose consumption. In contrast, PK11195 treatment did not alter sucrose consumption at either dose after 4 or 12 weeks of sucrose consumption. To assess if the effect seen from etifoxine is TSPO specific, a third group of 12 mice were pre-treated with 10 mg/kg PK11195 30 minutes prior to receiving a 50 mg/kg etifoxine injection. Pre-treatment with PK11195 blocked the consumption-reducing effect of etifoxine. Together, these results demonstrate that etifoxine acts through TSPO to reduce sucrose consumption in sucrose overconsuming mice. Given the well-documented safety profile of etifoxine, this study provides preliminary supporting evidence for its potential repurposing as an anti-obesity medication.

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