Anosmia impairs the feeding response to 2-deoxy-D-glucose in rats

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In two separate studies, adult female rats with olfactory bulbectomies displayed no increase in food intake during the first 2 h after an intraperitoneal injection of 350 mg/kg 2-deoxy-D-glucose (2-DG). Behavioral testing demonstrated that the rats with olfactory bulbectomies were anosmic. Rats made anosmic by application of zinc sulfate to the olfactory mucosa also did not display a feeding response to 2-DG. Rats given olfactory bulbectomies also displayed a greatly attenuated feeding response in the first hour after an intraperitoneal injection of 4 U insulin, and displayed a normal drinking response after an intraperitoneal injection of 1 M hypertonic saline. The results with 2-DG can not be attributed to debilitation as the body weights and daily food intakes of rats with olfactory bulbectomies did not differ from control animals at any time during the studies. A previous study found that rats with olfactory bulbectomies did not increase their food intake after dilution of their powder diet with nonnutritive bulk. Other studies have implicated neural pathways mediating taste in the feeding response to 2-DG, and the present results indicate that olfactory pathways are also critically important in the feeding response to 2-DG.
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Anorexigenic effects of the brain derived neurotrophic factor (BDNF)

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Treatment with BDNF was found to attenuate weight gain or even cause weight loss in rats. Furthermore, within the dorsal vagal complex, BDNF has been shown to be involved in the control of food intake. Two studies have been conducted (1) to test the electrophysiological response of duodenal vagal afferents to BDNF and (2) to investigate the nature of BDNF-induced food intake depression. In male rats the activation of duodenal vagal afferents in response to BDNF injection (10 ng) within the blood supply of the duodenum was recorded *ex vivo*. Basal vagal afferent neurons' spontaneous discharge was increased by 156% after BDNF administration. In the second study rats underwent surgery for implantation of a cannula in their fourth ventricle. Food ingestion patterns were recorded every minute for 14 days using an adapted acquisition system. During this period, the animals were treated on specific days with an injection of BDNF (1 μg) or an equivalent volume of saline (NaCl 0.9%) via their intra-cerebro-ventricular cannula. BDNF induced a significant decrease in food intake during the 12 h following injection, but it did not have an effect on the delay in meal onset or on rate of ingestion and meal frequency. These results indicate that the intake depression is more likely to result from an increased satiety rather than an aversive effect of BDNF. Both studies confirm the hypothesis that peripheral BDNF may act as an anorexigenic factor in the dorsal vagal complex by increasing satiety.
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Influence of a high-fat diet on brain-derived neurotrophic factor (BDNF)

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BDNF and its high affinity receptor TrkB play a critical role in the synaptic activity and plasticity of mature neurons and enhance adult neurogenesis. Furthermore, treatment with BDNF was found to attenuate weight gain or even cause weight loss and suppress appetite in rats. The aim of this study was to look at the effect of nutrient intake on BDNF concentrations and cellular proliferation in the brain. Adult male Wistar rats were given one of three diets for 6 weeks: high-carbohydrate, high-fat and high-fat pair fed. Rats were sacrificed at the end of the feeding period and BDNF concentrations in the dorsal vagal complex (DVC), hypothalamus and plasma were measured by ELISA on protein extracts of these samples. The cellular proliferation in the DVC was quantified by Ki-67 immunohistochemistry. Neither BDNF levels nor proliferation were modified by the diet. Secondly, using rats that received the same diets, real time PCR was performed in the DVC, hypothalamus and nodose ganglia in order to compare TrkB receptor levels after fasting or refeeding the animals. Results showed significantly lower TrkB levels in the hypothalamus and nodose ganglia of fasted rats given the high-fat diet compared to the other dietary groups. These two complementary methodological approaches suggest that there might be a relationship between long-term dietary intake and BDNF but further investigations are needed.
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Arcuate POMC neurons suppress food intake by direct action on MC4 receptors expressed on vagal afferents in the NTS

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Meal size can be modulated by brainstem administration of melanocortin receptor-3/4 (MC3/4R) ligands, but the source of endogenous ligands and the mechanism of modulation are not known. Here we show that food intake suppression induced by local activation of arcuate nucleus POMC neurons with leptin in rats is abolished by pretreatment of the caudal brainstem with the MC3/4 antagonist SHU9119 delivered either into the 4th V (e.g. 12-h food intake on day after injection: sal/sal, 13.1 ± 1.2 g; sal/lep (30 pmol), 6.3 ± 0.8 g, $p < 0.01$; SHU (100 pmol)/sal, 14.2 ± 1.0 g, ns; SHU/lep, 11.6 ± 1.3 g, ns) or directly into the NTS. Patch clamp recordings from 140 NTS neurons showed both excitatory and inhibitory effects of α-MSH and its stable analog MTII on frequency but not amplitude of spontaneous and electrical solitary tract stimulation-evoked glutamate currents, consistent with mainly presynaptic modulation. Western blotting revealed presence of MC4 but not MC3-receptor mRNA in rat nodose ganglia. These results are consistent with a role for arcuate-medullary POMC projections in the control of meal size by modulating satiety signaling from the gut through MC4R on central terminals of vagal afferents. In addition, other excitatory inputs to NTS neurons such as projections from the PVH, and vagal motor neurons are likely targets of descending melanocortinergic modulation.

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