NOP receptor selective antagonism decreases binge-like alcohol drinking in mice

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The N/OFQ receptor (NOP) is found throughout the brain, spinal cord and dorsal root ganglia, supporting a role of the N/OFQ-NOP system in the modulation of central functions, such as learning and memory, reward, mood, feeding, stress as well as sensory nociceptive processing. Activation of NOP receptors with exogenously administered N/OFQ or synthetic agonists blunts the reinforcing and motivating effects of many abused drugs including alcohol. The role of the endogenous N/OFQ-NOP system in response to drug-mediated behaviors is however still unclear.
In the present study we investigated the effects of NOP receptor activation and inhibition on alcohol consumption by using the 'drinking in the dark' model, a paradigm that reflects binge-like drinking behavior in the mouse.
Male C57BL/6J mice received 20% alcohol in place of water, beginning 3 hours into the dark cycle for 2 hours on day 1 and for 4 hours on day 2. Mice were given an injection of the NOP antagonist SB612111 (0, 3, 10, 30 mg/kg, ip) or the NOP agonist MT7716 (0.0, 0.1, 0.3, 1.0 mg/kg, ip) on day 2 and alcohol consumption was monitored. Additional control experiments assessed the 4-h drinking of 10% sucrose and water following SB612111 administration.
We found that treatment with MT7716 did not alter binge-like alcohol drinking, while treatment with SB612111 (30 mg/kg) significantly decreased excessive alcohol intake. This finding was replicated in mu knockout mice (also on a C57BL/6J background), suggesting that the effect is not due to SB612111 blocking the mu receptors. Finally, consumption of neither 10% sucrose nor water was altered following SB612111 treatment.
Altogether, these experiments provide novel evidence that the endogenous N/OFQ signaling might be recruited in response to excessive drinking in mice and suggest that NOP antagonists may serve as useful approach to prevent binge-like alcohol drinking in humans.