Cocaine- and amphetamine-regulated transcript (CART) peptide immunoreactivity in the brain of the obese OLETF rat

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Cocaine- and amphetamine-regulated transcript (CART) peptide is expressed in brain areas that play a role in homeostatic regulation and reward. CART has been shown to reduce food intake in rodents but the underlying mechanisms and the relevance of this effect to obesity yet remain unknown. Therefore, the present study investigated CART peptide immunoreactivity (CARTir) in various brain regions of adult (35–40 weeks) Otsuka Long-Evans Tokushima Fatty (OLETF) rats. The OLETF rat is a null-mutant to the CCK-1 receptor, and used as a model for dietary obesity due to its chronic hyperphagia, and increased avidity for palatable foods. Whereas the distribution of CARTir neurons and axonal networks was identical in OLETF and age-matched lean LETO rats, intensity of CARTir was significantly reduced in the rostral part of the nucleus accumbens ($p < 0.01$), the basolateral complex of the amygdale ($p < 0.02$), and the rostro-medial nucleus of solitary tract ($p < 0.001$) of the OLETF rats. These areas are involved in reward and integration of taste and viscerosensory information and have been previously associated with altered functions in this strain. The findings suggest that in addition to previously described deficits in peripheral satiety signals and augmented orexigenic regulation in the hypothalamus, the anorectic effect of CART may also be diminished in OLETF rats.

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Regulation of food intake and anxiety by α-MSH reactive autoantibodies

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α-Melanocyte-stimulating hormone (α-MSH) is a neuropeptide critically involved in regulation of energy and emotional homeostasis. Autoantibodies (autoAbs) reactive with α-MSH have been recently identified in human subjects while their levels correlated with psychological traits in patients with eating disorders. So far it was unknown if these autoAbs are involved in the regulation of feeding and anxiety and if their production can be influenced by stress. In the present work, we found that α-MSH reactive autoAbs are present in rat blood and that repeated exposure to mild stress increase their levels and affinity and that this change is associated with modifications in feeding and anxiety during exposure to strong stress such as food restriction. Using passive transfer, we show that high affinity α-MSH autoAbs from rats exposed to repeated mild stress are able to suppress food intake and anxiety and modify the gene expression of hypothalamic neuropeptides involved in the regulation of appetite in naïve rats. These data provide the first evidence that α-MSH autoAbs are involved in regulation of feeding and mood, assigning a new role for the immune system in the control of motivated behavior and stress-response.

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Methotrexate-induced anorexia is associated with alteration of hypothalamic neuropeptide expression and plasma levels of α-MSH reactive autoantibodies

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Anorexia and enterocolitis are side effects caused by a cancer chemotherapeutic methotrexate (MTX). To investigate mechanisms of MTX-induced anorexia, Sprague Dawley male rats received MTX (2.5 mg/kg s.c. for 3 days), while pair-fed and ad libitum-fed control rats received saline. Rats were fed powdered standard chow and food intake and body weight were monitored. Rats were killed on days 5 or 19 after first injection of MTX. Day 5 in MTX-treated rats was characterized by maximal suppression of food intake and body weight and presence of inflammation in colonic mucosa. On day 19 no signs of intestinal inflammation were found but MTX-treated rats still exhibited significantly lower body weight. In pair-fed rats, hypothalamic NPY mRNA was increased ($p < 0.05$) and POMC mRNA were decreased ($p < 0.05$) on day 5, providing evidence of negative energy balance. However, in MTX-treated rats no significant changes of NPY or POMC mRNA were found suggesting that their acute anorexia may be related to altered expression of hypothalamic neuropeptides triggered by intestinal inflammation. The levels of free α-MSH reactive autoAbs were decreased at day 5 ($p < 0.05$), but increased at day 19 ($p < 0.05$) in MTX-treated rats suggesting that in the absence of intestinal inflammation α-MSH reactive autoantibodies can be involved in wasting syndrome persisting after MTX treatment.

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Exercise modifies body weight set-point in diet-induced obesity-prone rats

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Background: Exercise has been suggested to prevent onset of obesity in juvenile obesity-prone rats probably by effecting the development of the neural circuits controlling obesity. **Materials and methods:** Young diet-induced obesity-prone (DIO) rats were placed in a running wheel cage immediately following weaning and allowed to exercise (voluntary) during a 2-week training period. Based on the training activity we then divided the rats into runners and non-runners. Non-runners were placed in a standard cage as a sedentary reference, while runners were stratified into 3 groups: (i) wheel access for additional 11 weeks, (ii) wheel access for additional 6 weeks followed by 5 weeks of blocked wheels, (iii) 11 weeks of blocked wheels. **Results:** We demonstrate that young DIO rats which was exercised (voluntary) for 8 weeks followed by a forced sedentary period of 5 weeks, displayed a similar body weight gain pattern, body composition, insulin sensitivity, and plasma lipid profile as rats exercising through the entire intervention period of 13 weeks. **Conclusion:** Our data suggests that exercise in young obesity-prone rats may protect against the development of obesity.

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