Glutamate agonists injected in the lateral hypothalamus stimulate ethanol intake

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Glutamate inputs to the hypothalamus are important in initiating ingestive behavior. The question is whether this includes ethanol intake, with a possible role in alcohol abuse. Male Sprague–Dawley rats ($N = 50$; $n = 12$–13 subgroup) were trained to drink 9% ethanol ad libitum and implanted with cannulas aimed at the lateral hypothalamus (LH). Microinjections of the glutamatergic agonist NMDA dose-dependently increased ethanol consumption, relative to vehicle injections given in counterbalanced order. Ethanol intake was significantly enhanced for 1 h after the 5.5 nmol dose (vehicle: 0.41 ± 0.08 g/kg; NMDA: 0.66 ± 0.15 g/kg) ($p < 0.05$) and for 6 hr after the 11 nmol dose (vehicle: 1.05 ± 0.22 g/kg; NMDA 2.01 ± 0.34 g/kg) ($p < 0.05$). Compared to the long-lasting effect of NMDA, the glutamatergic agonist AMPA produced milder but similar results in the LH. At 1.07 nmol, AMPA significantly enhanced ethanol consumption for 4 h post-injection (vehicle: 0.70 ± 0.11 g/kg; AMPA: 1.04 ± 0.15 g/kg) ($p < 0.05$). Water and food intake were unaffected in all tests. These results show that glutamate, which also stimulates feeding when injected into the LH (Stanley et al., 1993), can instead induce 9% ethanol intake in rats that have learned to drink it, having an effect that lasts up to 6 h. Thus, glutamate inputs to the LH have excitatory control over the initiation and maintenance of ethanol intake and thus may be a site where glutamatergic drugs, e.g., acamprosate, act to control ethanol consumption.

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Increased amygdala response and decreased influence of internal state on amygdala response to food in overweight compared to healthy weight individuals

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Neuroimaging studies in healthy weight (HW) individuals have demonstrated that the amygdala responds to food cues and that this response is attenuated by feeding to satiety, suggesting that the value of the food cue is represented there. To test the hypothesis that amygdala response to food is greater in overweight (OW) compared to HW individuals, we used fMRI to examine brain response to the taste and smell of highly palatable milkshakes in 26 individuals (13 HW and 13 OW). Perceptual ratings of the stimuli and of internal state were collected before and after scanning. Between group analyses of variance based on random effects models were performed in SPM5. Peaks were considered significant following correction for multiple comparisons across all voxels in the amygdala. Greater amygdala response was observed in the comparison of milkshake vs. tasteless and of food aromas vs. odorless in OW compared to HW individuals. This response did not vary as a function of stimuli pleasantness. However, hunger, which did not differ between groups, was positively associated with amygdala response to milkshake in the HW group, whereas no association was observed in the OW group. Additionally, amygdala response to the food aromas predicted weight gain one-year post scan. These findings suggest that heightened amygdala response to food, coupled with reduced influence of internal state upon this response, may lead to overeating.

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Role of dopamine in dorsal medial prefrontal cortex in yohimbine-induced reinstatement of food seeking in rats

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In humans, relapse to maladaptive eating habits during dieting is often provoked by stress. We adapted a drug relapse-reinstatement model to study the role of stress in relapse to food seeking (Nair et al., Prog. Neurobiol., 2009). In our model, the anxiogenic drug yohimbine, an alpha-2 adrenoceptor antagonist, that causes stress-like responses in humans and laboratory animals, reliably reinstates food seeking. We recently found that yohimbine-induced reinstatement of food seeking is attenuated by systemic injections of SCH23390 (a D1-family receptor antagonist) but not clonidine (an alpha-2 adrenoceptor agonist). Here, we studied the role of the medial prefrontal cortex (mPFC) in yohimbine-induced reinstatement. We trained food-restricted rats to lever-press for 35% high-fat pellets every other day (9–15 3 h sessions). We then extinguished the food-reinforced operant responding for 10–14 days by removing the pellets. Subsequently, we tested the effect of systemic injections of yohimbine (0, 2 mg/kg) on reinstatement of food seeking. In Exp. 1 we found that yohimbine-induced reinstatement was associated with strong induction of Fos (a marker of neuronal activity) in the dorsal mPFC and weaker Fos induction in the ventral mPFC. In Exp. 2 we found that dorsal but not ventral mPFC injections of the D1-family receptor antagonist SCH23390 (0.5, 1.0 μg/side) decreased yohimbine-induced reinstatement of food seeking. Our data indicate a critical role of dorsal mPFC dopamine in reinstatement food seeking induced by the pharmacological stressor yohimbine.

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Effect of *Rhodiola rosea* extracts on binge eating in female rats

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Stress is a determinant of binge eating. *Rhodiola rosea* (ROR) extracts modulate stress responses. The present study evaluated the effect of ROR dry extract and its active principles in rats in which binge eating for highly palatable sweet food (HPF) was evoked by stress and repeated food restrictions. Female Sprague–Dawley rats were submitted to three 8-day cycles of food restriction/refeeding (4 d 66% of the usual chow intake, 4 d food ad libitum) and to acute stress on d25. Stress was induced by preventing access to HPF for 15 min, while rats were able to see and smell it. 4 groups of rats were used: NR + NS rats were normally fed and not stressed on the test day (d25); NR + S rats were similarly fed but were stressed on d25; R + NS rats were exposed to 3 cycles of yo-yo dieting but not stressed; R + S rats were exposed to 3 cycles of yo-yo dieting and stressed on d25. ROR dry extract (containing 3% rosavin and 3.12% salidroside) or the purified principles were given by gavage 1 h before access to HPF. Food restrictions and stress induced binge eating in R + S rats, increasing HPF intake of about 50% in the first 15 min. 10 mg/kg of ROR extract significantly reduced and 20 mg/kg abolished the HPF binge in R + S rats, but did not modify HPF intake in NR + NS, NR + S or R + NS rats. Rosavin or salidroside, 600 or 636 μg/kg (i.e. the amounts in 20 mg/kg of extract) significantly reduced HPF intake in R + S rats; when given together they completely abolished the binge response. Thus, ROR extracts or its active principles, rosavin and salidroside, may be interesting agents for treatment of bingeing-related eating disorders.

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