Loss of control of food intake among children during the school lunch

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anorexia as expected, and formerly HF-fed rats showed a significant response of the same magnitude (8%) during both tests. Next, we examined the time course of the development of the impairment. Another group of rats was tested for response to 1 μg/kg Ex4 while on chow diet; all were responsive. They were then put on HF diet and the Ex4 response was tested again 3, 7, 14, and 21 days later. The 1 μg/kg dose of Ex4 significantly reduced 24-h food intake after 3 days on HF diet, but the effect was marginal at 7 days ($p = 0.05$), and no longer present after 14 and 21 days on HF diet. We conclude that the mechanism for this impairment must be an effect of HF diet maintenance that is not immediate but emerges within 2 weeks, and that it is reversible with return to LF feeding. Supported by: NIH DK078779.
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Modeling impulse controls deficits. Relevance for addictive behaviors?
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A growing body of evidence indicates that high levels of impulsivity are a significant risk-factor for the development of substance abuse, particularly with regards to stimulant drugs. However, recent data also suggest an important link between deficits in impulse control and other putative addictions, such as problem gambling, and overeating. Regarding these conditions, it can be difficult to determine whether high trait impulsivity is predictive of engagement in problem behaviors, or whether the development of the addiction itself exacerbates impulsive responding. Such questions are difficult to resolve using clinical populations, and animal models could make an important contribution in this regard. For example, the rodent five-choice serial reaction time task has been developed as an analogue for the human continuous performance test, and both provide measures of premature responding i.e. the inability to withhold from making a prepotent motor response, also known as impulsive action. Research using this model suggests that high levels of this form of impulsivity increases vulnerability to cocaine addiction, and also that self-administration of cocaine can lead to impulse control deficits during withdrawal. Ongoing research is exploring whether similar relationships exist between poor inhibitory control and other addictive behaviors, such as gambling. In addition, we have found that the level of impulsive action varies depending on the number of sugar pellets at stake, such that larger rewards may be capable of inducing higher levels of impulsivity. Supported by: CIHR, NSERC, MSFHR.
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Flip-flop memory circuit uses a synaptic AMPK-dependent positive feedback loop and is switched by hunger state
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Synaptic plasticity in response to changes in physiologic state is coordinated by hormonal signals across multiple neuronal cell types, but the significance and underlying mechanisms are unclear. Here, we combine cell type-specific electrophysiological, pharmacological, and optogenetic techniques to dissect neural circuits and molecular pathways controlling synaptic plasticity onto AGRP neurons, a population that regulates feeding. We find that food deprivation elevates excitatory synaptic input, which is mediated by a presynaptic positive feedback loop involving AMP-activated protein kinase. Potentiation of glutamate release was triggered by the orexigenic hormone ghrelin and exhibited hysteresis, persisting for hours after ghrelin removal. Persistent activity was reversed by the anorexigenic hormone leptin, and optogenetic photostimulation demonstrated involvement of opioid release from POMC neurons. Based on these experiments, we propose a memory storage device for physiological state constructed from bistable synapses that are flipped between two sustained activity states by transient exposure to hormones signaling energy levels. Supported by: Howard Hughes Medical Institute.
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The leptin signaling cascade and pediatric obesity
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The prevalence of overweight and obesity in children has tripled during the past 40 years. This alarming rise in body weight has likely occurred because the current environment affords easy access to calorie-dense foods and requires less voluntary energy expenditure. However, this environment has not led to severe obesity in all children; rather, it has unmasked a select group of individuals whose body weight regulatory systems are not able to control body adiposity with sufficient precision in our high calorie/low activity environment. This presentation will review genetic syndromes affecting the leptin signaling cascade that have been demonstrated to be associated with pediatric-onset obesity, concentrating on genes other than leptin and the melanocortin 4 receptor. This research was supported by the Intramural Research Program of the NICHD, NIH.
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Understanding the nature of the reinforcer in human flavour-nutrient learning
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In flavour-nutrient learning (FNL), repeated experience of a novel flavour and subsequent ingestion of nutrients has been hypothesised to increase subsequent flavour liking and consequent intake. However, although there are published studies consistent with this effect, other studies have failed to find evidence of changes in liking or intake through flavour nutrient associations. Here a series of recent studies attempted to clarify the nature of the reinforcing effects of ingested nutrients and whether this could explain variability in human FNL. First, the importance of nutrient load is considered. A simple FNL model would predict greater liking as energy intake increases. However, excessive nutrient intake could be aversively over-satiating, implying an inverted U-shape function between ingested nutrients and change in liking, and evidence is presented consistent with this latter view. Second, the issue of nutrient relevance is considered. If a person's primary control of intake was based on cognitive rather than physiological signals, then FNL effects would be weaker. Evidence that restrained eaters show weak liking changes through FNL is consistent with this view. Finally, whether nutrients are expected or not is considered, with evidence that prior expectation that a food is high calorie preventing liking change through FNL. Together these data suggest that FNL operates most effectively where ingested energy matches short-term needs, is unexpected and does not contradict restrained attitudes. Together these findings imply considerable cognitive influence on FNL in humans.
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Loss of control of food intake among children during the school lunch
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In an observational and experimental study in a secondary school in Stockholm the cumulative food intake was studied in 18 girls and 12 boys individually and after experimentally increasing or decreasing the speed of eating or maintaining its control level

by computer during the school lunch. All children had their school lunch in a shorter period of time than when eating individually (girls: 5.6 (1.2) min vs 10.7 (2.1) $P < 0.001$; boys: 6.8 (1.3) min vs 8.8 (1.8), $P = 0.003$). Only two girls and one boy maintained their food intake at the individual level when eating their school lunch; nine girls ate 30% less food and seven girls ate 33% more food and 11 boys ate 35% more food. These changes were prevented by providing feedback via computer to maintain the control pattern of eating during the school lunch and they were replicated by experimentally increasing the speed of eating by computer feedback. The conditions at the school lunch increased the speed of eating such that the children were unable to maintain their individual pattern of food intake. Interestingly, the increase and decrease in food intake which emerged are comparable to those previously reported after administration of orexigenic (ghrelin) and anorexigenic (PYY) peptides in humans. While the former changes could be prevented by feedback on how fast to eat during the course of the lunch, the latter effects have never been reversed. Supported by: Mando Group AB.
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NTS leptin signaling contributes to meal size control and suppression of food intake by intestinally-derived satiation signals

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Leptin receptors (LepR) expressed in the medial nucleus tractus solitarius (mNTS) are required for normal energy balance control. Here, the contribution of mNTS LepR signaling to the mediation of the intake suppressive effects of intraduodenal nutrient infusion and meal parameter (meal size and frequency) control is evaluated. Intestinal nutrient (Intralipid; 8 ml at 0.5 kcal/ml) infusion at a subthreshold concentration for intake suppression and a subthreshold dose of 4th ventricle leptin (5 μg), combined to significantly decrease food intake in rats. To assess the roleof *endogenous* mNTS LepR signaling in mediating the intake suppressive effects of intestinal nutrient delivery, knockdown of LepR in the mNTS and area posterma (AP) (mNTS/AP LepRKD) via adeno-associated virus short hairpin RNA-interference (AAV-shRNAi) was employed. Rats with LepRKD in the mNTS showed attenuated 30 and 60m food intake suppression by intraduodenal infusion of a complete liquid meal (Ensure) in a concentration dependent fashion. The endogenous role of mNTS LepR signaling in control of within-meal satiation signaling was further examined following LepRKD by analysis of *ad libitum* meal parameters. mNTS LepRKD increased daily food intake by increasing average meal size but not frequency, whereas LepRKD restricted to the AP did not influence overall energy intake. Current findings demonstrate an endogenous contribution of mNTS LepR signaling in sensitivity to intestinal satiation signals and meal size control. Supported by: NIH DK21397.
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Structural and functional dissection of the central connections of hindbrain A1 and A2 noradrenergic (NA) cell groups

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NA signaling pathways are implicated in diverse autonomic, endocrine, and behavioral adjustments associated with the central control of food intake and energy homeostasis. NA neurons within the nucleus of solitary tract (A2) and caudal ventrolateral medulla (A1) appear to innervate similar regions of the brainstem, hypothalamus, and limbic forebrain, and also appear to share central sources of axonal input. However, some evidence suggests that A1 and A2 projection fields are discrete. To determine the extent to which A1 and A2 regions participate in similar or discrete neural circuits, we employed a double co-injection neural tracing paradigm (Thompson and Swanson, PNAS, 2010). A cocktail of phaseolus vulgaris leucoagglutinin/cholera toxin B was delivered iontophoretically into either the A1 or A2 region, and in the same rat a combination of biotinylated dextran amine/FluoroGold was delivered into the alternate region. Two weeks later, rats were injected with cholecystokinin (CCK) and perfused with fixative. Tissue sections were processed for immunocytochemical detection of nuclear cFos together with various combinations of tracers. Results confirm the utility of the quadruple neural tracing approach, and have revealed that ascending projections arising from the A1 and A2 regions tend to target discrete subregions of the parabrachial nuclei, paraventricular hypothalamus, and bed nucleus of the stria terminalis. Ongoing analyses will probe for potential areas of collateralized or discrete inputs to the A1 and A2 regions, together with identification of inputs that are activated by CCK. Supported by: NIH #MH59911.
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Caffiene conditions flavor preferences in adolescents

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Beverage manufacturers say that caffeine is added to drinks to enhance their flavor, but many researchers speculate that caffeine is added to enhance preferences for these drinks. Previous studies in adults have shown that caffeine can condition flavor preferences for novel flavored teas, but similar studies involving adolescents have not been conducted. The purpose of this study was to test the hypothesis that caffeine added to novel flavored drinks would increase liking and preference in adolescents. Adolescents ($n = 112$) between the age of 12 and 17 were brought into the laboratory for 6 visits. They tasted 7 novel soda drinks and provided liking ratings and ranked the beverages in order from most to least liked. The drink ranked #4 was chosen as the target beverage. Participants returned to the lab for 4 consecutive conditioning trials, during which they were randomly assigned to consume the target beverage with either caffeine (1 mg/kg or 2 mg/kg) or placebo. On the final visit, participants re-tasted the 7 soda beverages and provided liking ratings and rankings. Participants in the caffeine group increased their liking of the target beverage over the exposure period, but there was no change in liking for those in the placebo group. These findings indicate that caffeine added to novel-flavored beverages increases liking and preferences of these beverages relative to those without caffeine. This conditioned preference represents an alternative mechanism for increased consumption of caffeinated beverages over time. Supported by: NIH.
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The sensitivity of AP neurons to amylin and GLP-1 is modulated by the feeding status

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The AP is sensitive to the anorectic hormones amylin and glucagon-like peptide 1 (GLP-1). Amylin-induced c-Fos expression and amylin's hypophagic effect is decreased by protein while 24 h fasting increases amylin-induced AP activation (c-Fos). Here we investigated whether the responsiveness of AP neurons to GLP-1 is also increased after 24 h fasting and whether the angiotensin II (AngII) mediated AP activation is independent of the feeding status because AngII primarily modulates cardiovascular function via