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Personality as a risk factor for adiposity and hyperinsulinaemia

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Personality may be a risk factor for weight gain and insulin resistance. We have studied this in rats that display either a proactive or a passive coping style. We found that passive rats are more prone to develop adiposity, and hyperinsulinaemia. Passive rats consumed more of a high fat diet than proactive rats. Subsequently, passive rats have a higher percentages of visceral adiposity. Additionally, baseline insulin levels were elevated in passive rats and in response to a glucose infusion (iv) passive rats showed increased insulin levels at both peak and plateau. Personality may also play a role in the treatment. When allowed to run voluntarily, passive rats display higher levels of running activity. This effect became more pronounced once the rats were switched to a high fat diet; passive rats increased running levels in response to a switch to the high fat diet, whereas proactive rats do not. Running decreased insulin responses in both personalities, although the effects were stronger in the passive rat. Second, treatment with RU486 decreased hyperinsulinaemia in passive rats, but had no effect in proactive rats. This suggests that the origin of hyperinsulinaemia in the passive rats might be related to enhanced HPA-axis activity. Taken together, these data indicate that passive rats are more prone to develop adiposity and hyperinsulinaemia. However, they are also more likely to respond well to a life style intervention program since passive rats voluntarily increase their daily activity when given the opportunity to run, and in this situation, plasma insulin levels are normalized. Supported by: AstraZeneca.

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Effect of insulin on dopamine neurons of the ventral tegmental area

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The prevalence of obesity has drastically increased over the last few decades. Exploration into how hunger and satiety signals influence the reward system can help us to understand non-homeostatic mechanisms of feeding. Previous research has implicated mesolimbic dopamine signaling in the incentive, reinforcing, and motivational aspects of food intake. Insulin receptors are expressed in dopaminergic neurons of the ventral tegmental area (VTA) and there is substantial evidence suggesting that insulin may act in the VTA to suppress feeding. However, the neural mechanisms underlying insulin effects in the VTA remain unknown. We demonstrate that insulin can cause a long-term depression (LTD) of excitatory synapses onto VTA dopamine neurons. This effect requires endocannabinoid-mediated presynaptic inhibition of glutamate release. Insulin-mediated LTD onto VTA dopamine neurons was disrupted in hyperinsulinemic mice. Using fast scan-cyclic voltammetry to measure subsecond dopamine concentrations in the VTA, we found that insulin dose-dependently reduced dopamine concentration by increasing the reuptake of dopamine through its transporter. Finally, insulin administered into the VTA reduces palatable food intake in mice. Taken together, these results demonstrate that insulin acts in the VTA to depress excitatory synaptic transmission of dopamine neurons as well as somatodendritic dopamine concentrations. Furthermore, insulin action in the VTA may serve to reduce palatable food consumption. Supported by: CIHR NSERC.

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LPS inhibits ghrelin-excited neurons and food intake via central nitric oxide signaling

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Nitric oxide (NO) is produced by inducible nitric oxide synthase NOS (iNOS). Lipopolysaccharide (LPS) induces high iNOS expression in the arcuate nucleus (ARC). Peripheral administration of the specific iNOS inhibitor 1400 W counteracts the anorectic effect of LPS. To evaluate the role of central iNOS signaling we conducted third intracerebroventricular (icv) injections of 1400 W in rats receiving LPS (100 µg/kg ip). Further, we analyzed the electrophysiological effects of 1400 W in ARC preparations that were obtained from rats 4 h after peripheral LPS treatment or after in vitro stimulation of the ARC with LPS. We also tested whether LPS induces an iNOS-dependent cGMP formation in the ARC. 1400 W (4 µg icv) attenuated the LPS-induced anorexia. Superfusion with 1400 W (10⁻⁴ M) increased neuronal activity in 37% of neurons recorded in ARC slices from LPS-treated rats (*n* = 19) but not from control treated animals. Similarly, 1400 W induced excitatory effects (45%) after in vitro stimulation with LPS (100 ng/ml). 1400 W sensitive neurons were excited by ghrelin (10⁻⁸ M). In vitro stimulation with LPS increased the number of cGMP positive cells in the ARC. This response was blocked by co-incubation with 1400 W. In conclusion, central NO signaling contributes to LPS anorexia and seems to inhibit ghrelin-excited ARC neurons via iNOS-dependent NO formation. This effect might be mediated by the NO dependent second messenger cGMP. A pharmacological blockade of NO formation might be a therapeutic approach to ameliorate disease-related anorexia. Supported by: Swiss National Science Foundation (SNF), Krebsliga Zurich.

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Mysterious fat. The different impact of fat content on toddlers' and adults' food intake

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Fat content of foods is often incriminated in the high prevalence of overweight and obesity. However, the role of fat on intake and perception is still a matter of debate. This work evaluated the impact of fat content of a creamy white cheese (CWC) on its intake, hedonic rating and sensory characteristics. The CWC variants were commercially available products with 0, 20 or 40% fat and sweetened with 5% added sugar. Study 1: 56 toddlers (2–3 years; 26 ♀–24 ♂) and 51 students (18–25 years; 26 ♀–25 ♂) took part to three afternoon snacks (*ad libitum* CWC, biscuits, milk and/or water). Study 2: the same students scored their liking and several sensory descriptors for the three CWC, in a separate sensory evaluation session. Children's intake of CWC was influenced by fat content (*P* = 0.013): 0% and 20% fat CWC were more consumed than the 40% one (196 ± 12, 186 ± 12 and 159 ± 11 g respectively). Fat content had no effect on students' CWC intake (*P* = 0.55; 190 ± 6 g on average). Children maintained an equivalent total energy intake from the three snacks (*P* = 0.58), this was not the case for the students (*P* = 0.006). Students liked the 40% fat CWC more than the 20% and the 0% fat CWC (*P* < 0.0001). They differentiated the three CWC according to thickness (*P* = 0.04), creaminess (*P* < 0.0001), dryness (*P* < 0.0001), sourness (*P* < 0.0001) and sweetness (*P* = 0.0003), but not according to fattiness (*P* = 0.43). These results highlight the discrepancy between intake and liking measurements in adults. They also shed light on the poorer ability of adults to maintain their energy intake when fat content varied in a common food contrarily to children. Supported by: The present work was funded by the Nutrition, Chemical Food Safety and Consumer Behaviour Division