Orexin A-induced activity is inversely correlated with body weight gain and may promote weight loss in rats

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Studies in humans and animals suggest that high levels of spontaneous physical activity (SPA) protect against weight gain. We are investigating whether orexin A (OXA) influences body weight by contributing to SPA levels in rodents. We hypothesized that (1) OXA responsiveness and OX receptor expression are correlated to SPA and body weight gain, and (2) that OXA injections would increase SPA and reduce body weight gain. To test this, adult male rats were treated with OXA via guide cannulae aimed at the rostral lateral hypothalamus. For experiment 1, we measured 2 h SPA following a single OXA injection (31.25 pmol). Body weights were monitored for 6 weeks post-treatment. Body weight gain over this period was significantly and inversely correlated to levels of OXA-induced SPA ($R^2 = 0.435$, $p = 0.038$), and to orexin 2 receptor expression in the rostral lateral hypothalamus ($R^2 = 0.686$, $p = 0.0260$). For experiment 2, rats were treated three times daily with OXA (500 pmol) or artificial cerebrospinal fluid (aCSF) for 5 days. OXA treatment significantly increased dark-period SPA in one group ($p < 0.05$). A second group receiving OXA showed weight loss (OXA: -32.8 ± 15.0 g; aCSF: -7.6 ± 8.4 g; $p = 0.18$), but the effect did not reach significance. We attribute this to the short duration and small animal numbers in this pilot study; a more extensive follow-up study is planned. These data suggest that OXA sensitivity and receptor expression level may predict body weight gain, and that OXA therapy elevates SPA and may reduce body weight.

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Suppressed intake of highly palatable food and dysfunctional of HPA axis response to restraint stress in adolescent rats that experienced neonatal maternal separation

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Sprague–Dawley pups were separated from dam daily for 3 h during PND 1–14 (MS) or left undisturbed (NH). All pups were subjected to a preference test with free choices of chow or chocolate cookie for 1 h every alternate day from PND 28, with (RR)/without (NR) 1 h of restraint stress prior to the test. Pups were sacrificed on PND 40; RR pups immediately after restraint session; and half of NR pups after a single restraint. Neither MS nor repeated restraint affected weight gain of pups. Cookie intake was significantly suppressed in MS pups. Restraint stress suppressed cookie intake of NH, but not of MS pups, and significantly increased c-Fos expression in the nucleus accumbens of NH pups, but not in MS. However, c-Fos-ir in the NAccb core was increased by MS. c-Fos expression in the paraventricular nucleus of MS and NH pups responding to restraint stress did not differ. Basal c-Fos expression in the central amygdala (CeA) of MS increased significantly, compared to NH. The CeA-c-Fos was markedly increased by single restraint in NH, but not in MS. Basal plasma level of corticosterone was elevated in MS compared with NH. A single restraint increased plasma corticosterone both in NH and MS, but the repeated restraint only in NH. These results suggest that neonatal maternal separation may suppress intake of highly palatable food in rats at adolescence, perhaps, due to dysfunction of the HPA axis.

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The effects of modified sham feeding and variety on sensory specific satiety and food intake in humans

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Sensory specific satiety (SSS) occurs in modified sham feeding (MSH) in the absence of postingestive feedback. MSF increases satiety and fullness ratings; gut humoral events associated with hunger and satiety are initiated by MSF. We compared intake and SSS following real and MSH feeding. Twenty-three participants (16 women, 7 men) from the US and UK ate lunch on four occasions in the laboratory in a repeated measures design with MSF (sham feed or eat in first course) and food variety (same or varied sandwich in second course) as factors. SSS was tested before and after each course. The first course was cheese sandwiches; the second was either cheese (same) or ham (varied) sandwiches. There were no differences in intake in the first course. Participants ate fewer sandwich units in the second course after eating than after MSF [$F(1,21) = 22.72$, $p < 0.001$]. Participants ate more in the varied than in the same condition [$F(1,21) = 11.40$, $p < 0.01$]. There was no difference in SSS to cheese for MSF and eating conditions. Thus, the pleasantness of the taste of the eaten food declined whether that food was sham fed or eaten [$F(5,110) = 20.32$, $p < 0.001$]. There was no interaction between MSF and variety conditions on food intake. Hunger ratings decreased after eating but not after MSF. The results suggest that while MSF can produce SSS, it does not lower food intake. Thus, sensory specific satiation is important in limiting food intake only when coupled with the relevant negative postingestive feedback.

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Conditioned taste aversion and Na-appetite after asymmetric brain lesions

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In rodents, the central gustatory system has monosynaptic projections from the pontine parabrachial nuclei (PBN) that distribute widely in the limbic forebrain. Unlike its thalamocortical counterpart, this ventral gustatory pathway is largely unilateral. Bilateral damage to the PBN eliminates the ability of rats to acquire conditioned taste aversions (CTA) or to exhibit Na-appetite (Na-Ap). Damage to the thalamic taste area has little effect on either of these taste guided behaviors. Thus, a lesion of the PBN on one side and damage to one of its limbic targets on the other should reveal if interaction between the two structures supports either CTA or Na-Ap. Experiments using this strategy demonstrated that, although the PBN is critical for both behaviors, connections with the lateral hypothalamus (LH) and the central nucleus of the amygdala (CNA) contribute differently to their elaboration. Asymmetric lesions of the PBN and the CNA failed to block a CTA but they increased the initial intake of a sucrose CS and considerably sped up extinction. Rats with bilateral CNA damage also displayed exaggerated CS intake on trial 1, but exhibited little if any extinction of a CTA. In the same two sets of animals both the induced Na-Ap and need-free NaCl intake were increased. Asymmetric lesions of the PBN and the LH slowed acquisition of a CTA and sped up its extinction. In the same PBN/LH rats, however, Na-Ap was essentially eliminated. Prelesion experience with Na-Ap protected PBN/LH rats from the deficits in stimulated salt intake.

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