Abstracts

Society for the Study of Ingestive Behavior: Annual Meeting 2005
12 - 17 July, Sheraton Station Square Hotel, Pittsburgh, PA, USA

Guest Editor: Christine Zuberbuehler*

Masterfoods Keynote Lecture Series:

Note: Authors marked with # were recipients of New Investigator Awards.

*** Present address: Physiology & Animal Husbandry, Institute of Animal Sciences, Swiss Federal Institute of Technology, ETH-Zentrum, CH-8092 Zurich, Switzerland; Tel.: +41 44 632 3268; fax: +41 44 632 1128.**
E-mail address: christine.zuberbuehler@inw.agrl.ethz.ch

Food intake regulation of chicks by N/OFQ/NOP receptor system.

M. ABBASNEJAD, H. JONAIDI , D.M. DENBOW, A.M. POUR RAHIMI.
Department of Basic Sciences, Shahid Bahonar University of Kerman (SBUK), 76169-133, Kerman, Iran.

Nociceptin/orphanin FQ (N/OFQ), the endogenous ligand of the opioid receptor-like receptor or nociceptin receptor (NOP), has been shown to induce feeding, locomotion, anti-stress and anxiolytic effects in rodents after central nervous system injection. In this study, the effect of intracerebroventricular (icv) injection of N/OFQ on feeding behavior was evaluated in male broiler-type chickens. The icv injection of N/OFQ caused a moderate but significant increase in feed intake similar to the classical opioid peptides in rats. It also increased feed pecking frequency and feeding time 1 hour after injection. These results suggest that N/OFQ can act within the central nervous system of chickens to increase food intake, probably acting at NOP receptors. Keywords: Feeding behavior; Chickens; Nociceptin/orphanin FQ.

The flavor of fat: preferences for Olestra, mineral oil, and corn oil in rats.

K. ACKROFF, Y.-M. YIIN, A. SCLAFANI.
Brooklyn College of CUNY, Brooklyn, NY 11210, USA.

Rats are attracted to the flavor of nutritive corn oil and nonnutritive mineral oil. This study compared Olestra, a nonabsorbable sucrose polyester oil, to the other oils in food-restricted male rats given 30 min/day sessions. In choice tests, 5% Olestra was strongly (89%) preferred to 5% mineral oil and was overconsumed in one-bottle tests (21.1 versus 10.0 g). The same rats consumed similar amounts of 5% corn oil and 5% Olestra in one-bottle tests (33.8 versus 32.9 g) but preferred corn oil (78%) in two-bottle tests. In threshold tests with emulsifier vehicle, 0.5% Olestra was the lowest concentration preferred, while corn oil was still preferred at 0.25%. In one-bottle tests with 5% to 40% oils, the rats consumed more Olestra than corn oil overall, presumably due to corn oil's postoral satiating action. A sham-feeding study with oil-naive rats revealed that corn oil was preferred (84%) to Olestra in two-bottle tests but the oils were consumed equally in one-bottle tests. To determine if Olestra has positive postingestive actions, rats were trained with flavored saccharin solutions paired with intragastric infusions of 15% Olestra or water. The Olestra infusions did not alter flavor acceptance or preference. Thus, Olestra is a potent oral, but not postoral stimulus to rats. Its orosensory acceptance is close to that of corn oil, although corn oil is preferred in choice tests and has reinforcing postoral actions. Further studies of Olestra and corn oil may elucidate the orosensory systems mediating the flavor of fat. Supported by NIH Grant DK31135.

Vagal signaling, eating and metabolism in male Zucker obese (fa/fa) rats.

M. ARNOLD[a], B. FERRARI[a], D. HÄBERER[a], D.X. GRAM[b], R.D. CARR[b], W. LANGHANS[a].
[a]*Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland;* [b]*Pharmacology Research, Novo Nordisk, Måløv, Denmark.*

We previously demonstrated that subdiaphragmatic vagal deafferentation (SDA), i.e., a left dorsal (afferent) rootlet section (DRS) combined with an ipsilateral subdiaphragmatic vagotomy, affects eating, body weight (BW) gain, basal plasma glucose and insulin in Zucker obese (fa/fa) rats. Here we examined the critical lesion for these effects by introducing another group (DRS) in which we cut only the left dorsal rootlets. Male Zucker obese (fa/fa) rats (BW ~ 318 g) underwent SDA, DRS or SHAM surgery (n = 10 each). Compared to SHAM, SDA and DRS reduced ($P < 0.05$) daily food intake (SDA: 30.2 ± 0.5, DRS: 30.4 ± 1.0, SHAM: 33.3 ± 0.6 g) and SDA also BW gain (SDA: 49 ± 2, DRS: 53 ± 1, SHAM: 55 ± 2

g) from day 16 to 25 after surgery. 32 - 35 days after surgery, basal plasma glucose in SDA and DRS rats was lower ($P < 0.05$) than in SHAM rats (SDA: 7.0 ± 0.2, DRS: 7.0 ± 0.2, SHAM: 7.8 ± 0.2 mmol/L) and lower than prior to surgery. In DRS and SHAM rats, basal insulin was higher ($P < 0.05$) than in SDA rats (SDA: 8.9 ± 0.6, DRS: 11.9 ± 0.8, SHAM: 14.4 ± 1.6 ng/mL) and higher than prior to surgery. Thus, in Zucker obese (fa/fa) rats, DRS is sufficient to reduce food intake and basal plasma glucose, whereas the gradual increase in basal plasma insulin was prevented by DRS combined with ipsilateral subdiaphragmatic vagotomy.

Absence of hyperphagia following middle cerebral artery occlusion (MCAO) in uncoupling protein-2 knockout mice.

D. ARSENIJEVIC[a], S. CLAVEL[b], W. LANGHANS[a], D. RICHARD[b].
[a]*Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland;* [b]*Department of Anatomy and Physiology, Laval University, Quebec, Canada.*

We have previously reported that MCAO results in a biphasic change in food intake in mice, with anorexia during day 1 and day 2 and hyperphagia during day 3 to day 6 (Arsenijevic et al., Appetite 40, 315, 2003). Furthermore, these changes were associated with changes in the expression of the uncoupling protein-2 (UCP2) in the arcuate nucleus. Arcuate nucleus UCP2 mRNA, measured by in situ hybridisation, was decreased on day 1 and increased on day 4. To determine whether UCP2 is involved in the feeding effects of MCAO lesion, we compared the lesion's effects on food intake in wild-type (WT) and UCP2 KO mice. After MCAO, WT mice ate less than UCP2 KO mice on day 1 (2.1 ± 0.2 versus 3.0 ± 0.3 g, $P < 0.01$, n = 6). Hyperphagia on day 3 to day 5 after MCAO occurred only in WT (4.9 ± 0.2 versus 4.2 ± 0.1 g, $P < 0.01$), but not in UCP2 KO mice. Without surgery, food intake did not differ between the two genotypes (day 1: 4.2 ± 0.2 in WT and 4.0 ± 0.1 g in UCP2 KO; day 4: 4.3 g ± 0.1 in WT and 4.2 g ± 0.1 in UCP2 KO). These data indicate that UCP2 is involved in the anorexia and is necessary for the hyperphagia following MCAO lesions. Whether this is due to an action of UCP2 in the arcuate nucleus remains to be determined.

Binge-eating "prone" rats respond differently than "resistant" rats to intake of palatable food (PF) when hungry and stressed.

A.I. ARTIGA, L. MADDOX, A.J. ELDRIDGE, P.C. CHANDLER, C.R. CAMERON, C. PRITCHETT, M.L. SMITH, M.M. BOGGIANO.
Department of Psychology, University of Alabama at Birmingham, Birmingham, AL 35294, USA.

Stress and dieting are common antecedents of binge-eating disorders. These and PF also trigger binge-eating. We observed that while rats do not differ in the amount of chow they consume, some rats will consistently eat twice as much PF when given a choice. Hence, PF consumption overtly expresses an inherent propensity towards binge-eating proneness (BEP) or binge-eating resistance (BER). If PF is given intermittently (one day per week), BEPs will not gain more weight relative to BERs. Bulimics and many with binge-eating disorder are of normal body weight but they binge; therefore the BEP/BER model is useful in studying the physiology of these disorders and worth exploring further. To do this, we subjected BEP and BER rats to hunger and footshock-stress with a choice of chow and PF (cookies). Stress caused both groups to decrease their total food intake. However, BERs mainly decreased their PF intake ($P = 0.058$), while BEPs mainly decreased their intake of chow ($P < 0.05$). After food-restriction, BERs increased their total kcal intake (mainly from chow), and while BEPs

consumed more chow than when not hungry, their total intake was no greater than when sated. Hence, BEPs normally eat as many kcals of PF as they eat when hungry. Other BEP/BER comparisons and those to the DIO-model will be discussed. The different responses to stress and hunger in this model point to diverse physiological systems mediating intake of PF that can be explored to understand human responses to PF that predispose some to eating disorders. Ultimately, the genes predisposing these differences can be explored. Supported by NIH-R03-DK066007 and UAB-CNRC-P30DK056336.

Estradiol selectively increases LPS-induced c-Fos expression in ovariectomized rats.

L. ASARIAN, N. GEARY, W. LANGHANS.
Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland.

Gram-negative bacterial lipopolysaccharide (LPS) causes a robust acute phase response (APR) that includes anorexia. We previously reported that LPS-anorexia is sexually differentiated and that estradiol is part of the mechanism that mediates this phenomenon (Physiol. Behav. 2004: 82:251). After i.p. LPS, females in estrus ate less than females during diestrus or males, and estradiol treatment increased LPS anorexia in ovariectomized females. Here we explored the neural mechanisms of the effect of estradiol on LPS-anorexia using ovariectomized Long-Evans rats that received either cyclic estradiol (2 µg every 4 d, s.c.) or oil treatment. Estradiol-treated rats, tested on the day modeling estrus, and oil-treated rats received either LPS (12.5 µg/kg, i.p., n = 6) or saline (1 ml/kg, i.p., n = 6) injections at dark onset and were sacrificed 90 min later for c-Fos immunocytochemistry. The numbers of cells expressing c-Fos after LPS in the median raphe nuclei and PVN were each significantly higher in estradiol-treated rats than in either saline-injected estradiol-treated rats or LPS-injected oil-treated rats. There were no significant differences in c-Fos expression following LPS or saline treatment in oil-treated rats. LPS did not elicit c-Fos expression in the NTS in either estradiol or oil-treated rats. These data indicate that estradiol acts to increase LPS-induced neuronal activity in brain areas supposed to mediate anorexia following peripheral LPS administration. This mechanism appears to be selective to LPS-anorexia because LPS did not induce c-Fos expression in the NTS, a brain site known to mediate at least some of the physiological effects of estradiol on food intake.

Increased body weight and decreased CCK-8 satiety in female heterozygous serotonin 2C receptor-deficient mice.

L. ASARIAN, W. LANGHANS, N. GEARY.
Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland.

The serotonin 2C receptor subtype (5-HT2CR) plays an important role in the serotonergic control of feeding. Male 5-HT2CR knockout mice are slightly hyperphagic and become overweight beginning about 7 wk of age. In addition, systemic administration of the 5-HT2CR antagonist metergoline blocked the satiating action of exogenous CCK-8 in rats. Here we investigated the role of the 5-HT2CR in the control of body weight and CCK-8 satiety in female wild-type (WT) and heterozygous 5-HT2CR deficient mice (HET). Body weight gain was measured between 7-12 weeks of age in WT (n = 8) and HET (n = 3) female mice. Then, mice received intraperitoneal injections of 6 µg/kg CCK-8 or saline (1 ml/kg) at dark onset, and 2-h food intake was monitored. HET mice gained significantly more weight than WT mice between 7 and 12 weeks of age (5.5 ± 0.5 versus 4.0 ± 0.3 g, $P < 0.03$) and were

significantly less sensitive to 6 μg/kg CCK-8 than WT mice (2-h food intakes after saline versus CCK-8 were 0.45 ± 0.11 versus 0.51 ± 0.08 g, ns, for HET mice and 0.61 ± 0.07 versus 0.39 ± 0.06 g, $P < 0.01$, for WT mice). These data indicate that heterozygous deletion of the 5-HT2CR gene is sufficient to increase body weight gain and suggest that this may be due in part to a decrease in CCK satiety.

8-OHDPAT attenuates development of activity-based anorexia.

D.P.D. ATCHLEY, L.A. ECKEL.
Program in Neuroscience, Florida State University, Tallahassee, FL 32306, USA.

Female rats develop activity-based anorexia (ABA) when maintained on a restricted-feeding schedule in the presence of running wheels (RWs). Such conditions induce hypophagia, hyperactivity, weight loss, and disruptions in estrous cyclicity. Because the serotonin system has been implicated in the etiology and high relapse rates of anorexia nervosa (AN), we used this model of AN to determine whether reduced serotonergic neurotransmission attenuates the development of ABA in female rats. Following adaptation to custom-designed cages connected to RWs, baseline food intake, RW activity, and body weight were monitored for one estrous cycle. Rats were then placed on a restricted-feeding schedule (2 h daily). Each day, 40 min prior to food access, rats were s.c. injected with 0.5 mg/kg 8-OHDPAT, a drug that decreases serotonin neurotransmission, or saline vehicle (n = 8/group). Drug treatment and restricted feeding were terminated when individual rats lost ~ 25% of their body weight or after 10 days, whichever occurred first. Food restriction suppressed food intake similarly in 8-OHDPAT- and saline-treated rats (60% and 68%, respectively, ns). 8-OHDPAT treatment prevented the increase in RW activity observed in saline-treated rats. Thus, 8-OHDPAT-treated rats lost less weight than saline treated-rats (49 g versus 58 g, respectively, $P < 0.05$), and reached the 25% weight loss criterion more slowly (4.9 days versus 6.9 days, respectively, $P < 0.05$). These data suggest decreasing serotonergic neurotransmission, by chronic 8-OHDPAT treatment, prevents the hyperactivity associated with food restriction and, thereby decreases susceptibility to ABA. Supported by NIH Ruth Kirschstein NRSA (DPDA) and MH 63932 (LAE).

Melanocortin 4 receptor (MC4R) knockout mice have increased food intake and meal size, and decreased sensitivity to post-oral nutrient stimulation.

A.V. AZZARA, B. SCHUSS, S. HONG, S.C. CHUA, G.J. SCHWARTZ.
Albert Einstein College of Medicine, Bronx, NY 10461, USA.

Pharmacological agonists of MC4R produce reductions in food intake attributable to meal size, while MC4R antagonists are potent orexigens. To evaluate the effects of genetic absence of MC4R signalling on food intake and meal pattern, we measured spontaneous 22 h feeding patterns in male MC4R knockout (MC4RKO) and wildtype (WT) mice maintained on standard chow or high fat (24%) diets. On standard chow, MC4RKO mice displayed only mild hyperphagia compared to WT controls. However, on high fat diet, MC4RKO mice consumed nearly twice as many pellets as WT. This increased intake was entirely due to an increase in meal size, with MC4RKO meal size averaging twice that of WT. MC4RKO increased meal size may result from decreased post-ingestive feedback from gut nutrient stimuli. Mice with intraduodenal catheters received duodenal nutrient preloads prior to glucose feeding tests. Preloads of glucose and fat were less effective in reducing subsequent glucose drinking in MC4RKO compared to WT. Together these results support the idea that

the MC4R is involved in determining the behavioral potency of oral stimulatory and feeding inhibitory nutrient signals critical in determining meal size. Supported by DK66618.

Peripheral ghrelin administration increases food intake, meal size, and progressive-ratio responding for food.

A.V. AZZARA, B. SCHUSS, S. HONG, G.J. SCHWARTZ.
Albert Einstein College of Medicine, Bronx, NY 10461, USA.

The gut peptide ghrelin has been identified as a potent stimulator of food intake and has been implicated in the overall control of energy homeostasis. To further characterize the orexigenic effects of ghrelin, we evaluated the effects of a range of peripheral (IP) ghrelin doses (0.1 – 10 nmol) on both the appetitive and consummatory phases of food intake in male C57/BL6J mice. Mice maintained on a 12:12 hour light cycle with lights on at 0700 h received a single bolus injection of ghrelin 6 hours prior to lights-out, and spontaneous meal patterns were assessed over the subsequent 22 h. Ghrelin decreased the latency to the first meal, and more than doubled food intake within the first hour post-treatment. This hyperphagia was still present at 4 hours, but 24-hour intakes did not differ. Ghrelin specifically increased meal size (> 2x), without altering meal frequency. Peripheral ghrelin administration also increased appetitive nose-poking (progressive ratio 5) and breakpoints for both solid (24 % fat pellets) and liquid (20% Intralipid fat emulsion) rewards. These results: 1) support the idea that ghrelin acts to modulate the potency oral and post-oral feedback signals that contribute to the control of meal size, and 2) suggest that increased ghrelin levels reported prior to meal taking may promote food seeking behavior. Supported by DK065790 and MH65024.

High protein diet stimulates liver gluconeogenesis but not glucose release from liver.

D. AZZOUT-MARNICHE, C. GAUDICHON, C. BLOUET, V. MATHÉ, C. BOS, J.F. HUNEAU, D. TOMÉ.
UMR 914 INRA-INAPG. 914 Physiologie de la Nutrition et du Comportement Alimentaire, 16 rue Claude Bernard, 75005 Paris, France.

We reported that adaptation to a high protein diet induces a decrease in food intake and body fatness and occurs by adjusting protein oxidation and carbohydrate metabolism to protein intake. In this study, we investigated glucose metabolism in rat adapted to a high protein diet (55%) (HP) for 15 days. In liver, the utilization of amino acids in HP rats is stimulated, as assessed by increased Alanine aminotransferase (AlAT) and Aspartate aminotransférase (AsAT) expression (3.5 and 4.6 fold, respectively, $P < 0.05$). The mRNA encoding phosphoenolpyruvate carboxykinase (PEPCK), the first gluconeogenic enzyme, was expressed at similar level in the fasted and fed-state in HP-fed rats, and higher than in NP-fed rats. However, the expression of glucose 6-phosphatase (G6PC1), which catalyzes the last step of gluconeogenesis, is similar in HP and NP rats in the fed state. In vitro glucose production was not different in hepatocytes isolated from HP or NP rats fed rats (respectively 490.4 ± 72.57 and 534.5 ± 129.13 nmol glucose/hour/106 hepatocytes) whereas it was 3.5 higher in hepatocytes isolated from HP compared to NP-fasted rats. These results suggested that HP diet stimulated the first step of gluconeogenesis, but that glucose is not released from hepatocytes because of the inhibition of G6PC1. This is the first evidence of a differential regulation of PEPCK and G6PC1 by nutritional state.

Effects of icv NPY on sucrose, saccharin, and water licking microstructure.

J.P. BAIRD, N.E. GRAY, S.G. FISCHER.
Department of Psychology, Amherst College, Amherst, MA 01002, USA.
Previously we showed that third intracerebroventricular neuropeptide-Y (NPY) injections (5 μg/5 μl) increased sucrose intake across a range of concentrations. Licking microstructure analyses indicated that NPY prolonged meal duration and increased burst counts but did not increase first minute lick rate or mean burst size. These effects were consistent with an effect of NPY on postingestive feedback rather than taste evaluation. In the present study we evaluated NPY effects on licking for 1M sucrose, 0.1% saccharin, and water solutions. The effects of NPY on 1 M sucrose were replicated: intake was doubled ($P < 0.02$), meal duration and burst count increased almost four-fold ($P's < 0.05$), and mean burst size and lick volume was reduced ($P's < 0.05$). Although NPY increased saccharin intake by 42% over the 2 h test period, there was no significant effect on the size of the first meal (only 5% intake increase) using a 10 min meal criterion. NPY had no effect on most measures of saccharin licking microstructure except that lick volume was reduced ($P < 0.03$). No effects of NPY on water ingestion were observed at all. Overall, results are consistent with the interpretation that the effects of NPY on ingestive behavior are food-specific and mediated through an increase in appetitive behaviors (spout engagements) and a diminution of post-ingestive (caloric) feedback rather than enhancement of taste evaluation.

Yohimbine promotes anorexia in rats lacking noradrenergic (NA) input to the bed nucleus of the stria terminalis (BNST).
L. BANIHASHEMI, L. RINAMAN.
Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA.
NA projections from the hindbrain to the BNST are implicated in behavioral and endocrine responses to stress. Yohimbine (YO), an alpha-2 receptor antagonist, increases transmitter release from NA terminals and is anxiogenic. We have shown that YO induces cFos activation in BNST-projecting brainstem neurons, and that NA inputs to the BNST are necessary for YO to activate cFos in the BNST and paraventricular nucleus of the hypothalamus (PVN). We hypothesized that the anorexigenic effect of YO also requires NA inputs to the BNST. To test this, NA inputs to the BNST were lesioned using DSAP (an antibody against dopamine beta hydroxylase, DBH, conjugated to saporin toxin) injected bilaterally into the ventrolateral BNST. After 10 - 14 days, DSAP-lesioned rats (n = 9) and sham-lesioned rats (n = 7) were food-deprived in their home cages for 24 hours. Thirty minutes after i.p. YO (0 or 5 mg/kg), food was returned and cumulative intake was recorded at 30 min, 60 min and 18 hr. In a separate experiment, DSAP and control rats were injected with YO (0 or 5 mg/kg, i.p.) and then perfused with fixative 90 – 120 minutes later. Brain sections were processed to reveal lesion extent and treatment-induced cFos activation. YO (5 mg/kg) induced a similar degree of anorexia in both sham-lesioned and DSAP-lesioned rats. ANOVA revealed a significant inhibitory effect of YO on food intake ($P < 0.001$), but no effect of lesion group ($P = 0.227$). We conclude that while NA inputs to the BNST are necessary for BNST and PVN cFos responses to YO, these inputs are unnecessary for the ability of YO to inhibit food intake.

Effects of High Fat Diets on the Blood-Brain Barrier Transport of Leptin.
W.A. BANKS.
VA and Saint Louis Univeristy School of Medicine, St. Louis, MO, USA.

The leptin resistance associated with diet-induced obesity first arises at the level of the blood-brain barrier (BBB). Decreased transport of leptin across the BBB can be both acquired and reversed and is mediated in part by substances circulating in the blood. We have shown that blood-borne triglycerides are an important regulator of leptin transport. Fasting, which lowers triglycerides, increases leptin transport, whereas starvation and high fat diets, which increase triglycerides, decreases leptin transport. Administration of the triglyceride triolein has a dose dependent effect on leptin transport and triglycerides inhibit leptin transport across an in vitro model of the BBB. Pharmacologic lowering of triglycerides also enhances leptin transport. These studies show that serum triglycerides are an important regulator of leptin transport across the BBB and could be important in the development of leptin resistance and obesity.

Hyperinsulinemia under conditions of hyperglycemia or hypoglycemia increase dopamine in the nucleus accumbens of the rat.

N.T. BELLO, A. HAJNAL.
Department of Neural and Behavioral Sciences, College of Medicine, The Pennsylvania State University, Hershey, PA 17033, USA.

Perturbations in metabolic states (i.e., food restriction, diabetes, and obesity) have been shown to alter the function of the mesoaccumbens dopamine system. We investigated if different concentrations of insulin influence basal dopamine levels in the nucleus accumbens of the rat. Adult male Sprague Dawley rats (n = 12) anesthetized with chloral hydrate were implanted with microdialysis probes in the caudo-medial nucleus accumbens and equipped with venous and arterial catheters for the hyperinsulinemic-euglycemic clamping procedure. During the microdialysis, each rat was infused with one of three concentrations of insulin (2.4, 4.8, and 9.6 mU/kg/min) while plasma glucose levels were maintained at ~ 100 mg/dl. Despite that dopamine and dihydroxyphenylacetic acid were not significantly different form baseline during the clamp procedure there was a great deal of variability in dopamine levels immediately after the insulin and glucose infusions ceased. Therefore, a follow-up experiment was performed, in which rats were infused with one concentration of insulin (9.6 mU/kg/min) and plasma glucose was maintained at either hypoglycemia (~ 50 mg/dl; n = 5) or hyperglycemia (~ 300 mg/dl; n = 5). Results showed an increase in dopamine over baseline levels [$F(11,88) = 2.84$, $P < 0.01$], irrespective of the actual glycemic condition. Post hoc tests revealed that dopamine was elevated over baseline during the last 20 min of the clamp procedure and after the infusions ceased ($P < 0.05$ for both). These results together suggest that hyperinsulinemia stimulates the mesoaccumbens dopamine system only when blood glucose levels deviate from euglycemia (i.e., in either direction). This finding further supports a role for mesoaccumbens dopamine in complex metabolic regulation. Supported by NIH grants NS046872 and DK065709.

Deletion of the syndecan-3 gene attenuates the hyperphagia and obesity of the agouti lethal yellow (Ay) mouse.

S.C. BENOIT[a], D.J. CLEGG[a], A.D. STRADER[b], O. REIZES[b].
[a]*University of Cincinnati, Cincinnati, OH 45237, USA;* [b]*Muscle/Obesity, Procter & Gamble Pharmaceuticals, Inc., Mason, OH 45241, USA.*

Recent data suggest that CNS plasticity may be important for the regulation of body weight. Syndecan-3 is a membrane-bound heparan-sulfate proteoglycan, important for learning, LTP, and hippocampal plasticity. Importantly, syndecan-3 is also expressed in hypothalamic nuclei known to regulate energy balance. We previously demonstrated that mice with targeted

disruption of the syndecan-3 gene are partially resistant to obesity inducing effects of a palatable, high-fat diet (Strader et al., *J. Clin. Invest.* 2004;114:1354-1360.). One possibility is that syndecan-3 facilitates the actions of endogenous melanocortin (MC) antagonists (i.e., AgRP and agouti protein). To test this hypothesis, we crossed syndecan-3 -/- and agouti lethal yellow (Ay) obese mice. Syndecan-3 deletion dose-dependently attenuated the Ay obese phenotype. Syndecan-3 -/-; Ay mice exhibited significantly reduced food intake, body weight and body fat compared to Ay mice. Additionally, syndecan-3 heterozygosity conferred ~ 50% protection to Ay mice, compared to syndecan-3 -/-; Ay double mutants. These data strongly implicate an important interaction between syndecan-3 and MC antagonists in the regulation of body weight. These findings also support the idea that molecular mechanisms of CNS 'plasticity' play important roles in the regulation of energy balance, in addition to learning and memory.

Long-term effects of post weaning running wheel access on food intake and body weight in OLETF rats lacking cholecystokinin (CCK) A receptors.

S. BI, J. CHEN, K.A. SCOTT, T.H. MORAN.
Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA.

Otsuka Long-Evans Tokushima Fatty (OLETF) rats lacking CCK-A receptors are hyperphagic and obese. We have demonstrated that voluntary exercise reduces food intake and normalizes body weight in OLETF rats and when a period of exercise begins at 8 weeks of age, there is a lasting reduction in the degree of obesity. To extend these findings, we assessed whether an 8 week period of voluntary exercise beginning at 4 weeks of age further reduce the eventual degree of food intake and body weight in OLETF rats. We found that during the 8 weeks of running wheel access exercising control LETO rats (LETO.RW) had increased food intake but decreased body weight gain compared to sedentary LETO rats. Exercise decreased food intake and prevented weight gain in OLETF rats (OLETF.RW). When returned to home cages, LETO.RW rats gradually regained body weight and reduced their increased food intake to levels similar to those of sedentary LETO rats. In contrast, when returned to home cages, the food intake and body weight of OLETF.RW rats did not return to those of sedentary OLETF rats. OLETF.RW rats attained a body weight intermediate between sedentary LETO and OLETF rats by 21 weeks of age. These data are similar to those obtained when running wheel access was begun at 8 weeks of age suggesting that the timing of the exercise during development is not a critical factor for the eventual phenotype of OLETF rats. Supported by DK57609. The OLETF and LETO rats were a gift of Otsuka Pharmaceutical, Japan.

Comparative effects of CCK and GLP-1 on appetite, energy intake and pyloric motility in healthy men.

I. BRENNAN[a], K.L. FELTRIN[a], M. HOROWITZ[a], A.J.P.M. SMOUT[b], J.H. MEYER[a], C. FEINLE-BISSET[a].
[a]*Departments of Medicine, University of Adelaide, South Australia;* [b]*Gastroenterology, University Hospital Utrecht, The Netherlands.*

Both small intestinal infusion of nutrients and intravenous administration of cholecystokinin (CCK) and glucagon-like peptide-1 (GLP-1) suppress appetite and energy intake and slow gastric emptying. The latter reflects the suppression of antral and duodenal pressures and stimulation of tonic and phasic pyloric pressures, suggesting a relationship between changes

in energy intake and motility, which has hitherto not been evaluated. Moreover it has been reported that electrical stimulation of the pylorus decreases energy intake in dogs (*Gastroenterology* 2005;128:43-50). We have evaluated the effects of i.v. CCK and GLP-1 on pyloric motility, appetite and energy intake. 9 healthy men were studied on three occasions. Appetite and pyloric pressures were measured during 150 min i.v. infusions of (i) isotonic saline (control), (ii) CCK-8 (1.8 pmol/kg/min) and (iii) GLP-1 (0.9 pmol/kg/min). At 120 min energy intake was quantified. CCK-8 increased fullness, decreased hunger and subsequent energy intake and increased phasic and tonic pyloric pressures ($P < 0.05$). GLP-1 failed to stimulate pyloric pressures, and had no effect on either appetite or energy intake. In conclusion, in the doses evaluated, exogenous CCK-8 and GLP-1 had discrepant effects on appetite, energy intake and pyloric pressures: CCK-8 stimulated pyloric pressures and suppressed subsequent energy intake, while GLP-1 did not stimulate pyloric pressures and had no effect on energy intake, consistent with the concept that pyloric pressure activity contributes to the regulation of energy intake.

Effects of interleukin-1b **on spontaneous meal patterns during the rat estrous cycle.**

P.C. BUTERA, M.M. FERRARO, C. COOGAN-BASSETT.
Niagara University, Department of Psychology, Lewiston, NY 14109, USA.

Proinflammatory cytokines (e.g., IL-1) are released by an activated immune system during infection, inflammation, and stress resulting in anorexia, aches and pains, hypersomnia, and lack of interest in usual activities. Previous findings indicate that the anorectic effect of IL-1β is enhanced in ovariectomized rats treated with a cyclic pattern of estradiol replacement, suggesting that estradiol modulates responsiveness to IL-1. However, it is unclear how the interaction between estradiol and IL-1 affects the microstructure of feeding behavior to bring about this inhibition of food intake. The purpose of this experiment was to determine whether the effects of IL-1 on meal patterns are influenced by changes in endogenous hormones during the ovarian cycle. Cycling female rats were given intraperitoneal injections of IL-1β (5.0 μg/kg) or physiological saline one hour before dark onset during diestrus and estrus stages of the ovarian cycle. Food intake, meal size, and meal number were recorded during the subsequent 12-hour nocturnal period of spontaneous feeding. The ANOVA revealed a significant interaction between estrous cycle stage and IL-1. Subsequent analyses indicated that the inhibitory effect of IL-1 on food intake during estrus resulted from a decrease in meal frequency without any significant effect on meal size. IL-1 had no significant effect on meal frequency during diestrus although there was a slight decrease in meal size during the first nocturnal quartile of diestrus. These findings suggest that different mechanisms control estradiol¹s physiological effects on eating, which occur as a change in meal size, from its pathophysiological actions on meal frequency during IL-1-induced anorexia. Supported by NIH grant HD40238.

Visceral inhibition of NaCl consumption by adrenalectomized rats.

M.R. BYKOWSKI, M.L. HOFFMANN, E.M. STRICKER.
Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA.

Rats consume large volumes of NaCl solution after bilateral removal of their adrenal glands. The present experiments sought to identify the postingestional signals that cause adrenalectomized (adrex) rats to stop consuming saline solution. For 7-10 days after surgery, adrex rats were given access to 0.15 M or 0.30 M NaCl for 5-6 hr daily; food and water were present ad libitum. In addition, some adrex rats were given 0.05 M NaCl to drink for 1 hr

daily and then, after a 30-min delay, 0.30 M NaCl was available for 5 hr. Adrex rats were observed to consume similar amounts of 0.05 M and 0.15 M NaCl in a 10-min drinking test, but they drank significantly less 0.30 M NaCl. Interestingly, the rats stopped consuming saline while almost all of the ingested solution was still present in the stomach and small intestine, and the osmolality of systemic blood was not yet affected. Gastric emptying varied as a function of concentration; the hypertonic solution emptied little in 10 min, whereas the more dilute solutions emptied quite rapidly. These and other findings suggest two dimensions for inhibition of saline consumption by adrex rats: distension of the stomach and small intestine, and increased osmolality (or Na^+ concentration) of visceral blood. Summation of these early postingestional signals may override the excitatory stimulus for saline ingestion by adrex rats.

C-fos expression in paraventricular nucleus of the hypothalamus after gastric infusion of ethyl oleate.

C.R. CAMERON, W. WANG, A. RANDICH, J.E. COX.
Department of Psychology, University of Alabama at Birmingham, Birmingham, AL 35294-1170, USA.

Intragastric ethyl oleate (EO) reduces food intake and body weight in rats. Previous electrophysiological and c-fos studies have revealed activation of neurons in the paraventricular nucleus of the hypothalamus (PVN) after gastrointestinal infusions of lipids (*AJP* 2004;286:R166-R173, *AJP* 1997;273:R2059-R2071). The present study examined which subnuclei of the PVN expressed c-fos two hours after intragastric infusions of either EO or vehicle. The amount of c-fos was rated as 0-none; 1-sparse; 2-moderate; or 3-dense, as a function of subnuclear locations within the PVN (anterior, medial, dorsal, ventral, and lateral parvocellular regions; anterior and posterior magnocellular regions). The results indicated that in EO-treated rats relative to vehicle-treated rats, the medial parvocellular subnucleus was densely labeled. This was followed by moderate to sparse labeling in the anterior, ventral, and dorsal parvocellular subnuclei. There also was sparse labeling of the posterior magnocellular subnucleus, but when this occurred, it was primarily on the medial border with the medial parvocellular subnucleus. These findings present a different picture than our previous electrophysiological studies involving jejunal administration of linoleic acid. In the present studies, we observed the strongest c-fos activation in mid PVN regions (~ -1.8 mm posterior to bregma) as compared to our previous report in which the strongest single unit activation occurred in the anterior PVN (~ - 0.9 – 1.3 mm posterior to bregma). However, differences in the location of the gastrointestinal infusions and type of lipids between these studies may have contributed to these discrepancies.

Dietary fat can increase alcohol intake.

C.A. CARRILLO[a], S.F. LEIBOWITZ[b], O. KARATAYEV[b], B.G. HOEBEL[a].
[a]Princeton University, Princeton, NJ 08544, USA; [b]Rockefeller University, New York, NY 10021, USA.

Ingestion of fat or ethanol can stimulate mRNA for galanin (GAL) in the PVN. Conversely, GAL injected into the PVN or third ventricle can stimulate the consumption of fat or ethanol. The question for this series of experiments is whether or not the ingestion of fat can directly stimulate ethanol consumption. Three experiments examined the effect of voluntary or involuntary fat intake in rats that had learned to drink ethanol. 1. In the first experiment, adult Sprague-Dawley rats were maintained on a high-fat diet (50% fat) for 7 days. Then they

switched to a lab chow diet while being trained to drink 9% (v/v) ethanol. The animals that had eaten the greatest amount of the high-fat diet subsequently drank the most ethanol. 2. In the second experiment, a 1-hr meal of a high-fat diet (50% fat) produced a significant increase in 7% ethanol consumption compared to an equicaloric, low-fat (10% fat) meal. 3. In the third experiment, injection of a fat emulsion, Intralipid (20%, 5.0 ml, i.p.), to eliminate orosensory effects, increased ingestion of 9% ethanol significantly. As a control, equicaloric, 50% glucose injection did the opposite by suppressing ethanol intake. These findings with acute tests provide new evidence suggesting that dietary fat can increase ethanol intake. This research is supported by USPHS grant AA-12882 and the Minnie and Bernard Lane Foundation and Wyeth, Inc.

Sex and estrous cycle differences in the behavioral effects of high-strength static magnetic fields: role of ovarian steroids.

A.M. CASON, M.J. DENBLEYKER, K.D. FERRENCE, J.C. SMITH, T.A. HOUPT.
Program in Neuroscience, Departments of Biological Science and Psychology, Florida State University, Tallahassee, FL 32306-4340, USA.

Magnetic fields (MFs) induce locomotor circling, suppresse rearing and induce conditioned taste aversion (CTA) in male and female rats. To determine if there are sex differences in response due to ovarian steroids, we compared males to intact females across the estrous cycle and to ovariectomized females (OVX) with or without chronic estrogen (E) or estrogen and progesterone (EP). Water-restricted rats received 1 (intact females) or 3 pairings (OVX females) of 0.125% saccharin (10-min access) with exposure to a 14 T MF or 0T for 30 minutes. Circling and rearing was measured by videotaping for 2 minutes after exposure. CTA was measured by 24-h, 2-bottle preference test for 12 days. Magnet-exposure (not sham-exposure) induced circling, suppressed rearing, and caused CTA in all groups. Intact females, especially estrus females, displayed more circling behavior than males but acquired CTAs of similar magnitude after 1 pairing; however, males extinguished but females failed to extinguish. Compared to intact rats, OVX increased circling; E decreased circling in OVX rats. After 3 pairings, males had greater CTA than intact and OVX females. However, E and EP increased extinction transiently in OVX females. Thus, the response to MFs is sensitive to sex and ovarian steroids. Because circling varied across the estrous cycle and was senstive to OVX and replacement, the locomotor response may be acutely modulated by ovarian steroids (activational effect). Because CTA was only weakly affected by OVX and steroids, the CTA response may be determined more by sex than acute steroids (organizational effect). Supported by NIDCD04607, DC006521.

Co-ingestion of alcohol and food: acute effects on energy intake.

S.J. CATON, L.E. BATE, M.M. HETHERINGTON.
School of Psychology, University of Liverpool, L69 3BX England, UK.

Alcohol ingestion is often coupled with energy overconsumption and could therefore contribute to positive energy balance. Our previous investigations have demonstrated the stimulatory effect of alcohol on food intake when given before a meal, as an aperitif. To compare the effects of alcohol on food intake when it is given either before or along with food, 10 lean, healthy males attended the laboratory on three occasions. On each occasion participants consumed a standard breakfast and then returned to the laboratory around four hours later for lunch. Participants received either 375 ml of red wine 20 min before lunch (aperitif), no-alcohol (baseline) or 125 ml of red wine with the starter course and 250ml of red

wine with the main course (co-ingestion). Subjective ratings of appetite and mood were taken before and after lunch. Ad libitum energy intake at lunch was greater when alcohol was consumed ($P < 0.05$) in both the aperitif (6394 ± 477 kJ) and the co-ingestion (6291 ± 461 kJ) conditions in comparison to the baseline condition (5123 ± 290 kJ). Energy intake at lunch in both the alcohol conditions did not vary. Total energy intake was higher in the aperitif (7465 ± 477 kJ) and the co-ingestion condition (7361 ± 461 kJ) in comparison to the baseline condition. Confirming our previous studies, a moderate dose of ethanol (3 units/24 g) stimulates food intake and contributes to greater total energy intake relative to no alcohol. This effect does not rely on a time delay between administration and access to food.

State dependent learning in caffeine conditioned flavour preference using a within subject design.

L. CHAMBERS, S. MOBINI, M.R. YEOMANS.
Department of Psychology, University of Sussex, Brighton, UK.

Previous studies have reported that moderate caffeine consumers acquire a liking for the flavour of a novel caffeinated drink when these drinks are consumed repeatedly in a caffeine-deprived, but not undeprived, state (e.g. Yeomans et al., *Psychopharmacology* 1998;137:401-409). Morover, expression of acquired liking for the caffeine-paired flavour was found to be acutely sensitive to current caffeine deprivation state. However, these studies all used between-subjects designs, where one group of participants consumed a caffeinated version of a drink, and a separate group acted as control and consumed the same drink without caffeine. These designs are open to interpretations which rely less on conditioned associations. The present study was designed to investigate these findings further using a more rigorous within-subject design, with one flavour consistently paired with caffeine (CS+) and the second the absence of caffeine (CS-). During four CS+ and four CS- training days, 32 moderate caffeine consumers alternatively consumed a novel caffeinated (100 mg) flavour and a novel non-caffeinated flavour on non-consecutive days. Participants evaluated these drinks before and after training sessions in two motivational states; caffeine deprived and undeprived. As predicted, participants gave higher pleasantness ratings for the caffeinated flavour in both the deprived and undeprived conditions. However, this increase in liking was only significant when tested caffeine-deprived. The results also confirmed positive psychostimulant effects of caffeine, with increased ratings of lively, clear-headed and energetic ratings following the consumption of caffeinated drink. Overall these data imply that expression of acquired liking for a novel caffeinated flavour depends on the actual need for the effects of caffeine at the time when the drink is evaluated.

Effect of intermittent versus chronic palatable-food (PF) on rat body-composition and endocrine parameters.

P.C. CHANDLER, A.I. ARTIGA, C.R. CAMERON, L. MADDOX, M.M. BOGGIANO.
Department of Psychology, University of Alabama at Birmingham, Birmingham, AL 35294, USA.

Intermittent access to PF (IPF) with caloric-restriction (R) is emerging as key in the neuroendocrinology of binge-eating but the effect of PF itself versus its intermittency on energy-regulating parameters is unclear. Therefore, we assigned rats to a diet of chow-only (C-only), chow and IPF (C+IPF), or chow and PF at all times (C+PF). Half of each group were cycled through 12 restriction-refeeding (R) bouts for 144 days. The C+PF diet doubled body-fat (16% versus 8% in IPF and C-only rats) and increased leptin levels (by 80%) despite

C+PF rats adjusting their intake to equal daily kcals of the IPF and C-only groups. Interestingly, even though the C+PF group consumed more PF kcal/cycle (64%) than the C+IPF group (28%), bone mineral density (BMD) was the same for these groups but 9.1% lower in both these groups versus C-only rats ($P < 0.001$). ACTH levels were also lower for PF groups and lowest in C+PF rats ($P < 0.01$). PF groups also had lower insulin:body fat ratios. A history of R only interacted with diet to increase glucose in C+IPF rats ($P < 0.001$). These results highlight the profound impact of PF (vs R) on endocrine parameters. Ad-lib PF's effect as "comfort food" in lowering ACTH may prove "uncomfortable" if body-fat is increased and BMD decreased. Ad-lib PF and, first evidenced here, IPF+R, produces a diabetic-like condition. The physiological changes imposed by PF should be considered in animal models and behavioral/dietary treatments of obesity and binge-eating. Support: NIH-R03-DK066007 and UAB-CNRC-P30DK056336.

A history of dieting and intermittent palatable food alters forebrain monoamine levels in ways consistent with depression, impulsivity, and binge-eating.

P.C. CHANDLER[a], E. CASTANEDA[b], A.I. ARTIGA[a], A.J. ELDRIDGE[a], L.C. MADDOX[a], C.R. CAMERON[a], M.M. BOGGIANO[a].

[a]*Department of Psychology, University of Alabama at Birmingham, Birmingham, AL 35294,USA;* [b]*Department of Psychology, Arizona State University, Tempe, AZ, USA.*

In eating disorders, dieting is a common antecedent and depression and impulsivity common comorbidities. Surprisingly, it is not known whether a history of dieting induces lasting neurochemical changes in forebrain areas involved in mood, motivation, and impulse-control. Rats were provided either with chow (C), chow and palatable food at all times (PF), or chow and intermittent access to PF (IPF). Within each of these conditions, half the rats were food restricted (R) on days 1-5, then allowed to freely-feed on days 6-12 (one cycle). The other halves were never restricted (NR). After 12 cycles NR rats, irrespective of diet condition, had a strong positive association between serotonin and dopamine turnovers in the nucleus accumbens, an association completely absent in R rats. This pattern was also found in an earlier study with IPF-R versus IPF-NR rats. In the medial prefrontal cortex (mPFC), serotonin and dopamine levels were 71% and 58% lower in IPF-R versus IPF-NR rats. We (and others) have found that rats subjected to IPF-R are vulnerable to binge-eating. In a subsequent experiment, mPFC-infusion of the serotonin antagonist, metergoline, increased chow intake (93%). Together, the results indicate that a history of dieting, despite normal body weight and food intake, can alter monoamine levels. Blunted 5HT-signaling in the mPFC via drugs or past caloric-restriction increases food intake and may increase susceptibility to binge-eat. Decreased mPFC-5HT and R-induced disruption of DA/5HT interactions in the nucleus accumbens may also help explain depression and impulsivity that commonly accompany binge-eating disorders. Supported by NIH-R03-DK066007.

Body composition and endocrine profile of long-term binge-eating rats.

P.C. CHANDLER, J.B. VIANA, K.D. OSWALD, M.M. BOGGIANO.

Department of Psychology, University of Alabama at Birmingham, Birmingham, AL 35294, USA.

We developed a rodent model of binge-eating where rats with past caloric-restriction (CR) binge on palatable-food (PF) when stressed (S; via footshock). In this study we used young female rats to examine the strength and duration of binge-eating after multiple CR/S cycles and the effect of these cycles on body composition and energy-regulating hormones. During

initial cycles, the binge-eating (CR+S) rats consumed 100 - 140% more PF kcals in 4 hrs than CR-only, S-only, and control rats. Just prior to sacrifice, after the 23rd cycle, they were still consuming 100% more than the other groups at 4 and 24 hrs ($P < 0.001$) following stress. Binge-eating in this model does not appear to wane with time (app. 5 months here). Body weights did not differ significantly across groups although there was a trend of decreased weight in S-only rats. Compared to the control condition, CR-history, alone, did not alter percent body fat and S-alone decreased it by 42% ($P < 0.001$), but CR+S prevented this decrease. DEXA-analyzed bone mass content and bone mineral density were not altered under any condition. Plasma leptin levels paralleled body fat levels. Plasma insulin levels were normal across all conditions as were plasma glucose levels except in the CR+S group, which had twice the plasma glucose levels ($P < 0.01$). The endocrine profile of the binge-eating-prone, CR+S rats, is strikingly similar to that reported for bulimics and binge-eaters (normal plasma leptin and insulin but elevated glucose) and may reflect a conditioned endocrine response adaptive in dealing with impending future episodes of dieting and stress. Supported by NIH-R03-DK066007 and UAB-CNRC-P30DK056336.

Intravenous infusion of ghrelin increases meal frequency and attenuates anorexigenic responses to peptide YY(3-36), glucagon-like peptide-1, and CCK in rats.

P.K. CHELIKANI, A.C. HAVER, R.D. REIDELBERGER.
VA-Nebraska Western Iowa Health Care System, Omaha, NE 68105, USA.

Ghrelin is an orexigenic brain-gut peptide whereas peptide YY(3-36) [PYY(3-36)], glucagon-like peptide-1 (7-36) (GLP-1), and CCK are anorexigenic brain-gut peptides. We investigated the dose-response effects of intravenous infusion of ghrelin on food intake and meal patterns, and assessed whether ghrelin attenuates anorexigenic responses to PYY(3-36), GLP-1, and CCK-8. In separate experiments, non-food-deprived rats received at dark-onset a 3-h i.v. infusion of (i) ghrelin (5 to 150 pmol/kg/min), (ii) PYY(3-36) (15 pmol/kg/min) alone or with ghrelin (15 or 50 pmol/kg/min), (iii) GLP-1 (15 pmol/kg/min) alone or with ghrelin (15 or 50 pmol/kg/min), and (iv) CCK-8 (15 pmol/kg/min) alone or with ghrelin (50 or 150 pmol/kg/min). Ghrelin infusion at 150 pmol/kg/min increased 3-h food intake by 40% by increasing meal frequency. PYY(3-36) infusion alone at 15 pmol/kg/min inhibited 3-h food intake by 31%; co-infusion of ghrelin at 15 and 50 pmol/kg/min attenuated this response by 82 and 83%, respectively. GLP-1 infusion alone at 15 pmol/kg/min inhibited 3-h food intake by 49%; co-infusion of ghrelin at 50 and 150 pmol/kg/min attenuated this response by 57% and 63%, respectively. CCK-8 infusion alone at 15 pmol/kg/min inhibited 3-h food intake by 53%; co-infusion of ghrelin at 50 pmol/kg/min attenuated this response by 27%. We conclude that intravenous infusion of ghrelin stimulates food intake during the dark period in rats by increasing meal frequency, and that ghrelin attenuates the inhibitory effects of PYY(3-36), GLP-1, and CCK on food intake. Supported by Department of Veterans Affairs and NIH grant DK55830.

Intravenous infusion of glucagon-like peptide-1 potently inhibits food intake, sham-feeding and gastric emptying in rats.

P.K. CHELIKANI, A.C. HAVER, R.D. REIDELBERGER.
VA Nebraska/Western Iowa Health Care System and Creighton University, Omaha, NE 68105, USA.

Glucagon-like peptide-1(7-36) (GLP-1) is postulated to act as a hormonal signal from gut to brain to inhibit food intake and gastric emptying. A mixed-nutrient meal produces a 2 - 3 h

increase in plasma GLP-1. Bolus systemic doses of GLP-1 have been reported to have little or no effect on food intake in rodents. We determined the effects of intravenous infusions of GLP-1 on food intake, sham feeding, and gastric emptying in rats to assess whether GLP-1 inhibits food intake in part by slowing gastric emptying. A 3 h intravenous infusion of GLP-1 (0.5 - 170 pmol/kg/min) at dark onset dose-dependently inhibited food intake in non-food-deprived rats with a potency (mean effective dose) and efficacy (maximal % inhibition) of 23 pmol/kg/min and 82%, respectively. Similar total doses of GLP-1 administered over a 15-min period were less potent and effective. In gastric emptying experiments, GLP-1 (1.7 - 50 pmol/kg/min) dose-dependently inhibited gastric emptying of saline and ingested chow with potencies of 18 and 6 pmol/kg/min and maximal inhibitions of 74 and 83%, respectively. In sham-feeding experiments, GLP-1 (5 - 50 pmol/kg/min) dose-dependently reduced 15% aqueous sucrose intake in a similar manner when gastric cannulas were closed (real feeding) and open (sham feeding). These results demonstrate that intravenous infusions of GLP-1 dose-dependently inhibit food intake, sham feeding, and gastric emptying with a similar potency and efficacy. We conclude that GLP-1 may inhibit food intake in part by reducing gastric emptying, yet can also inhibit food intake independently of its action to reduce gastric emptying. Supported by Department of Veterans Affairs and NIH grant DK55830.

Characterization of the feeding inhibition and neural activation produced by dorsomedial hypothalamic cholecystokinin (CCK) administration.

J. CHEN, K.A. SCOTT, T.H. MORAN , S. BI.
Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA.

We have demonstrated that neuropeptide Y (NPY) expressing neurons in the dorsomedial hypothalamus (DMH) are colocalized with CCK-A receptors and that administration of CCK into the DMH inhibits food intake and decreases NPY gene expression in both the DMH and arcuate nucleus (ARC). We have suggested that DMH CCK-NPY signaling system plays an important role in the control of food intake and body weight. However, the neural circuitry underlying the actions of DMH CCK in feeding control haves not yetto been determined. In these experiments, we determined examined the time course of feeding inhibitory effects of DMH CCK administration and characterized the activation brain sites activated by of DMH CCK administration using c-Fos like immunohistochemistry determination as a maker of neuronal activation. We found that 0.5 nmol of parenchymal DMH CCK administration decreased food intake with a maximum effect at 4 hours. While total food intake remained inhibitedory for the entire 22 hour observation period, the intake from 4 - 22 hours was not significantly suppressed compared to vehicle treatment. Moreover, we found that relative to vehicle treatment, DMH CCK administration increased the number of c-Fos positive cells in a variety of feeding related brain regions including the DMH, ARC, paraventricular nucleus, suprachiasmatic nucleus, and median eminence. DMH CCK did not result in increased c-Fos in, but not the ventromedial nucleus, and nucleus tractus solitarius or area postrema. How These data suggest that DMH CCK and the subsequent reduction in DMH NPY signaling activates multiple signaling systems involved in feeding control. Supported by MH067638.

Chronic effects of olanzapine on food intake and weight gain in male and female rats.

S. CHOI, J. UNANGST, S. COLE, J.D. FERNSTROM.
University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA.

Antipsychotic drugs cause weight gain in humans. A rat model would help in studying the basis for this effect, but thus far, female and male rats respond differently to antipsychotic drugs with regard to weight gain. Thus, the rat might not be a good human model. Earlier studies administered drug by injection. The plasma half-lives of antipsychotics are short in rats (a few hours); single daily dosing thus exposes the rat transiently to high plasma drug levels. Moreover, a sex difference in metabolism might account for different biologic responses to single daily injections. We examined these issues using olanzapine. We first injected adult male and female rats with olanzapine (5 mg/kg, i.p.) and killed groups 15, 30, 60, 180, 420 min later. Plasma olanzapine was measured. Pharmacokinetic analysis indicated that females metabolize the drug more slowly than males. In the second study, we implanted male and female rats with Alzet minipumps to receive 5 mg olanzapine/kg/day. Female rats (initial weight, 214 ± 2 g) increased body weight more with olanzapine (final weight, 251 ± 5 g) than with vehicle (229 ± 2 g). Food intake was also greater in olanzapine-treated than vehicle-treated females. In contrast, males treated identically showed no difference in body weight or food intake (olanzapine versus vehicle). Plasma olanzapine levels were 17 ± 2 ng/ml in females and 19 ± 3 ng/ml in males. Male and female rats thus respond differently to olanzapine, even when chronic drug exposure is similar. Supported by NIH/NIMH.

Training to estimate and control blood glucose levels before meals improves metabolic control in infants with functional bowel disorders.

M. CIAMPOLINI.
Firenze Università, Meyer Hospital, 50132 Firenze, Italy.

In previous investigation, two-thirds of adults initiated meals 15 mg/dl before blood glucose was allowed to fall further to hunger-producing levels. Higher postprandial hyperglycemia and hyperinsulinemia followed this habit (producing metabolic risk factors) than allowing blood glucose levels to fall further before meal initiation. To assess the possibility of lowering the high preprandial levels, we proposed mothers of infants with recurrent diarrhea to find the hunger-producing level in their infants possibly below 85 mg/dl by using standard glucose monitors before meals. The measurement did not trouble 83 of 170 infants aged up 4 years. Mother-infant pairs acquired the ability to recognize the infant's hunger-producing level, and focused entirely on the associated manifestations as signal for meal initiation, only beginning a meal when estimated blood glucose fell to the infant's personal hunger-producing level. Furthermore, they adjusted meal-size and content to near the subsequent attainment of hunger-producing level with next mealtime. 40 of 83 infants who's mothers undertook this training and who exhibited 94.0 ± 6.4 mg/dl glycemic pre-prandial average (all over 85.4 mg/dl) by 7d-diary before training, decreased to 77.6 ± 7.5 mg/dl and reduced energy intake by maintaining past activity. The effect of training was not significant in 43 infants who exhibited 78.8 ± 5.2 mg/dl preprandial blood glucose and were all below 85.4 mg/dl (ordinary hunger-producing level) before training. Thus, 43 infants had freely chosen this ordinary level at baseline, and further 30 mothers discovered and habituated their infants (73/83 = 88%) to attain it after training. Feeding infants after manifestations of attaining hunger-producing levels prevented diarrhea and habituated to an improved metabolic control.

Decreased extracellular leptin induces nitric oxide (NO) production in ventromedial hypothalamic (VMH) neurons.

D.D. CINCO, J.G. POTIAN, J.J. MCARDLE, V.H. ROUTH.
Departments of Pharmacology & Physiology, NJ Medical School, Newark, NJ 07101, USA.

The diffusible messenger, nitric oxide (NO), is a central regulator of food intake. Inhibition of NO synthase (NOS) decreases food intake. Neuronal NOS (nNOS) knock-out mice are refractory to neuropeptide Y- and orexin-induced feeding. Subcutaneous leptin reduces body weight and hypothalamic NOS activity in mice. Both activity and mRNA of NOS are elevated in the hypothalamus of leptin-deficient obese (*ob/ob*) mice. We have shown that physiologic decreases in extracellular glucose cause NO production in cultured neurons derived from the ventromedial hypothalamus (VMH), a key region in the regulation of energy balance. Thus, we hypothesized that leptin would reduce NO production in VMH neurons. To test this hypothesis we measured NO production in primary cultures of VMH neurons with diaminofluorescein (DAF), an NO sensitive dye. Since this method detects only an increase in DAF fluorescence (DAF-FL), we incubated VMH neurons in 10 nM leptin for 1 hour and then measured changes in DAF-FL in response to leptin removal. DAF-FL was measured every min for an hour. If, as we hypothesized, leptin reversibly reduces NO production, then we should measure increased DAF-FL when the VMH neurons were placed in leptin-free artificial cerebral spinal fluid (ACSF). Indeed, leptin removal increased DAF fluorescence in 49 ± 9% of 197 VMH neurons. The non-selective NOS inhibitor L-NAME (1 mM) reduced the number of VMH neurons which increased DAF fluorescence to 14 ± 7% of 129 neurons (P = 0.02). These data suggest that NO signaling mediates, in part, the physiological responses of VMH neurons to leptin. Supported in part by NIDDK55619, 64566, NS045979.

Development of a rodent model examining the role of obesity and dietary fats in mammary carcinogenesis.

D.J. CLEGG, S.C. BENOIT, J. SCHNEIDER, J. SCHURDAK, M.Y. YAN, R.B. GEAR, S.C. HEFFELFINGER.
Departments of Psychiatry and Pathology, University of Cincinnati, Cincinnati, OH 45237, USA.

Epidemiological data demonstrates links between diet and some forms of cancer. Different dietary fatty acids may affect susceptibility to cancer, and there is a strong correlation between obesity and known risk factors for cancer. The purpose of this study was to characterize well-controlled, nutritionally-matched diets of different fatty acid composition on food intake, body weight, body composition, adipose distribution and mammary gland development in female rats. Toward this end, young female rats (50 days old) were maintained for 6 or 12 weeks on diets containing monounsaturated fat (olive oil), n-6 polyunsaturated fat (safflower oil), or n-3 polyunsaturated fat (menhaden oil). Rats received either high fat (40% kcal), low fat (20% kcal), or were pair fed the high fat diet at intake levels matching the low fat cohort. An additional control group was maintained on AIN-93. Total daily caloric intake was similar across all groups. Rats in all groups gained similar amounts of body weight and body fat as measured by NMR, although adipose tissue distribution differed somewhat. Fatty acid composition of both adipose tissue and mammary glands were dramatically different among groups ingesting different sources of fat, as well as between high and low fat groups. Studies of mammary gland composition are ongoing. Results of these studies will direct future work to assess the effects of dietary fatty acids on the development of mammary gland carcinogenesis. Importantly, this model allows us to separate effects of specific dietary fatty acids from common effects of obesity.

Central administration of an insulin mimetic, but not insulin, reduces food intake in rats on a high-fat diet.

D.J. CLEGG, L.M. BROWN, B.B. ZHANG, S.C. WOODS, S.C. BENOIT.
University of Cincinnati, Cincinnati, OH 45237, USA.
Central administration of insulin reduces food intake and body weight when animals are maintained on a low-fat (LF) chow diet. Animals maintained on a high-fat (HF) diet develop obesity and central insulin resistance. Compound 1 (Cpd1) is a small-molecule insulin mimetic that reduces peripheral insulin resistance. We compared the ability of insulin and Cpd1 to reduce food intake and body weight in rats maintained on either a HF or a LF diet. Intra-third ventricular (i3vt) Cpd1 decreased 24-h food intake in rats maintained on either the HF or the LF diet (50 % and 20% respectively relative to vehicle; $P < 0.05$). In contrast, i3vt insulin reduced food intake comparably (40% relative to vehicle) to Cpd1 in the LF group ($P < 0.05$) but had no effect on rats in the HF condition. HF rats had a 50% reduction in hypothalamic insulin receptor mRNA relative to the animals maintained on chow. Insulin increased pAKT (30% relative to vehicle; $P < 0.05$) in LF chow animals, but had no effect in animals on HF. Cpd1 increased pAKT comparably (30% relative to controls) in LF and HF animals. Insulin and Cpd1 reduced hypothalamic AgRP mRNA comparably (-35% relative to vehicle; $P < 0.05$) in chow rats whereas Cpd1 but not insulin reduced hypothalamic AgRP (-20%; $P < 0.05$) in HF rats. These data demonstrate that Cpd1 differentially impacts hypothalamic neuropeptide systems that control energy homeostasis and imply that this may lead to approaches to circumvent central insulin resistance. Supported by NIH-DK-DK064885.

Exploring the effects of hunger, food stimuli, restrained eating, and relative weight on BOLD responses with fMRI.

M. COLETTA[a], M. LOWE[a], S. PLATEK[a], F. MOHAMED[b].
[a] *Drexel University, Philadelphia, PA 19102, USA;* [b] *Temple University Hospital, 3401 N. Broad Street, Philadelphia, PA 19140, USA.*
Normal weight restrained eaters have been used as a model of "obese behavior" in past research. One purpose of this study was to examine this analogy through the investigation of neurobiological correlates when deprivation state (hungry, full), food exposure cues (pictures of high versus moderate palatability food versus nonfood items) were manipulated in three groups of subjects: restrained normal weight females (N = 3; avg. BMI = 21), unrestrained normal weight females (N = 3; avg. BMI = 21), and overweight females (N = 2; avg. BMI = 37). Level of restraint was assessed using Herman and Polivy's Restraint Scale. Data was analyzed using SPM'2 software. Within groups analyses across all groups showed that in a fasted state, high relative to moderate palatability images yielded significantly ($P < 0.001$, uncorrected) greater activation in the left superior frontal gyrus, right middle temporal gyrus, and right inferior parietal lobule. When comparing these two conditions after feeding, the high palatability condition yielded activation of the left caudate tail, right anterior cingulate gyrus, and right precuneus. When fasted and fed, moderate relative to high palatability images yielded nearly the mirror image of activation of the high relative to moderate comparison. These findings are consistent with past research that has demonstrated differential brain activation depending on hunger state and palatability level of food stimuli. In addition, preliminary between group analyses, although lacking in statistical power, suggest differences in activation when comparing the three groups.

The effects of short-term overfeeding on intake behaviors and neuronal activity in obese-resistant women and men.

M.A. CORNIER, S.S. VON KAENEL, J.R. TREGELLAS, D.H. BESSESEN.
University of Colorado Health Sciences Center, Denver, CO, USA.
Individuals who appear to be resistant to weight gain in an obesigenic environment may sense positive energy balance more appropriately influencing their intake. Seventeen thin individuals (12 women and 5 men) were studied twice in a randomized crossover design. Measures of intake behaviors were obtained before and after each meal during 3 days of eucaloric feeding (EU) and 3 days of 30% overfeeding (OF). Ad libitum energy intake was then measured for three days. fMRI studies were performed in a sub-cohort (n = 12) in the overnight fast state on the 3rd day of EU and OF. Functional imaging was performed with visual stimuli of three categories (objects, hedonic foods, utilitarian foods). OF resulted in a significant reduction in hunger and increase in satiety in the women but not the men. OF also resulted in reduced subsequent energy intake in women. There was significant bilateral activation of inferior temporal visual and posterior parietal cortex, as well as posterior cingulate and insular cortex in response to the food stimuli. Hedonic foods resulted in further bilateral activation of inferior temporal visual cortex and posterior parietal cortex. During OF, food stimuli led to significant activation of the prefrontal cortex as compared to EU, which was especially dramatic in the women. In summary, obese-resistant women appear to sense positive energy balance effectively and appropriately with changes in intake favoring a rapid return to energy balance. In addition, these individuals appear to sense positive energy balance with activation of brain regions important in the regulation of behaviors.

Effects of sucrose access and concentration on shortening bingeing in rats.
R.L. CORWIN, F.H.E. WOJNICKI.
Nutritional Sciences Department, Penn State Universitv, University Park, PA 16802, USA.
Previous studies showed that limited access to shortening can promote binge-type eating in non-food deprived rats. This study examined the effects of limited access to sucrose on sucrose intake and on subsequent shortening intake. Non food-deprived male rats were given 2-h access to a low (L; 3.2% w/v), medium (M; 10% w/v) or high (H; 32% w/v) concentration sucrose solution on a daily (D) or a more restricted (R; Mon, Wed., Fri.) access schedule. The 6 groups (n = 10/group) were: DL, DM, DH, RL, RM, RH. Access schedule had no effect on sucrose intake at any concentration. This differs from our previous work in which the R schedule increased shortening (fat) intake compared to the D schedule. After 9 weeks, sucrose was no longer provided. Instead, all rats were given 2-h access to shortening on the same access schedules as above for 4 weeks. While the schedule differences (R > D) were generally the same as those reported in previous shortening studies, the RH group ate significantly more shortening than any other group ($P \leq 0.0012$). To examine the relationship between sucrose history and current access schedule, all rats were next given access to shortening on the R schedule for 6 weeks. Even though all rats were now on the R shortening access schedule, the RL and RH groups ate significantly more ($P < 0.01$) shortening than their D counterparts (DL and DH, respectively). There was no difference between DM and RM groups. These results demonstrate that both the schedule access history and the sucrose concentration affect subsequent shortening consumption. Supported by RO1-MH067943.

Effect of basomedial hypothalamic lesions on suppression of food intake by peripheral PYY3-36 and MT-II.
J.E. COX, A. RANDICH.

Department of Psychology, University of Alabama at Birmingham, Birmingham, AL 35294-1170, USA.
The median eminence (ME) and adjacent hypothalamic tissue, especially the arcuate nucleus (ARC), may be important in the anorectic effects of both the hormone PYY3-36 and the melanocortin receptor agonist MT-II after peripheral administration. We conducted feeding tests with these substances in adult, male Sprague-Dawley rats in controls (N = 8) and in animals with bilateral electrolytic lesions targeting the ARC (ARC-X group, N = 11). Rats were maintained on Harlan-Teklad 16% protein pellets ad libitum except for 1 h prior to onset of feeding tests. Injections were given 15 – 20 min prior to lights-out, at which point food hoppers were replaced. Cumulative food intake, corrected for spillage, was measured 6 and 23 h later. For the first set of tests, rats received intraperitoneal injections of saline and 60 mg/kg PYY3-36 on consecutive days. As we have previously observed, in controls this peptide reduced 6-h intake (17.6 ± 4.7%; $P < 0.01$). Hypothalamic lesions attenuated this effect by 57% (7.6 ± 3.5%; $P < 0.05$). In subsequent tests, rats received subcutaneous injections of saline and 1 mg/kg MT-II. ARC lesions resulted in MT-II producing greater suppression than in controls at both 6 h (89.0 ± 3.0% versus 78 ± 2.1%) and 23 h (57.9 ± 6.5% versus 38.3 ± 2.7%; P values < 0.025). Our results are consistent with an important role for the basomedial hypothalamus in mediating the anorectic effect of PYY3-36 but not that of peripherally administered MT-II. Instead, tissue within this region may normally oppose the action of MT-II.

Differences in opioid related feeding in alcohol-preferrring (AA) and alcohol-avoiding rats (ANA).

D.L. CRANKSHAW[a,b], J.E. BRIGGS[b], M.K. GRACE[b], P. HYYTIA[c], A.S. LEVINE[a,b].
[a]*University of Minnesota, Saint Paul, MN 55108, USA;* [b]*Veterans Affairs Medical Center, Minneapolis, MN 55417, USA;* [c]*Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, POB 33, 00251 Helsinki, Finland.*
Endogenous opioids are known to affect intake and preference of both food and alcohol. The differences between alcohol-preferring and alcohol-avoiding rats in propensity for alcohol ingestion and preference have in part been attributed to differences in endogenous opioid circuitry. We investigated whether opioid effects on food intake were also significantly different in these line pairs (AA-alcohol preferring; ANA-alcohol-avoiding). The opioid antagonist, naltrexone and the opioid agonists, morphine and butorphanol had no effect on the food intake of alcohol-avoiding rats over a four-hour time period. In contrast, naltrexone reduced intake of food deprived and satiated alcohol-preferring rats. Morphine and butorphanol dose dependently induced a significant increase in food consumption in alcohol-preferring rats. We also found that ANA rats did not ingest laboratory chow (placed on the cage floor) when the lights were on following a period of nocturnal feeding. In contrast, satiated AA rats readily ingested chow when placed on the floor cage during the light on period. The striking differences in opioid regulation of food intake in the AA and ANA rats support the idea that these two lines of rats have genetically-determined differences in endogenous opioid tone. Alcohol-preferring and alcohol-avoiding rats provide an animal model for alcoholism, and may also provide a model to study opioid-induced feeding. Supported by NIAAA and the Department of Veterans Affairs.

Conditions of metabolic syndrome (obesity, insulin resistance, dyslipidemia) altered by varied sources of dietary fat in the C57BL/6 mouse.

T.M. CUNHA[a], R.G. PETERSON[b], T.A. GOBBETT[c].
[a]*TestDiet, Purina Mills, Richmond, IN 47374, USA;* [b]*Anatomy and Cell Biology, Indiana University School of Medicine, Indianapolis, IN 46202, USA;* [c]*PreClinOmics, Indianapolis, IN 46268, USA.*
Nine-week-old mice (C57BL/6NCrlBR) placed on high-fat purified diets in 6 groups (N7-9) for 100 days: low-fat (12% kcal fat) control, TestDiet #58G7, and high-fat (60% kcal) diets, identical but for fat source: #58G9 (lard), #5T97 (hydrogenated vegetable oil, "Crisco"), #5T98 (½ lard – ½ Crisco), #5T99 (coconut oil), and #5TA1 (butterfat) from Purina. Obesity was highest in Crisco and butterfat groups (49.4 g and 53.0 g, 97 d). Crisco and lard/Crisco groups had virtually identical weight-gains (49.4 g and 49.0 g, 97 d); lard and coconut oil groups gained least of the high-fat groups (47.9 g and 47.6 g, 97 d). All high-fat-fed mice had higher glucose levels than controls, highest being butterfat. At 84 days insulin levels were high (30 ng/ml) in all groups except control (4 ng/ml) and coconut oil (15 ng/ml). Day 85 cholesterol: butterfat 262 mg/dl; coconut oil 243 mg/dl; lard 211 mg/dl; lard/Crisco 195 mg/dl; Crisco 180 mg/dl; and control 148 mg/dl. Triglycerides presented differently. Both Crisco (81 mg/dl) and lard/Crisco (108 mg/dl) produced lower levels than low-fat (lard-based) control (114 mg/dl). Remaining high-fat diets had increasing levels, butterfat (121 mg/dl), lard (143 mg/dl), and coconut oil (195 mg/dl). Results demonstrate that different fat sources have dramatically different effects on development of metabolic syndrome factors.

Estrogen augments PEG-induced Fos immunoreactivity in specific brainstem nuclei of ovariectomized rats.

K.S. CURTIS, R.J. CONTRERAS.
Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL 32306, USA.
Previous studies have reported estrogen-dependent sex differences in water intake and cardiovascular responses after body fluid loss. This study used immunolabeling for the Fos protein, a marker of neuronal activation, to determine whether estrogen affects activity in the brainstem of female rats after non-hypotensive hypovolemia produced by polyethylene glycol (PEG). Adult female Sprague-Dawley rats were bilaterally ovariectomized (OVX) and allowed to recover for at least seven days. OVX rats then were given either estradiol benzoate (EB; 10 µg/0.1 ml, s.c.) or oil vehicle (OIL; 0.1 ml, s.c.) on two consecutive days. On the fourth day, rats were injected with PEG (40% w/v; PEG 8000; 1.35 ml/100 g BW, s.c.) or 0.15 M NaCl vehicle (1.35 ml/100 g BW, s.c.). Rats were sacrificed six hours later, at which time blood samples were taken for assessment of hematocrit and plasma protein concentration. Brains were processed for detection of the Fos protein using standard immunocytochemical methods. In both groups, PEG produced comparable volume depletion (~ 25 - 35%) and increased Fos immunoreactivity (Fos-IR) in the nucleus of the solitary tract and in the area postrema, the hindbrain circumventricular organ. However, in OVX rats given EB, PEG-induced Fos-IR was augmented in both the lateral parabrachial nucleus and in the rostroventrolateral medulla, the sympathoexcitatory area. These results show that estrogen has selective effects on neural activation elicited by non-hypotensive hypovolemia. Thus, estrogen-dependent sex differences in compensatory fluid intake and cardiovascular responses to hypovolemia may be attributable, in part, to differential activation of specific brainstem nuclei. Supported by DC 06360 and DC 04785.

Fat pad-specific effects of lipectomy on appetitive and consummatory ingestive behaviors in Siberian hamsters (*Phodopus sungorus*).

M. DAILEY, T.J. BARTNESS.
Department of Biology, Georgia State University, Atlanta, GA 30302, USA.

Both appetitive and consummatory behaviors contribute to the overall energy strategy of animals. After food deprivation, Siberian hamsters increase foraging and food hoarding, instead of increasing food intake as do most other animals. We previously demonstrated that increases in food hoarding, an appetitive ingestive behavior, are triggered by directly decreasing body fat levels through partial surgical lipectomy (LIPX). In that experiment, however, we did not assess foraging behavior and also did not test whether there was a relation between the magnitude of the lipid deficit and the size of the food hoards. Therefore, in the present experiment, we tested the effect of a graded lipid deficit on both appetitive and consummatory ingestive behaviors in Siberian hamsters using a semi-natural foraging/hoarding apparatus. This was accomplished by removing both epididymal white adipose tissue (EWAT) pads, both inguinal white adipose tissue (IWAT) pads, or both EWAT and IWAT pads and measuring foraging, food hoarding and food intake in Siberian hamsters. The magnitude of the lipid deficit did not correspond to a proportional change in appetitive or consummatory ingestive behaviors when animals were required to forage for their food. Specifically, when a foraging effort was imposed (10 revolutions/pellet), both appetitive ingestive behaviors (foraging and food hoarding) increased and the consummatory ingestive behavior (food intake) decreased. Collectively, these results suggest that body fat loss is not directly related to levels of foraging/food hoarding and that energy expenditure, such as occurs with foraging, can interact with the body fat loss to affect appetitive and consummatory ingestive behaviors.

Increased NaCl consumption, but not water intake by a double isoleucine-substituted analog of angiotensin II.

D. DANIELS, D.K. YEE, L.F. FAULCONBRIDGE, L. LUO, A. SUZUKI, S.J. FLUHARTY.
Departments of Animal Biology, Pharmacology, Psychology, Institute of Neurological Sciences, University of Pennsylvania, Philadelphia, PA 19104, USA.

Injection of angiotensin II (AngII) into the brain of awake, behaving rats results in dramatic increases in water and NaCl intake. These effects of AngII occur largely through stimulation of the AngII type 1 (AT_1) receptor. Stimulation of the AT_1 receptor *in vitro* leads to a number of intracellular events, including the release of inositol trisphosphate (IP_3) from the plasma membrane and activation of mitogen-activated protein kinase (MAP kinase). While previous studies suggested that activation of MAP kinase requires IP_3 formation, recent experiments using mutated receptor constructs or AngII analogs revealed that MAP kinase activation can occur without IP_3 release. The present experiments used *in vitro* and *in vivo* approaches to clarify the cellular and behavioral responses to the AngII analog, Sar^1,Ile^4,Ile^8-angiotensin II (SII). Studies using COS-1 cells, transiently transfected with AT_1, confirmed previous findings that treatment with AngII led to increases of IP_3 formation and MAP kinase activation, while treatment with SII increased MAP kinase activation, but failed to increase IP_3 formation. Injection of SII into the third ventricle of male rats failed to increase water intake, but did increase early consumption of 1.5% NaCl similar to that stimulated by AngII. These findings suggest that IP_3 formation is required for the increased intake of water, but not of NaCl, that is stimulated by AngII. Furthermore, these data argue that divergent intracellular signals from a single receptor type can give rise to separable behavioral phenomena.
Supported by NIH awards DK064012 (DD), HL058792 (DKY), and DK052018 (SJF).

Increased satiation induced by isocaloric, isonitrogenous, high fat diet in rats.

C.N. DARCEL[a,b], G. PAULINO[a,b], F. MILHAS[a,b], D.W. GIETZEN[a], D. TOMÉ[b], H.E. RAYBOULD[a].
[a]Department of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine, *University of California-Davis, 1321 Haring Hall, Davis, CA 95616, USA;* [b]*Unite INRA 914 Physiologie de la Nutrition et du Comportement Alimentaire, INA/P-G, 16, rue Claude Bernard, 75231 Paris cedex 05, France.*

Dietary fat is sensed within the intestine and induces signals that participate in the regulation of gastrointestinal function and ingestive behavior. Lumenal fat in the gut is thought to induce satiation (i.e. termination of the meal). HYPOTHESIS: Elevated dietary fat will promote greater satiation. METHODS: 8 Sprague Dawley male rats were divided into 2 groups fed either a normal fat diet (10% energy; NF) or a high fat (38% energy; HF); the NF and HF diets were isonitrogenous (21% energy) and isocaloric (3.4 kcal/g). To allow rigorous comparison between experimental groups, HF diet was offered ad libitum and NF rats were pair-fed based on HF fed rat caloric intake. Feeding pattern (number of meal, duration of meal, meal size, eating rate) was continuously measured using food intake monitoring cages. RESULTS: Feeding pattern was different between HF and NF treated-rats. When compared to F-treated rats, HF-treated rats had more frequent meals (+44%), with reduced meal size and eating rate (-32% and -33%, respectively). CONCLUSION: HF-treated rats seemed to show increased satiation (shorter meals). This result is consistent with an elevated CCK plasmatic level consecutive to fat ingestion, since CCK mediates satiation.

CCK-1 receptor deficient OLETF rats increase intake but not gastric emptying of solid and liquid meals.

B.C. DE JONGHE[a], A. HAJNAL[b], M. COVASA[a].
[a]*Department of Nutritional Sciences, Pennsylvania State University, University Park, PA 16802, USA;* [b]*Department of Neural and Behavioral Sciences, Pennsylvania State University, College of Medicine, Hershey, PA 17033, USA.*

Obese CCK-1R deficient OLETF rats are hyperphagic relative to control, non-mutant LETO rats. This study sought to assess whether overeating observed in the OLETF rat is associated with increased gastric emptying. To determine whether OLETF rats are less responsive to gastric volume, feeding responses to gastric distension were also addressed via gastric balloon inflation. Our results showed that gastric emptying of a limited, 5 g chow test meal was not significantly different between strain at either 1hr ($P = 0.948$), 2 hr ($P = 0.756$) or 4 hr ($P = 0.933$) postingestion. OLETF rats consumed more chow than LETO rats after 1 hr ($P < 0.01$), 2 hr ($P < 0.01$) or 4 hr ($P < 0.01$) ad libitum access. Gastric emptying following 1 hr ($P = 0.4820$), 2 hr ($P = 0.7130$), or 4 hr ($P = 0.864$), ad libitum food access however, was not statistical different between strains. No significant difference in gastric emptying of an intragastric 15 ml load of a 25% semisolid chow mixture was noted between OLETF and LETO rats at either 1hr ($P = 0.561$) or 2 hr ($P = 0.208$). Finally, OLETF rats showed increased sham intake ($P < 0.05$) relative to LETO controls during a 20-min gastric distension by 5 cc or 10 cc balloon inflation. These findings demonstrate that OLETF rats, despite increased food intake, do not exhibit deficits in emptying rates. Thus, it is unlikely that hyperphagia in these animals is due to increased delivery of nutrients to the small intestine.
Supported by NIH grant DK065709.

Increased sensitivity to D1 and D2 receptor antagonism in sucrose feeding OLETF rats.

B.C. DE JONGHE[a], A. HAJNAL[b], M. COVASA[a].

[a]*Department of Nutritional Sciences, Pennsylvania State University, University Park, PA 16802, USA;* [b]*Department of Neural and Behavioral Sciences, College of Medicine, Pennsylvania State University, Hershey, PA 17033, USA.*

CCK-1R deficient OLETF rats exhibit enhanced preference for sucrose compared to control, LETO rats. To assess specific involvement of dopamine receptors underlying this difference in food reward, OLETFs and LETOs were injected with either a selective D1 (SCH23390: 0, 50, 200, 400, 600, 800 nMol/kg, i.p.) or D2 (raclopride: 0, 50, 200, 400, 600, 800 nMol/kg, i.p.) antagonist, 15 min prior to presentation of 0.3 M sucrose solution. The threshold dose of SCH23390 required to reduce 30- and 60-min intake in OLETFs was 400 nMol/kg ($P < 0.0001$, $P < 0.0004$; for 30 and 60 min) while 600 nMol/kg was needed to reduce intake significantly in LETOs ($P < 0.0001$, $P < 0.0005$; for 30 and 60 min). The threshold raclopride dose required to reduce 30-min intake in OLETFs was 400 nMol/kg ($P < 0.0001$), in contrast to LETO rats, which required an 800 nMol/kg dose to reduce intake significantly ($P < 0.0001$). At 60 min OLETFs decreased intake after 600 and 800 nMol/kg ($P < 0.0001$) while raclopride had no effect in LETO rats at any dose tested. In a parallel experiment we assessed the effects of brief sucrose access on prepulse inhibition (PPI), a measure of sensorimotor gating known to be modulated by dopamine receptors. No significant sucrose effect on PPI was noted in OLETFs whereas sucrose receiving LETOs had a significantly lower ($P < 0.05$) PPI percentage than controls. To conclude, OLETFs express hypersensitivity to antagonism of both D1 and D2 receptors, as well as deficient sensorimotor gating following sucrose ingestion. These effects are indicative of altered dopamine regulation and may contribute to the hyperphagia characteristic of OLETF rats. Supported by DK065709.

Stress-induced modifications of food intake and food choice in rats.

A. DIANE, G. FROMENTIN, D. TOME, C. LARUE-ACHAGIOTIS.

INRA, UMR 914 Physiologie de la Nutrition et du Comportement Alimentaire, 16, rue Claude Bernard. 75231 Paris cedex 05, France.

Modification of food intake by stress in the rat has been proposed as a model of depression and anorexia nervosa. Studies do not allow to determine whether stress modifies appetite or affect the avoidance (or preference) for a specific macronutrient. Methods: 20 Wistar rats (10 males, 10 females) were individually housed in stainless cages in a temperature controlled room (22 ± 2 °C) and submitted to a reverse cycle (night: 10 - 22 h). They were provided ad libitum with separate sources of the three macronutrients: protein, fat and carbohydrate. Rats were weighed daily and food intake was recorded every 3 hours. After 2 weeks of habituation, rats were submitted to a swimming stress (15 min/day) at the beginning of the dark cycle for 3 consecutive days. Thereafter a catheter was inserted in the right lateral jugular vein for blood samples collecting before, just after, and 1 hours, 3 hours after the stress in order to determine corticosterone and insulin levels. Results: In the basal state, the animal choosed a high level of protein (25 - 35%) and fat (40 - 70%). Stress induced a decrease in total food intake only during the first 3 hours after the stress that affected protein, fat and carbohydrates intakes in both sexes. Body weight gain was decreased (males: baseline = 7 g/d versus 3.1 g/d and females: 5.1 g/d versus 1.8 g/d). In females, fat ingestion was enhanced 6 hours after the stress. Corticosterone was increased after stress while the opposite was found for insulin. These results suggested that stress mainly modified appetite.

Effect of green tea on resting energy expenditure and substrate oxidation during weight loss in overweight females.

K. DIEPVENS[a], E.M.R. KOVACS[b], M.S. WESTERTERP-PLANTENGA[a].
[a]*Maastricht University, Maastricht, The Netherlands;* [b]*Unilever Health Institute, Unilever R&D, Vlaardingen. The Netherlands.*

We assessed the effect of ingestion of green tea (GT) extract along with a low-energy diet (LED) on resting energy expenditure (REE), substrate oxidation and body weight (BW) since GT has been shown to increase energy expenditure (EE) and fat oxidation in the short-term in both animals and humans. 46 overweight females (BMI 27.6 ± 1.8 kg/m^2) were fed in energy balance from day 1 to 3, followed by a LED with GT (1125 mg tea catechins + 225 mg caffeine/day) or placebo from day 4 to 87. Caffeine intake was standardized on 300 mg/day. EE was measured on day 4 and 32. Reductions in BW (4.19 ± 2.0 kg placebo, 4.21 ± 2.7 kg GT), BMI, W/H ratio, fat mass (FM) and fat free mass (FFM) were not statistically different between treatments. REE as a function of FFM and FM was significantly reduced over 32 days in the placebo group ($P < 0.05$), but not in the GT group. Dietary restraint increased over time ($P < 0.001$) in both groups, while disinhibition and general hunger decreased ($P < 0.05$). The GT group became more hungry over time, less thirsty and had increased prospective food consumption compared to placebo ($P < 0.05$). Taken together, ingestion of GT along a LED had no additional benefit for any measures of BW or body composition. Although the decrease in REE as a function of FFM and FM was not significant with GT treatment, whereas it was with placebo treatment, no significant treatment over time effect was seen, suggesting that a robust limitation of REE reduction during a LED was not achieved by GT.

Learning associations between sweet nutritive and non-nutritive diets and caloric consequences: impact on food intake and body weight regulation.

A.M. DOERFLINGER, T.L. DAVIDSON, S.E. SWITHERS.
Department of Psychological Sciences and Ingestive Behavior Research Center, Purdue University, West Lafayette, IN 47901, USA.

The homeostatic regulation of food intake is one of the most pressing challenges to an organism. Certain foods may, unpredictably, provide either an over-abundance or a deficit of energy and nutrients. The present series of experiments examines the influence of the learned associations between taste stimuli and nutritive or non-nutritive consequences on food intake and body weight regulation following both short- and long-term exposure to such diets. Experiment 1 examines whether consuming artificial sweeteners impairs caloric regulation. The prediction is that the ability of the animals to compensate for the calories contained in sweet-tasting foods would be impaired following experience with diets in which sweet tastes inconsistently predicted the caloric value of the diet, as compared to the animals that received foods that were always sweet tasting and always had associated caloric consequences. Results suggest that animals given experience with nutritive sweeteners (glucose and sucrose) sometimes and non-nutritive sweeteners (saccharin) sometimes are less able to regulate food intake following a preload challenge during a 24-h intake test compared to animals that always receive the sweet, nutritive diet. Experiment 2 examines the long-term effects of training with stable sweet-calorie relationships versus unstable sweet-calorie relationships. Results indicate that following long-term exposures, body weight differences were evident between groups. Experiment 3 replicated findings of Experiment 1, but included additional control groups. Following exposure and test phases, Dual X-Ray Absorptiometry (DXA) analysis was made on each subject in order to more closely examine body composition differences between groups.

Calcium and sodium intake during brief access tests by inbred mouse strains.

S.A. DOMAN, E.A. BYERLY, M.G. TORDOFF.
Monell Chemical Senses Center, Philadelphia, PA 19104, USA.

In previous work using long-term two bottle choice tests, we found that the BTBR T^{+}tf/J, JF1/Ms and PWK/PhJ strains of mice drank considerably more of various calcium solutions than did 37 other strains tested. Here, we investigated whether this avidity for calcium was due to oral factors. We used a "Davis rig" lickometer to compare the calcium acceptance of two of these strains (BTBR and PWK) with two strains having moderate calcium preferences in long-term tests (C57BL/6J and CBA/J). After training and adaptation to the lickometer, the mice received five test sessions with three presentations of various concentrations of calcium chloride, other calcium salts, other mineral chlorides, or other taste solutions. Each taste solution was available for 5 sec and was interspersed between 5-sec tests with water. We found that water-licking rates of the four strains were similar (licks/5 sec: B6 = 32 ± 3; CBA = 40 ± 6; BTBR = 32 ± 5; PWK = 40 ± 2) but the calcium-liking strains drank more calcium (licks/5 sec of 50 mM $CaCl_2$; B6 = 26 ± 5; CBA = 26 ± 5; BTBR = 34 ± 3; PWK = 38 ± 5). Consistent with NaCl preferences in long-term choice tests, the CBA strain drank little 200 mM NaCl (16 ± 6 licks/5 sec) relative to the other three strains (licks/5 sec: B6 = 36 ± 3; BTBR = 30 ± 6; PWK = 34 ± 3). Thus, intake during brief exposure tests reflected intake during long-term choice tests. This suggests that in the mice strains tested here, oral mechanisms may account for the acceptability of calcium and sodium.

Baclofen fails to alter highly palatable food intake in hindbrain lesioned rats.

G.L. EDWARDS, K.G. FREEMAN.
Department of Physiology and Pharmacology, University of Georgia, Athens, GA 30602, USA.

The GABA-B agonist, baclofen, is reported to increase chow and highly palatable food intake. Additionally, baclofen facilitates operant behavior for food following peripheral injection (Ebenezer & Pringle, *Neuropharm.* 1992;31:39-42; Ebenezer, *Eur. J. Pharmacol.* 1995;273:183). Baclofen is also suggested to antagonize the satietogenic actions of cholecystokinin (CCK) (Ebenezer, *Brain Res. Bull.* 1996;41:269-271). Lesions in the dorsal vagal complex result in enhanced intake of highly palatable foods and alter the response to gastrointestinal hormones such as CCK (Edwards & Ritter, *Brain Res.* 1981;216:265-276; Edwards et al., *AJP* 1986;251:R971-R977). Thus, baclofen potentially has actions on hindbrain systems reported to influence food intake. We have examined the ability of baclofen to facilitate food intake in rats with lesions centered on the area postrema (AP) in the dorsal vagal complex. Baclofen was administered at doses of 0.003, 0.01 and 0.03 mmol/kg intraperitoneally. We found that baclofen increased intake of sweetened condensed milk, a highly palatable food, in sham-lesioned control rats, but food intake was not elevated in rats with lesions centered on the AP. These data support a role for GABA-B receptors in control of highly palatable food intake and suggest that lesions centered on the AP may alter GABAergic pathways and thereby enhance intake of highly palatable foods. Supported by UGA Physiol. & Pharmacol.

Reducing the energy density of the diet as a strategy for weight management.

J.A. ELLO-MARTIN, L.S. ROE, B.J. ROLLS.

Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA 16802, USA.
Consuming foods low in energy density (kcal/g) has been shown to decrease short-term energy intake; therefore, reducing energy density may be an effective tool for weight loss. We tested two strategies to reduce dietary energy density on weight loss over one year in obese women. One group (n = 49) was counseled to reduce fat intake and the other group (n = 48) to increase intake of water-rich foods (e.g., fruits and vegetables) and to reduce fat intake. No limits for energy or fat intake were assigned; subjects were instructed to eat *ad libitum* amounts of food while following the principles of their diet. Results showed that both groups lowered the energy density of their diets; however, dietary energy density was lower for the group counseled to eat more fruits and vegetables ($P < 0.0001$). This group also consumed a greater weight of food ($P < 0.0025$). Subjects in both groups lost significant amounts of weight after 6 months ($P < 0.025$); the group advised to eat more fruits and vegetables lost more weight (9.0 ± 0.5 kg) than the group advised to reduce fat intake (6.7 ± 0.5 kg). Subjects in both groups showed good maintenance over the second six-month period. Thus, both strategies for reducing dietary energy density resulted in weight loss without specific goals for calories or fat grams. Incorporating fruits and vegetables into a reduced-fat diet resulted in a further reduction in energy density and enhanced weight loss. Supported by NIH grant R37DK0391778.

Changes in glucose, lipid and protein oxidation in rats adapted to a high protein diet.
P.C. EVEN, C. GAUDICHON, C. LUENGO, D. TOMÉ.
UMR 914 INRA-INAPG Physiologie de la Nutrition et du Comportement Alimentaire, 16 rue Claude Bernard, 75005 Paris, France.
Rats switched from a 14% (P14) to a 50% (P50) protein diet decrease body adiposity and food intake, and exhibit metabolic adaptations favouring utilisation of amino acids as energetic substrates. In this study we quantified post prandial rates of glucose, lipid and protein oxidation, and the part of the de-aminated amino acids that entered non oxidative disposal. Rats adapted 15 days to a P50 diet ingested a 45 kJ test meal and the changes in oxygen consumption and carbon dioxide production were measured during six hours. Amino-acid catabolism was assessed throughout the calorimetric measurements from urinary nitrogen excretion and changes in blood urea. The test meal was enriched with a mixture of four ^{13}C or ^{15}N-labelled amino acids (Leucine, phenylalanine, glycine, alanine) and de-amination versus oxidation of the amino acids brought by the meal was assessed from $^{13}CO_2$ enrichment in the expired air and ^{15}N enrichment of urea. Comparison of amino acid catabolism and oxidation showed that 77 ± 8% of the de-aminated amino acids were readily oxidized. It is concluded that a small part of the amino acids are stored into glycogen and/or lipids. The increased gluconeogenesis from amino acids cannot compensate for the decrease in dietary glucose availability as demonstrated by the decrease in Gox. This decrease in glucose availability probably also produced a decrease in glucose-derived fatty acid synthesis and subsequently in Lox and triglycerides synthesis. These results fitted with the low levels of glycogen in liver and the leanness of the rats fed a HP diet.

Distinct roles for the NPY Y5 and NPY Y1 receptors in the mediation of ghrelin hyperphagia.
L.F. FAULCONBRIDGE, H.J. GRILL, J.M. KAPLAN.
University of Pennsylvania, Department of Psychology, Philadelphia, PA 19104, USA.

We previously established the presence of independent forebrain and caudal brainstem (CBS) GHS-R triggers for the hyperphagic response to ghrelin administration, and that stimulation of NPY Y1-R in the CBS (but not forebrain) is always necessary for the response. We also provided evidence for a forebrain contribution of a different NPY-R (based on work with an antagonist that does not bind Y1-R, but is not otherwise subtype-selective). The present work addresses the hypothesis that the Y5-R is the relevant subtype, and assesses the relative contribution of CBS and forebrain Y5-R stimulation to centrally elicited ghrelin hyperphagia. The selective NPY Y5-R antagonist, L-152,804 (30 μg/4 μl) or vehicle was: 1) administered with ghrelin (150 pmol/1 μl) to either the 3rd or 4th ventricle: or 2) delivered to the ventricle opposite to the ghrelin delivery site. For all conditions, the cerebral aqueduct was (verifiably) occluded to restrict the flow of ligands between the ventricles. L-152,804 reversed the orexigenic response to ghrelin when both ligands were delivered to the same ventricle but not when delivered to different ventricular sites. The current results affirm an Y5-R contribution for the expression of ghrelin hyperphagia that, moreover, differs dramatically from the Y1-R requirement. The necessary Y5-R activation appears to be local to, or at modest distances from, the specific GHS-R targets. Supported by N.I.H. R01 DK-42294 and DK-21397.

Fat digestion is required for the lipid-induced modulation of ghrelin, peptide YY and pancreatic polypeptide secretion in healthy men.

C. FEINLE-BISSET[a], M. PATTERSON[b], M. GHATEI[b], S. BLOOM[b], M. HOROWITZ[a].
[a]*Department of Medicine, University of Adelaide, South Australia;* [b]*Imperial College London, Hammersmith Campus, London, UK.*

We have demonstrated recently that the stimulation of cholecystokinin and glucagon-like peptide-1 secretion by fat is mediated by the products of fat digestion (Feinle et al. Am J Physiol 2003;284:G798-807). Ghrelin, peptide YY (PYY) and pancreatic polypeptide (PP) appear to play an important role in appetite regulation and their release is modulated by food ingestion, including fat. It is, however, not known, whether fat digestion is a prerequisite for their suppression (ghrelin) or release (PYY, PP). Moreover, it is not known whether small intestinal exposure to fat is sufficient to suppress ghrelin secretion. 16 healthy men received, on two occasions, 120 min intraduodenal infusions of a long-chain triglyceride emulsion, at 2.8 kcal/min, (i) without (FAT) or (ii) with (FAT-THL) 120 mg of the lipase inhibitor, tetrahydrolipstatin (THL). Blood samples for ghrelin, PYY and PP were taken at regular intervals. Infusion of FAT reduced plasma ghrelin ($P = 0.0001$) and increased PYY and PP ($P = 0.003$ for both). While PP release was relatively immediate, PYY and ghrelin changed progressively over time ($P = 0.009$ for both). FAT-THL abolished the FAT-induced changes in plasma ghrelin, PYY and PP. In conclusion, in healthy humans (i) the presence of fat in the small intestine suppresses ghrelin secretion and (ii) fat-induced suppression of ghrelin and stimulation of PYY and PP secretion are dependent on fat digestion.

Intraventricular (IVT) insulin and leptin decrease sucrose self-administration in rats.

D. FIGLEWICZ LATTEMANN[a,b], J. BENNETT[b], C. DAVIS[b], A.J. SIPOLS[c], J.W. GRIMM[d].
[a]*VA Puget Sound Health Care System, Seattle WA 98108, USA;* [b]*University of Washington, Seattle WA;* [c]*University of Riga, Riga LV;* [d]*Western Washington University, Bellingham WA, USA.*

We have hypothesized that insulin and leptin decrease the reward value of foods, and have demonstrated that IVT insulin and leptin reverse palatable food-induced place preference. In this study we tested whether IVT insulin or leptin decrease motivation to consume sucrose.

Non-deprived rats were trained to self-administer 5% sucrose under a progressive ratio schedule of reinforcement. Rats then received CSF, 5 mU insulin, or 0.2 μg leptin IVT (n = 30, within-subjects, randomized order). CSF injections did not alter sucrose self-administration behavior compared to non-injection control sessions. In contrast, both IVT insulin and leptin decreased the number of active lever presses versus controls (69 ± 9 and 67 ± 7 versus 87 ± 7, *P's* < 0.05) and the number of rewards received versus controls (6.6 ± 0.3 and 6.7 ± 0.3 versus 7.6 ± 0.4, *P's* < 0.05). Insulin also decreased the cumulative time interval preceding the last sucrose delivery versus controls (19 ± 3 versus 31 ± 3 min, *P* = 0.01). These effects were prevented either by increasing the concentration of sucrose to 10%, or by maintaining the rats on a higher fat diet (separate comparison groups). We conclude that insulin and leptin can decrease motivation for sucrose, but that this can be blocked either by increasing the concentration of sucrose, or by a dietary intervention that induces resistance to the action of these hormones at the CNS.

Experimental dissociation of 'liking' and 'wanting' in humans.

G. FINLAYSON, N. KING, J. BLUNDELL.
Institute of Psychological Sciences, University of Leeds, Leeds LS2 9JT, UK.

Brain substrates of food reward have been described by Berridge (*Neurosci. Biobehav. Rev*. 1996;20:1-25) who identified distinct components of 'liking' (primarily involving opioid transmitter systems and brainstem primary gustatory relays) and 'wanting' (via mesotelencephalic dopamine projections). In terms of food choice and food preference it is tempting to treat the concepts of liking and wanting as synonymous. If someone wants the food they are eating then they probably like it. However, it is possible to like a food without wanting it at a particular moment. Liking and wanting probably overlap but can they be separately manipulated? A computerized procedure has been developed to measure these components in humans. 'Liking' (using palatability ratings) and 'wanting' (using forced-choice photographic procedure) were assessed for foods that varied in the generic categories of fat (high or low) and taste (savory or sweet). 53 subjects completed the program when hungry and following ad-libitum consumption of a test meal. When hungry, subjects 'wanted' high-fat savory > low-fat savory with no corresponding difference in 'liking', and 'liked' high-fat sweet > low-fat sweet but did not differ in 'want' for these foods. When satiated, subjects 'liked', but did not 'want', high-fat savory > low-fat savory, and 'wanted' but did not 'like' low-fat sweet > high-fat sweet. Greater differences between 'liking' and 'wanting' were observed when hungry than when satiated. Findings indicate a state dependent, partial dissociation between 'liking' and 'wanting' for generic food categories. This procedure provides proof of concept that 'liking' and 'wanting' can be dissociated in humans and can be developed for foods varying along different dimensions.

The effects of beverage type and portion size on beverage consumption and lunch intake.

J.E. FLOOD, L.S. ROE, B.J. ROLLS.
Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA 16802 USA.

Previous research has shown that consuming caloric beverages before or during a meal results in an increase in total energy intake at that meal. In addition, research has shown that increasing the portion size of various foods leads to increased energy intake. The influence of beverage portion size on beverage and food intake has not been explored. In the present study, we tested the hypothesis that serving a larger portion of a caloric beverage with a meal would

result in increased energy intake at that meal. Men and women reported to the laboratory for breakfast and lunch once a week for six weeks. During each lunch, one of three types of beverages (cola, diet cola, or water) was served in one of two different portion sizes (360 g or 540 g). The same standard lunch, consisting of a pasta dish, a salad, a roll, and cookies, was served at each lunch, and all foods and beverages were consumed ad libitum. Preliminary results show that in both men and women, increasing beverage portion size significantly increased the weight of beverage consumed, but did not affect the weight of food eaten. Therefore, when a caloric beverage was consumed, portion size affected beverage energy intake, leading to an increase in total energy intake at lunch. These findings suggest that habitual consumption of large portions of caloric beverages may contribute to positive energy balance.

Concurrent orosensory stimulation and intestinal nutrient infusions suppress sham feeding more than the additive effects of either stimuli alone.

L.A. FOSTER, S. MIHELEK, E.A. COGGER.
Department of Animal & Veterinary Science, California Polytechnic University, Pomona, CA 91768, USA.

Fourteen male Sprague Dawly rats were equipped with gastric fistulas and an intestinal catheters. Prior to each experimental session the gastric fistulas were opened and the stomachs flushed with warm saline. Therefore, when the rats drank, the fluid drained out through the fistula. During the first 10 min of an experimental session rats were either: 1. given access to two bottles (one containing lipid (0.125 kcal/ml) the other sucrose (0.5 kcal/ml)) to sham feed; 2. given a lipid (0.75 kcal/ml) or sucrose (0.75 kcal/ml) infusion; 3. allowed to sham feed concurrently with a nutrient infusion; or, 4. were placed in the testing cage but were neither infused nor allowed to sham feed. After the first 10 min, all rats were given access to two bottles (sucrose and lipid) to sham feed for 20 min. All rats received all treatment combinations and data were subjected to repeated measures ANOVA with three within factors (oro-stim, infusion-type, infusion). Total sham intake was suppressed most by a nutrient infusion concurrent with oro-stimulation ($P < 0.05$). Total intake was suppressed less by a sucrose infusion alone ($P < 0.05$). Sham intake of lipid was suppressed by concurrent oro-stim and lipid infusion ($P < 0.001$). Sham intake of sucrose was suppressed by both nutrient infusions concurrent with oro-stimulation, and by a sucrose infusion alone. The results of this study support the hypothesis that orosensory stimuli concurrent with intestinal nutrients lead to a greater sense of satiety.

High fat diet exaggerates social stress-induced obesity.

M.T. FOSTER[a], M.B. SOLOMON[b], K.L. HUHMAN[b], T.J. BARTNESS[a].
[a]*Deptpartment of Biology,* [b]*Department of Psychology, Center for Behavioral Neuroscience, Georgia State University, Atlanta, GA 30302, USA.*

Non-traumatic stress stimulates food intake and body and lipid mass in many humans. In most non-human animals, non-traumatic stress (e.g., social stress or restraint in laboratory rats) decreases body and lipid mass. By contrast, we have shown that Syrian hamsters exposed to repeated social defeat (as few as four defeats) exhibit significant increases in food intake and body mass, reflected exclusively as increases in white adipose tissue (WAT). Because stress increases consumption of preferred foods, such as high fat diets, we asked: Will a high fat diet exaggerate the repeated social stress-induced increases in food intake and body and lipid mass? Hamsters were fed either a high fat diet (33% added fat by weight) or standard

powdered chow and either were defeated or not defeated. Repeated social defeat did not significantly increase caloric intake in hamsters given either diet. In hamsters fed standard chow, there was no significant difference in WAT masses in defeated versus non-defeated groups; however, in hamsters fed the high fat diet, defeated hamsters exhibited significantly increased WAT masses (inguinal, retroperitoneal, and epididymal, but not mesenteric WAT). These results suggest that repeated social defeat in Syrian hamsters mimics non-traumatic stress in humans in terms of increases in body fat that are exaggerated with high fat diet feeding. Supported by NIH R01 DK 35254 to TJB, NIH MH62044 to KLH and the Center for Behavioral Neuroscience NSF IBN 0349042.

Hypothalamic de novo fatty acid synthesis mediates leptin's anorectic effects.

S. GAO[a], K. KINZIG[b], S. AJA[b], E.E. LADENHEIM[b], T.H. MORAN[b].
[a]*Department of Biological Chemistry, bDepartment of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.*

Recently the hypothalamic de novo fatty acid synthetic pathway has been suggested to play an important role in mediating rodent feeding behavior and the regulation of global energy homeostasis. Here we investigated the relation between the activity of acetyl-CoA carboxylase (ACC), the rate determining enzyme of fatty acid synthesis pathway, and leptin's effect on rodent feeding control. Our data demonstrated that in arcuate nucleus ACC activity was reduced by food deprivation but elevated in response to leptin administration. Chronic lateral ventricular infusion of 5-(tetradecyloxy)-2-furoic acid (TOFA), an acetyl CoA carboxylase inhibitor, abolished the inhibition of feeding by central bolus injection of leptin in rats demonstrating the necessity of acute elevation of the enzymatic activity of ACC for the feeding inhibitory action of leptin. Thus these data suggest that hypothalamic de novo fatty acid synthesis mediates leptin's effects on the regulation of feeding and energy homeostasis.

D-cycloserine potentiates conditioned flavor-taste preference learning.

G.J. GOLDEN, T.A. HOUPT.
Department of Biological Science, Program in Neuroscience, The Florida State University, Tallahassee, FL 32306, USA.

NMDA receptor activation requires binding of both glutamate and glycine. D-cycloserine (DCS) is an agonist at the glycine-binding site that potentiates learning in several paradigms. We recently demonstrated that DCS can potentiate one form of ingestive learning, conditioned taste aversion. To determine if DCS could also potentiate preference learning, we tested the effect of DCS on the acquisition of a conditioned flavor-taste preference induced by pairing Kool-Aid flavors with the sweet taste of fructose. On 16 conditioning days, food-restricted rats (n = 23) were injected with DCS (15 mg/kg, n = 11) or saline vehicle (1 ml/kg, n = 12). One hour later, rats were given 2-h access to grape- or cherry-flavored 8% fructose (CS+, odd days) or alternate-flavored 0.2% saccharin (CS-, even days). Two-bottle preference test days were interspersed every fourth conditioning day: all rats were injected with saline and given access to both CS+ and CS- in 0.2% saccharin in 2 bottles. During 2-bottle tests the DCS group had significantly higher intake of CS+ (21 ± 3 ml) versus CS- (12 ± 3 ml, $P < 0.05$) after 8 conditioning days, while the vehicle group required 12 days to form a preference. Furthermore, after 12 days of conditioning the DCS group had significantly higher CS+ intake (34 ± 3 ml) compared to vehicle group (25 ± 3 ml, $P < 0.05$) during 2-bottle tests. Thus DCS potentiated conditioned flavor-taste preference learning by accelerating acquisition and increasing CS+ intake. Because DCS is a glycine agonist at the NMDA receptor, these results

implicate NMDA receptors in flavor-taste learning and suggest that endogenous glycine is a limiting factor. Supported by NIDCD03198.

Metabolic adaptations in the nonhuman primate (NHP) fetus: Effects of diet induced gestational hyperinsulinemia/hyperleptinemia.

K.L. GROVE, S.M. WILLIAMS, X.Q. XIAO, S.E. JOACHIM, M.S. SMITH.
Division of Neuroscience, Oregon Nation Primate Research Center, Beaverton,OR, USA.

Because of the dramatic increase in obesity amongst women in the United States, the occurrence of gestational diabetes (10%) has also risen. Furthermore, there has been a dramatic increase in obesity among children/infants. While there are likely many causes of this increased occurrence of adolescent obesity, maternal health (i.e., gestational diabetes/obesity) and diet may be a critical cue in the development of metabolic control in the offspring. Gestational diabetes has already been identified as a major health hazard to the developing fetus; however, the effect of a more subtle maternal phenotypes is uncertain. The third trimester of pregnancy has been identified as a critical period of development of hypothalamic circuits. These studies used a NHP model to investigate the effects of diet-induced gestational diabetes/obesity on the development of metabolic systems in the fetus. Fetuses were obtained during the 3rd trimester from mothers on a control diet or on a high fat diet for 1 - 3 years. These mothers displayed progressively worse hyperinsulinemia/hyperleptinemia in years 2 and 3 on the high fat diet, especially during the 3rd trimester of pregnancy. Real time PCR and high density microarray analysis was used to profile changes in expression for metabolic gene in skeletal muscle from the fetuses. Surprisingly, even fetuses from moms on the high fat diet for 1 year, displaying mild hyperinsulinemia/hyperleptinemia, showed several abnormalities in genes involved in regulation of fatty acid and glucose transport and oxidation. These results suggest that full gestational diabetes is not needed to cause the development of metabolic abnormalities in offspring.

The role of cholecystokinin1 receptor in mediating CCK induced Fos-like immunoreactivity in brainstem and myenteric neurons in the rat.

S. GULLEY[a], S.K. SHARMA[a], K.M. GADIYARAM[a], C.N. SULLIVAN[a], G.M. GREEN[b], T.H. MORAN[c], A.I. SAYEGH[a].
[a]*Gastroenterology Laboratory, Department of Biomedical Sciences, College of Veterinary Medicine, Tuskegee University, Tuskegee, AL 36088, USA;* [b]*Department of Physiology, University of Texas, San Antonio, TX 78284, USA;* [c]*Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.*

We performed a series of experiments examining the role of the cholecystokinin1 (CCK_1) receptor in mediating CCK-8 induced neural activation in the brainstem and the myenteric plexus of various rat strains. We compared CCK-8 induced Fos-Like immunoreactivity (Fos-LI), in 5 - 10 and 12 - 19 week old male Otsuka Long-Evans Tokushima Fatty (OLETF) lacking the CCK_1 receptor, control Long-Evans Tokushima Otsuka (LETO), standard Long Evans (SLE) and Sprague Dawley (SD) rats. We employed a dose range of exogenous CCK-8 administered intraperitoneally (5, 10, 20, and 40 μg/kg) in all groups and camostat stimulated endogenous CCK in OLETF and LETO rats. All doses of CCK-8 increased Fos-LI more than saline in the brainstem in all but the OLETF rats. The CCK-8 induced Fos-LI in the myenteric plexus was strain specific. CCK did not induce significant Fos-LI in OLETF rats. Only 40 μg/kg CCK-8 increased Fos-LI in the myenteric neurons in the young LETO rats, and 20 and

40 increased it in older LETO and SLE rats. In SD rats, all doses of CCK-8 increased myenteric Fos-LI. Finally, camostat increased Fos-LI more than saline only in the NTS of LETO rats. These data indicate that the CCK_1 receptor mediates CCK-8 induced Fos-LI in the brainstem and myenteric plexus. However, in the myenteric neurons, CCK-8 induced Fos-LI was strain and age specific, suggesting potential age and strain differences in myenteric CCK_1 receptor expression. Otsuka Pharmaceutical Co. [Tokushima, Japan] provided the OLETF and LETO rats. Supported by NIH S06/GM08091-31 and The Birmingham Racing Commission.

Effect of eating rate on binge size in bulimia nervosa (BN).

J.L. GUSS, H.R. KISSILEFF, M. TORRES, H. LOFINK, M.J. DEVLIN, E. ZIMMERLI, B.T. WALSH.
St Luke's-Roosevelt Hospital and Columbia University, New York, NY 10025, USA.

BN is an eating disorder characterized by episodes of excessive food ingestion (i.e. binges). Many studies report that BN patients eat more rapidly than do normal individuals, especially during binges, but no studies have directly manipulated consumption rate to compare its influence on intake during a binge. The aim of this study was to assess the influence of eating rate on binge size in BN, in order to determine whether binge size is mediated, in part, by ingestion rate. Women with and without BN (n = 9 per group) were instructed to 'let yourself go and binge eat' just before consuming an ad-libitum yogurt shake that was served at a rapid rate (140 g/min) on one occasion and at a slow rate (70 g/min) on another. Consumption rates were controlled by a computer pump. Patients consumed more, though not significantly so, than controls (1089 g versus 863 g; $P = 0.25$). Controls consumed significantly more when eating at faster rates than when eating at slower rates (by 354 g ± 146.6 SED; t = 2.41; $P = 0.02$). In contrast, consumption rates failed to influence patient's binge size. Therefore, patients ate 348 g more than controls (± 180.3 SED; t = 1.93; $P = 0.06$) when eating at slow rates, whereas patients and controls ate similar quantities when eating rapidly (patients: 1143 g ± 358.6 SE; controls: 1040 g ± 424.4 SE). These findings suggest that eating rate modulates meal size in normal individuals, but that BN patients either ignore such modulatory factors, or have deficiencies in physiological signals upon which such modulatory factors act. Supported by MH42206 & DK37352.

Adaptation to high-isomaltulose feeding improves postprandial glucose metabolism but does not affect food intake in rats.

D. HÄBERER[a], L. THIBAULT[b], W. LANGHANS[a], N. GEARY[a].
[a]*Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland;* [b]*School of Dietetics and Human Nutrition, McGill University, Ste-Anne de Bellevue, Quebec, Canada.*

Isomaltulose (a-D-glucosylpyranosyl-1.6-D-fructofuranose) is a natural disaccharide that is structurally similar to sucrose (a-D-glucosylpyranosyl-1.2-D-fructofuranose), but more slowly hydrolyzed in the intestine. Here we tested the effects of feeding isoenergetic 62% starch, sucrose or isomaltulose diets on metabolism and eating in rats. Diet palatability was not controlled. Spontaneous eating was measured for the first 8 d; then, at dark onset, 12-h fasted rats were offered 30 min-test meals of their diets, containing paracetamol to test gastric emptying (GE). Isomaltulose-fed rats ate less on d1 (14.4 ± 1.0 versus 29.2 ± 0.9 and 22.0 ± 1.5 g in sucrose- and starch-fed rats, $F(2,21) = 22.145$, $P < 0.001$) due to decreased meal size ($F(2,21) = 3.47$, $P < 0.06$) versus starch and decreased meal size and number ($F(2,21) = 8.51$, $P < 0.01$) versus sucrose. By d5 food intake differences had disappeared, and 8d body weight gains were similar. Test meal GE was similar among groups. Sucrose-fed rats had increased

plasma glucose (8.0 ± 0.2 mmol/l, $F(12,84) = 2.91$, $P < 0.01$), fructose (328.3 ± 44.5 mmol/l, $F(12,84) = 8.69$, $P < 0.001$) and insulin (7.3 ± 1.2 µmol/ml, $F(12,84) = 2.14$, $P < 0.05$) compared to isomaltulose-fed rats (7.3 ± 0.2 mmol/l, 67.5 ± 8.7 mmol/l and 3.7 ± 0.3 µmol/ml) and starch-fed rats (6.8 ± 0.2 mmol/l, 20.9 ± 8.9 mmol/l and 4.3 ± 1.2 µmol/l) 15 min after meal end. Thus, adaptation to high-isomaltulose feeding does not have a long lasting effect on rats' eating or weight gain and affects postprandial glucose metabolism more like starch than sucrose.

Hindbrain administration of 5-HT3 receptor antagonist, ondansetron attenuates systemic CCK-induced satiation.

M.R. HAYES, M. COVASA.
Department of Nutritional Sciences, College of Health and Human Development, The Pennsylvania State University, University Park, PA 16802, USA.

We have previously shown that systemic administration of ondansetron attenuates cholecystokinin (CCK)-induced suppression of both solid and liquid food intake. The location of serotonin type-3 (5-HT3) receptors mediating these actions is not clear and may involve hindbrain 5-HT3 receptor populations. Therefore, we tested the hypothesis that administration of the selective 5-HT3 receptor antagonist, ondansetron, into the fourth ventricle would attenuate CCK-induced satiation. Overnight food deprived rats received a 3.0 µl 4th ventricular injection of either ondansetron (6.0, 10.0, and 25.0 µg/rat) or vehicle immediately before an intraperitoneal (IP) injection of either CCK or saline. Administration of ondansetron alone did not alter 15% sucrose intake compared to control at any dose tested. IP CCK (0.5, 1.0, 4.0 µg/kg) reduced 30-min sucrose intake by 35, 45 and 76%, respectively compared to control. Prior treatment with ondansetron (10.0 µg/kg) significantly attenuated suppression of 30-min sucrose intake induced by 1.0 (50%) and 4.0 (33%) but not by 0.5 µg/kg dose of CCK. Higher doses of ondansetron (25.0 µg/kg) also attenuated CCK (1.0 µg/kg)-induced satiation by 52%. The lowest dose of ondansetron (6.0 µg/kg) had no significant effect on suppression of intake by CCK. These results extend on the well documented role of 5-HT3 receptor in control of food intake and demonstrate that 5-HT3 receptors located in the hindbrain also mediate systemic CCK-induced suppression of food intake.

Automated video-based behavioral assays in metabolic research.

J.U. HEIMAN, J.B. CHAMBERS, D.J. CLEGG, P. PFLUGER, M. TSCHOP, S.C. BENOIT.
University of Cincinnati, Department of Psychiatry, Cincinnati, OH 45237, USA.

Genetic manipulations and selective breeding represent crucial technologies in metabolism and ingestive behavior research. Behavioral testing is required to dissect the specific phenotypic components of such models with varying metabolic profiles. At our new core facility in the University of Cincinnati, we have recently developed a panel of specific high through put assays to quantify numerous behaviors, using a combination of modern technologies and techniques. We have refined two novel computer-based technologies for the analysis of rodent ingestive and locomotor behavior (CleverSys, Inc., Reston, VA). These programs implement digital video analysis in numerous rodent behavioral tests. The animal's activity scored by the specifically developed software that provides a detailed and broad matrix of behaviors over time, including velocity, distance traveled, sniffing and maze exploration, to just name a few. Use of this technology can provide a functional assessment of behavioral differences in genetically differing animals. The research implications are twofold in that we are able to: a) observe behaviors that may elucidate why, how and when changes in

bodyweight and/or body composition occur, and b) characterize changes in learning, anxiety, motivation, and other behaviors caused by genetic manipulation and/or metabolic deficit. As additional molecular targets and rodent models of are made available to the research community, there is a rapidly increasing need for high throughput behavioral phenotyping to understand and characterize the behavioral components involved. The technology described here will likely offer one important solution to the increased demand for behavioral phenotyping in modern obesity and anorexia research.

Lateral hypothalamic (LH) injection of D-AP5 suppresses behavior indicative of sensory specific satiety.

S.R. HETTES, G.R. DAVIS, Jr.
Biology Department, Wofford College, Spartanburg, SC 29303, USA.

Though LH neural activity fluctuates with sensory specific satiety (Rolls et al, Brain Research 1986), neurotransmitters regulating this activity are not known. Glutamate has been shown to regulate feeding by acting at LH NMDA receptors (Stanley et al, Am. Physiol, 1996). We tested whether D-AP5 (NMDA receptor antagonist) suppresses sensory specific satiety. Preliminary testing demonstrated that rats prefer Froot Loops® over Tekland rodent chow. Food-deprived rats fed chow to satiety, were microinjected into the LH via indwelling guide cannulas with 0.3 µl artificial cerebral spinal fluid (aCSF, control) or 10 nmol D-AP5 in 0.3 µl aCSF, then offered a second meal (60 min) of chow or Froot Loops®. After aCSF injection, rats exhibited sensory specific satiety by consuming more Froot Loops® (1.6 ± 0.28 g) than chow [0.3 ± 0.3 g ($F(1,13) = 17.7$; $P = 0.001$)]. Further, average latency to eat Froot Loops® (19 ± 4.3 min) was less than to eat chow [46.2 ± 4.3 min, ($F(1,13) = 36.9$; $P < 0.001$)]. Upon D-AP5 injection, Froot Loops® intake (0.6 ± 0.3 g) decreased so that there was no difference compared to chow intake (0.1 g ± 0.2 g; $P > 0.05$). Likewise, latency to feed was similar for Froot Loops® (34.3 ± 4.4 min) and chow (47 ± 4.4 min; $P > 0.05$). These findings suggest that endogenous glutamate released in the LH acts on NMDA receptors to increase intake during sensory specific satiety.

Sensory specific satiety is intact in amnesic patients who eat multiple meals.

S. HIGGS, A.C. WILLIAMSON, G.W. HUMPHREYS.
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK.

It has been suggested that the eating of multiple meals in amnesic patients highlights role for memory of recent eating in the control food intake, since in the absence of such memory meals are larger than normal. However, little is known about the specific mechanisms underlying this phenomenon. One possibility is that representation of the sensory properties of foods is disrupted in amnesics and this prevents the usual decline in pleasantness of an eaten food relative to uneaten foods, known as sensory-specific satiety. In the present study, sensory-specific satiety was measured in 3 amnesic and 7 control participants. Appetite and liking ratings were measured before and after an ad libitum lunch (sandwiches). Each of the sample foods was selected to provide a different set of sensory properties than the sandwiches: cookies, rice pudding, and potato chips. Our results showed that for both patients and controls there was a greater decrease in ratings of liking and prospective consumption for the eaten food compared to the uneaten foods. Since additional data from the same amnesic patients shows overeating in response to multiple meal presentation, the results indicate that a failure to show sensory specific satiety is unlikely to underlie such overeating. The results

also suggest that explicit memory of an eating episode is not required for the expression of sensory specific satiety, because none of the present patients were aware of having just eaten.

Olanzapine treatment reduces activity-based anorexia in rats.

J.J.G. HILLEBRAND, A.A. VAN ELBURG, M.J.H. KAS, R.A.H. ADAN.
Rudolf Magnus Institute of Neuroscience, Department of Pharmacology and Anatomy, University Medical Center Utrecht, Utrecht, The Netherlands.

The activity-based anorexia (ABA) model is based upon scheduled feeding in combination with wheel running. Following introduction of a feeding schedule (1 hr food access per day) rats loose body weight, become hyperactive, reduce food intake and the HPA axis is activated. Hence, similar to human anorectics, ABA rats have a severe negative energy balance but are (paradoxically) hyperactive. It was examined whether the development of ABA could be influenced by chronic treatment with the atypical antipsychotic olanzapine. Rats exposed to the ABA model were treated with olanzapine (7.5 mg/kg/day) for 7 days (using osmotic minipumps). Olanzapine-treated ABA rats lost less body weight and were less active in the running wheel as compared to vehicle-treated ABA rats. Olanzapine treatment also prevented starvation-induced hypothermia and reduced activation of the HPA axis in ABA rats. Therefore it was concluded that olanzapine treatment diminished the development of ABA. The clinical importance of these results will be discussed.

Effects of area postrema (AP) lesions on inhibition of vasopressin (VP), gastric emptying, and water intake by dehydrated rats.

M.L. HOFFMANN, J.A. SVED, E.M. STRICKER.
Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA.

Dehydrated mammals appear to have an adaptive mechanism for the early inhibition of VP secretion and thirst when drinking water. Ramsay and Thrasher's seminal work on this subject showed that oropharyngeal signals inhibited VP secretion and thirst in dogs. Subsequent work extended these findings to sheep, monkeys, and human subjects. However, recent work in our laboratory showed that rats have different mechanisms of inhibition related to the rapid, postingestive consequences of fluid consumption. Inhibition of VP secretion appears to result from osmotic dilution as might be sensed by a visceral osmo- (or Na^+-) receptor, whereas inhibition of thirst appears to result from a distension signal associated with the volume of ingested fluid in the stomach and small intestine. To examine whether the AP is necessary for the early inhibition of VP secretion and thirst, rats with discrete lesions of the AP were deprived of water overnight and then given water to drink. They consumed 5 - 7 ml in 3 - 4 min, amounts comparable to those consumed by intact control rats. Gastric emptying of ingested water was comparable in the two groups (~ 50%). Ingested fluid traveled deep into the small intestine in rats with AP lesions, further than in control rats (~ 55 cm versus ~ 35 cm in 3 min), yet the decreases in plasma levels of Na^+ and VP were comparable in the two groups. These results suggest that the AP does not play a critical role in mediating the early inhibition of VP secretion or thirst when dehydrated rats drink water.

Hypoglycemic response to gastric evacuation in schedule-fed rats.

J.M. HORMES, K.A. HAGUE, H.J. GRILL, J.M. KAPLAN.
University of Pennsylvania, Department of Psychology, Philadelphia, PA 19104, USA.

We previously observed a reliable and persistent hypoglycemic response in rats undergoing gastric evacuation following breakfast in a scheduled-feeding paradigm with three 60 min access periods (IMI = 3.5 h) during the dark phase. This response may be the simple result of loss of nutrients that would otherwise empty from the stomach, or alternatively reflect an interaction between reduced nutrient delivery and events specifically associated with the prior ingestion of a large meal. To address these possibilities, glycemic effects of evacuation (30 min after breakfast) were evaluated against results of a restricted-breakfast condition in which rats ate only the amount estimated to empty from the stomach during the full breakfast. A breakfast-omission condition was run to gauge the magnitude of the hypoglycemic response to evacuation. Mock-evacuation (after full breakfast meal) provided the baseline reference. Tail-blood was taken before and after the first meal, midway through the IMI and 20 min before lunch. The evacuation-induced hypoglycemia was replicated (about 20% below baseline for the latter two blood samples) and comparable in magnitude to that observed with meal omission. Importantly, the glucose response to the restricted meal was not significantly different from that observed after ingestion of a full meal. The mechanism underlying the evacuation response is currently unknown. The effect may reflect an altered pattern of nutrient delivery to the intestine, or a mismatch between the actual amount delivered to the system and that "anticipated" based on signals arising from ingestion of a large breakfast (e.g. elevated prandial insulin). Supported by DK42284, DK21397.

Hindbrain administration of competitive NMDA receptor antagonist, AP-5 increases food intake and body weight in the rat.

C. HUNG[a], M. COVASA[a], R.C. RITTER[b], G.A. BURNS[b].

[a]*Department of Nutritional Sciences, College of Health and Human Development, The Pennsylvania State University, University Park, PA, 16802, USA;* [b]*Department of Comparative Anatomy, Pharmacology and Physiology, College of Veterinary Medicine, Washington State University, Pullman, WA, 99164, USA.*

Hindbrain administration of MK-801, a non-competitive NMDA channel blocker, increases meal size. However, MK-801 reportedly antagonizes some non-NMDA ion channels. To further assess hindbrain NMDA receptor participation in food intake control, we measured deprivation-induced intakes of 15% sucrose solution or rat chow following intraperitoneal (IP), 4th ventricular (4V), or nucleus of the solitary tract (NTS) injection of either saline or D-AP5, a competitive NMDA receptor antagonist. IP AP5 (0.05, 0.1, 1.0, 3.0 and 5.0 mg/kg) did not alter 30-min sucrose intake at any dose (10.7 ± 0.4 ml, saline) (11.0 ± 0.8, 11.2 ± 1.0, 11.2 ± 1.0, 13.1 ± 2.2, and 11.0 ± 1.9 ml, AP5 doses, respectively). 4V AP5 (0.2 µg/3µl) significantly increased both 30 min (15.0 ± 0.6 ml, AP5 versus 13.1 ± 0.6 ml, saline) and 60 min (17.1 ± 0.5ml, AP5 versus 14.1 ± 0.5 ml, saline) sucrose intake. 24 hr cumulative chow intake also was increased compared to saline (31.5 ± 0.5 g, AP5 versus 27.1 ± 0.6 g saline). Finally, NTS AP5 (20 ng/30 nl) significantly increased 30 (17.1 ± 0.5 ml, AP5 versus 14.6 ± 0.7 ml, saline), and 60 min (19.3 ± 0.4 ml, AP5 versus 15.5 ± 0.7 ml, saline) sucrose intake and 24 hr chow intake (31.1 ± 0.8 g, AP5 versus 26.1 ± 0.6 g, saline). Surprisingly, NTS AP5-injected rats gained more weight over a 15-day post-injection period (11.2 ± 1.1%) than saline-injected rats (4.6 ± 1.4%). These results support hindbrain NMDA receptor participation in control of food intake and suggest that they may contribute to the control of body weight. Supported by DK-52849, NS-20561.

Opiate-dependent learning of conditioned place preferences (CPPs) to solid, high-calorie "snack foods" in rats.

P. JAROSZ, P.K. SEKHON, A. MALIK, D.V. COSCINA.
Departments of Psychology and Nursing, Wayne State University, Detroit, MI 48202, USA.

Previous research has shown that food-deprived rats acquire CPPs to sweet liquids that can be attenuated by systemic administration of the opiate antagonist naltrexone (NAL). This study determined if ad-libitum chow-fed rats can learn CPPs when given relatively brief exposures to different, solid "snack foods" – one high in sugar (Froot Loops cereal: FLs) versus one high in fat (Cheetos; Cs). Separate groups of 16 male rats were trained for 20 min every other day to eat either FLs or Cs on one side of a 3-chambered CPP apparatus versus chow on the opposite side of the apparatus on alternating days over 20 days. Both foods generated statistically higher consumptions (about 23 kcal each) than chow (about 7 kcal each) the last 4 days of training. Subsequent tests of CPPs for 10 min when no foods were available demonstrated significant learning regardless of the type of "snack food" used for training. Within-subject tests of CPPs after 0, 0.1, 1.0, 2.5 and 5.0 mg/kg NAL subcutaneously revealed dose-dependent suppression of both CPPs. These data demonstrate that, despite the absence of food restriction and regardless of macronutrient type, repetitive exposure to solid high-calorie "snack foods" can generate conditioned "reward" to environmental cues which appears to be maintained by stimulation of endogenous opiate systems.

***NO PUBLICATION in APPETITE.

Ghrelin and neuropeptide Y produce discriminative stimulus effects similar to 22 hours food deprivation.

D.C. JEWETT[a], T.W. LEFEVER[a], D.P. FLASHINSKI[a], M.N. KOFFARNUS[a], C.R. CAMERON[a], M.K. GRACE[b], A.S. LEVINE[b,c].
[a]*Department of Psychology, University of Wisconsin – Eau Claire, 54702, USA;* [b]*VA Medical Center, Minneapolis, MN 55417, USA;* [c]*Department of Food Science and Nutrition, University of Minnesota, St. Paul, MN 55108, USA.*

We trained rats to discriminate between 2 and 22 hrs of acute food deprivation in an operant choice paradigm. During generalization tests, acute food deprivation produced time-dependent increases in 22 hr responding. During other tests, rats were food restricted for 22 hrs and responded appropriately. When rats were then given access to food for 20 min (mean consumption = 5.7 g, SD = 1.3 g) and placed in the operant test, rats reliably selected the lever associated with 2 hrs food deprivation, indicating that food consumption eliminates discriminative stimuli associated with 22 hrs food deprivation. Saccharin (0.032 – 3.2%) or sucrose (0.32 – 32%) consumption did not appreciably alter the discriminative stimulus effects of 22 hrs food deprivation. During other tests, rats were food restricted for 2 hrs and responded appropriately. Rats were then injected with ghrelin, neuropeptide Y (NPY), or saline in the PVN. Saline resulted in continued 2 hr responding. Ghrelin and NPY produced dose dependent increases in 22 hr appropriate responding indicating ghrelin and NPY produced effects that are recognized as similar to those of acute food restriction. These findings suggest that discriminative stimuli produced by 22 hrs food deprivation are mimicked by neurochemicals administered into brain areas important for the feeding regulation. These discriminative stimulus effects may be sensitive to factors altering food consumption and may serve as a model to examine dietary and neurochemical factors that alter internal states associated with eating. Supported by the University of Wisconsin – Eau Claire Faculty/Student Research Collaboration grant, NIH and Department of Veterans Affairs.

The hippocampus and energy regulation.

S.E. KANOSKI[a], A.L.TRACY[a], E.K.WALLS[a], T.L.DAVIDSON[a], L.E. JARRARD[b], D. CLEGG[c], S.C. BENOIT[c].

[a]*Purdue University, West Lafayette, IN 47907, USA;* [b]*Washington & Lee University, Lexington VA 24450, USA;* [c]*University of Cincinnati, Cincinnati, OH 45237, USA.*

Although specification of physiological substrates will be central to any comprehensive account of food intake regulation, it is now clear that such accounts must also describe the role of learning and memory in the control of eating and appetitive behavior. From this perspective, food intake regulation and, ultimately body weight, is likely to depend on the ability to inhibit responding to orosensory and other food related stimuli that are associated with rewarding consequences of eating. New data and new interpretations of older findings suggest that this type of inhibitory ability may depend on the hippocampus, a brain structure long implicated as a substrate for learning and memory. Encouraged by variety of physiological and behavioral evidence, this presentation will evaluate the hypothesis that the regulation of food intake and body weight is, at least in part, a hippocampal-dependent function. We present data showing that selective neurotoxic lesions of the hippocampus are accompanied by increased food intake and body weight gain. We also report that such damage is accompanied by reduced glucose tolerance and sensitivity to cholecystokinin. The effects of damage confined to selected regions of the hippocampus (e.g., dorsal, ventral) that differ in terms of their connections to hypothalamic regions involved with food intake will also be discussed, as will the effect of diets high in fat and processed sugar on hippocampal neuronal activity and on performance on learning problems that rely on the hippocampus.

Fasting- and ghrelin-induced stimulation of food hoarding and food intake is attenuated by icv MTII injection.

E. KEEN-RHINEHART, T.J. BARTNESS.

Department of Biology, Center for Behavioral Neuroscience, Georgia State University, Atlanta, GA 30302, USA.

Mechanisms underlying appetitive ingestive behaviors (foraging, food hoarding) are relatively unknown compared to their consummatory counterpart (food intake). In Siberian hamsters, fasting increases food hoarding, decreases central alpha-melanocyte stimulating hormone and increases circulating ghrelin, suggesting their possible interaction controlling appetitive ingestive behavior. We used the melanocortin-3/4 receptor agonist, melanotan II (MTII), and the peripheral hormone, ghrelin to test their effects on food intake and food hoarding. We asked: 1) Will icv MTII inhibit fasting-induced increases in food intake and food hoarding? and 2) Because peripheral ghrelin increases food intake and hoarding similar to fasting, will icv MTII inhibit these responses? In Experiment 1, hamsters were food deprived 48 h and received either MTII (0.3, 1.0, or 2.5 nmol) or saline into the 3rd ventricle. In Experiment 2, hamsters received i.p. ghrelin (30 mg/kg) + icv MTII (2.5 nmol), i.p. ghrelin + icv saline, i.p. saline + icv MTII and i.p. saline + icv saline in a counterbalanced design. Food intake and hoarding were measured 1, 2, 4, 24, 48, 72, and 96 h post-injection. Food deprivation stimulated food intake and hoarding. MTII inhibited food deprivation-induced food intake up to 96 h post-injection, but only at 2.5 nmol. The two highest MTII doses inhibited food deprivation-induced food hoarding 24 - 96 h post-injection. Ghrelin stimulated food intake initially and food hoarding later, similar to fasting. MTII injection inhibited ghrelin-induced stimulation of food intake and hoarding. These results suggest food deprivation and ghrelin

stimulate similar ingestive behaviors, and the melanocortins are important for both food deprivation- and ghrelin-induced stimulation of consummatory and appetitive behaviors in Siberian hamsters. Supported by NSF IBN-9876495.

Estrogen signaling through estrogen receptor alpha (ERa) regulates food intake, body weight, and leptin sensitivity.

C. KEMP, S.C. BENOIT, D.J. CLEGG.
Obesity Research Center, Department of Psychiatry, University of Cincinnati, Cincinnati, OH 45237, USA.

Following ovariectomy (OVX), there is a significant increase in food intake and body weight that persists for 4 weeks. Mirroring the hyperphagia, we have found increased whole hypothalamic gene expression (measured by qPCR) of AgRP and NPY, and decreased POMC, that persists for the duration of hyperphagia, and that returns to the level of sham-operated females once the hyperphagia subsides. These data indicate that removal of the ovaries (and consequent reduction in plasma estrogen) changes the level of defended body weight through transient increases in hypothalamic orexigenic and reductions in anorexigenic gene expression. We have confirmed that one of the estrogen receptors, ERα, is located in the ARC and VL VMN. Additionally we have found, consistent with estrogen's regulation of POMC neurons, that ERα in the ARC is co-localized with POMC. Because several reports demonstrate that ARC POMC neurons also express the long form or signaling form of the leptin receptor, OB-Rb, these data suggest a direct mechanism by which estrogen signaling through ERα in the ARC may regulate food intake and body weight. Consistent with this, we have also found that following i3vt leptin, ERα is co-localized with pSTAT3, an intracellular marker of leptin receptor activation. These observations are consistent with the hypothesis that estrogen enhances leptin sensitivity by signaling through ERá. Since the OB-Rb gene has an Estrogen Response Element (ERE), the implication is that estrogen directly alters OB-Rb expression in POMC neurons, thereby explaining the differences in leptin sensitivity of intact versus OVX versus OVX + estrogen-treated females.

Meal-realted endocrine responses in anorexia nervosa.

K.P. KINZIG, G.W. REDGRAVE, J.W. COUGHLIN, T.H. MORAN, A.S. GUARDA.
Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.

Prolonged malnutrition in individuals with anorexia nervosa (AN) has been associated with alterations in endocrine function. We hypothesized that in AN there are reversible abnormalities in endocrine responses to ingestion of a meal that depend upon weight restoration. We measured meal-induced endocrine responses in subjects with AN at 3 time points during hospitalization: before refeeding (n = 13, mean BMI = 16.7), after two weeks of refeeding (n = 11, mean BMI = 18.0), and in the weight-restored state (n = 11, mean BMI = 20.3). Control subjects (BMI = 19 - 24.9) were tested once. Tests were 2.5 hour sessions in which blood was drawn every 15 minutes before, during, and after a 700 kcal test meal. Subjects rated hunger, satiety, nausea, and anxiety on visual analog (VA) scales at each blood draw. Among AN subjects, leptin levels were unchanged between trials 1 and 2 (4.07 ± 1.16 versus 4.71 ± 1.04 ng/ml) and were significantly increased at trial 3 (9.66 ± 2.78 ng/ml, $P < 0.05$). Relative to controls, peak levels of insulin and glucose in response to ingestion of the test meal were delayed, with response patterns in the third trial similar to those of controls. In contrast to controls, hunger and satiety ratings on VA scales did not correlate with endocrine

responses to ingestion of the test meal in AN subjects at any of the three test sessions. These data indicate that while endocrine responses to a meal improve with weight gain in AN subjects, ratings of hunger and satiety remain different from those of normal weight controls.

Chronic food restriction increases ambulatory activity and the hypothalamic 5-HT content in the rats experienced postnatal maternal separation.

H.J. KIM, J.G. KIM, J.W. JAHNG.
Department of Pharmacology, BK21 Project for Medical Science, Yonsei University College of Medicine, Seoul, 120-752, Korea.

It has been reported that postnatal maternal separation (MS) modulates the central serotonergic (5-HT) neural function and feeding behavior at adulthood, and that chronic food restriction (CFR) alters the activity of brain 5-HT system. We have previously reported that the raphe expression of 5-HT reuptake transporter (5-HTT) is markedly decreased at adulthood of the MS group, compared to the non-handled control (NH). CFR given at adulthood decreased the 5-HTT expression in the NH group, and produced no effect in the MS group. In this study, we measured the brain levels of 5-HT and its metabolite 5-HIAA and the ambulatory activity after the treatments of MS and CFR. Male Sprague-Dawley pups were either removed from their home cage and dam for 180 min every morning during PND 1 - 14 (MS) or left undisturbed (NH). Half of rats from the MS and NH groups received 50% of food (CFR), the rest were freely fed, during PND 28 – 60, and then all rats were either subjected to the ambulatory activity test or sacrificed for the measurement of brain 5-HT and 5-HIAA contents by HPLC. 5-HIAA contents in the midbrain and the hypothalamus did not differ among the groups. MS effect on the brain 5-HT levels were not found, however, CFR appeared to increase the hypothalamic 5-HT content in the NH group and the CFR effect was more obvious in the MS group. Ambulatory count of the first test day was reduced in the MS group compared with the NH group. CFR did not affect the ambulatory activity of the NH group, however, increased one of the MS group. These results suggest that MS may alter the central 5-HTergic function via modulating 5-HT release responding to nutritional stress. Supported by a KISTEP Grant (JWJ).

Brain 5-HT system may not mediate glucocorticoids suppression in feeding and weight gain.

N.Y. KIM, J.W. JAHNG.
Department of Pharmacology, BK21 Project for Medical Science, Yonsei University College of Medicine, Seoul, 120-752, Korea.

Stress has a major impact on feeding behavior. Plasma glucocorticoids and the hypothalamic release of 5-hydroxytryptophan (5-HT) sensitively respond to stress and feeding. We previously reported that synthetic glucocorticoid dexamethasone (DEX), which suppresses food intake and weight gain, decreases the brain 5-HT levels in rats, and the decrease appeared to be related with an increase in its metabolite 5-HIAA level. In order to determine the molecular mechanism by which glucocorticoids down-regulate the brain 5-HT level, we examined mRNA expressions of tryptophan hydroxylase (TPH), monoamine oxidase A (MAOA) and serotonin reuptake transpoter (5-HTT) in the raphe nucleus of rats treated with DEX, by using in situ hybridization. Male Sprague-Dawley rats (250 - 260 g) received 4 daily injections of DEX (0, 0.1 or 1.0 mg/kg), and were then transcardially perfused with 4 % paraformaldehyde. The mRNA level of TPH was markedly increased in the DEX treated groups. A dose-dependent increase in MAOA and 5-HTT expression by DEX was also

detected. The mRNA levels of TPH, MAOA and 5-HTT in the raphe of the pair-fed group did not differ from the saline injected control. These results together with our previous report suggest that DEX-induced increases of MAOA and 5-HTT expression might have caused a decrease in brain 5-HT level, perhaps an increase in its turn over as well. It appears that TPH expression level was increased as a part of compensatory regulation for the decreased brain 5-HT level. Lastly, DEX-induced suppression in feeding and weight gain does not appear to be mediated by brain 5-HT system. Supported by KISTEP Grant (JWJ).

Ratings as predictors of ad-libitum intake: reliability and effect of weight loss.

H.R. KISSILEFF, J.C. THORNTON, J.L. GUSS, R.L. LEIBEL, M. ROSENBAUM, M. TORRES.
St. Luke's/Roosevelt Hospital and Columbia University, New York, NY 10025, USA.

To validate ratings at certain intakes as measures of satiation, ad libitum food intake and appetite-related feelings were collected from three men and three women (obese [mean starting BMI = 46.1] inpatients in a 6 month study on a liquid formula diet). Subjects ate two ad libitum meals and two 975-g fixed meals, interrupted at 75 g aliquots to rate feelings, both before and after 15% weight loss. In the fixed meals subjects rated fullness ("0 = none", "150 = most imaginable") and satisfaction with eating (0 = "so little I'd always eat more", 150 = "so much I'd always eat less", and 75 = "at this amount I'd usually be comfortably satisfied") on 150 mm lines. Intake at the maximum rate of fullness increase per g eaten (IMAX) was computed from an exponential fit of fullness ratings to intake. Optimal intake (OI) was the amount eaten at 75 mm on the satisfaction question. Reliability between days and inter-correlations among ad libitum intake (AI), OI, and IMAX were tested. Reliabilities (r's) between days were 0.57 for AI, 0.82 for OI, and 0.53 for IMAX. Responses to weight loss were similar and non-significant on all three variables (eg. actual intakes pre-loss = 588 g, post-loss = 606 g, SED = 66.64, $P = 0.79$). Fullness at IMAX correlated with fullness at the end of ad libitum meals (r = 0.59, $P = 0.002$).There were significant correlations between AI and OI (r = 0.65) and between AI and IMAX (r = 0.56). Ratings could be used to measure the origin of sensations that control meal termination.

The development of a human sham-feeding paradigm.

D.A. KLEIN[a], J.S. SCHEBENDACH[a], M.J. DEVLIN[a], G.P. SMITH[b], B.T. WALSH[a].
[a]*Columbia University College of Physicians and Surgeons/NYSPI, New York, NY 10032, USA;* [b]*Weill Medical College and New York-Presbyterian Hospital, Westchester Division, White Plains, NY, USA.*

Although it is possible that binge eating and other forms of hyperphagia in humans are due to increased responsiveness of orosensory excitatory controls of eating, there is no direct evidence for this because food ingested during a test meal stimulates orosensory excitatory and postingestive inhibitory controls. To overcome this problem, we have adapted the modified sham feeding technique previously used in humans for the study of the orosensory control of autonomic and neuroendocrine mechanisms to measure the orosensory excitatory control of intake. Ten healthy women were randomly presented with cherry Kool-Aid unsweetened or sweetened with one of four concentrations of sucrose (2.5, 5, 10, or 20%) in a closed opaque container fitted with a straw. They were instructed to sip as much as they wanted of the liquid during 2-minute trials and to spit the fluid out into another opaque container. At the end of a trial, they used Visual Analogue Scales to rate the sweetness and liking of the fluid that they had just sipped and spit. Volume of intake and VAS ratings increased significantly as a monotonic function of sucrose concentration ($P's \leq 0.038$). These

effects of sucrose were due to orosensory stimulation in the absence of postingestive effects because the volume of liquid spit out did not differ significantly from the volume sipped. Thus, these results demonstrate for the first time the feasibility and apparent validity of this technique for measuring orosensory excitatory controls of eating in humans.

Central thyrotropin-releasing hormone (TRH) infusion attenuates the bradycardia induced by caloric restriction.

W.D. KNIGHT, S.J. SWOAP, A.D. PARSONS, J.M. OVERTON.
Florida State University, Tallahassee, FL 32306-4340, USA.

Central TRH infusion increases blood pressure and heart rate in anesthetized rats. Caloric restriction (CR) leads to negative energy balance and a decrease in the expression of TRH in the PVN accompanied by both reduced thyroid hormone levels and bradycardia. We tested the hypothesis that central infusion of low dose TRH would attenuate the cardiovascular responses to CR. Male Sprague Dawley rats were instrumented with telemetry devices for measurement of heart rate (HR) and blood pressure (BP) and a lateral intracerebroventricular (ICV) guide cannula for central infusions. After recovery, rats were given either ad libitum (AL) or CR treatments for seven days, which produced a pronounced decrease in light phase HR of approximately 50 bpm. Half of each group was given continuous infusions of TRH (600 nmol/day) or saline for seven days. Saline pump implantation had a mild transient effect on food intake and body weight, but no effect on MAP or HR. TRH also produced similar transient reductions in food intake, but produced slight increases in MAP and HR. The CR rats receiving saline continued to exhibit bradycardia while the TRH rats exhibited significant increase in HR from the saline-infused controls; these results were seen in both the light and dark phases. Furthermore, the magnitude of tachycardia observed in CR rats was greater than that observed in AL rats infused with TRH. The results indicate that reduced hypothalamic TRH signaling may contribute to the bradycardia observed during CR. Supported by NIH Grant HL56732.

Developmental changes in fos expression in the CNS in response to viscerosensory stimulation in the rat (Rattus norvegicus) by injection of lithium chloride.

T.J. KOEHNLE, L.M. RINAMAN.
Department of Neuroscience. University of Pittsburgh. Pittsburgh, PA 15260, USA.

There is good evidence that young mammals can acquire and express conditioned responses to odors and flavors paired with viscerosensory stimuli. Although the neural substrates that support these behaviors are widely studied in adults, there is essentially no information available concerning their genesis and functioning during early development. It is known that viscerosensory circuits assemble within the first two weeks of postnatal life in rats. To determine whether the functional circuitry supporting these behaviors is similar perinatally to that found in adults, we have studied the expression of fos protein in the brains of rat pups (aged 0, 7, 14, 21, and 28 days) after i.p. injection of either 0.15 M LiCl or 0.15 M NaCl. Litters were isolated from their dams for 1h prior to injection in an incubator. After injection, pups were perfused with fixative and their brains evaluated for fos protein using nickel intensified diaminobenzidine immunohistochemistry. Fos expression in the nucleus of the solitary tract increased slightly over development, whereas fos staining in the paraventricular nucleus of the hypothalamus showed marked elevation after P14. Fos staining in the bed nucleus of the stria terminalis, already significantly elevated by P14, increased further until P28. By contrast, fos staining in the central nucleus of the amygdala asymptoted with the

level at P28 as by P14. These results demonstrate the functional elaboration of viscerosensory circuits across postnatal ontogeny, and will permit the further identification and study of neural pathways that modulate conditioned responses to noxious stimuli in young and adult animals.

Parent feeding strategies and their perceived effectiveness in promoting intake of certain foods in young children.

T.V.E. KRAL, K.L. KELLER, A. PIETROBELLI, M.S. FAITH.
University of Pennsylvania, Philadelphia, PA 19104, USA.

Changing children's food choices to promote healthy eating is a challenge for many parents. Few studies have examined the strategies parents use to encourage consumption of certain foods, many of which their children often dislike (Rozin, *Appetite* 1989;12:171-182). This study tested the frequency with which mothers of 3 – 7 year-old children use 4 strategies to promote intake of certain foods: 1. offer special reward (e.g., gift); 2. offer verbal praise; 3. provide easy access to foods mothers want their children to eat; 4. restrict access to foods mothers do not want their children to eat. The sample included 65 mothers and their twins, all of whom were participants in a larger pediatric twin study. Mothers rated the frequency of strategy use on a 7-point scale (1 = never; 7 = always), and the strategies' effectiveness on a 5-point scale (1 = completely ineffective; 5 = completely effective). Mothers provided separate ratings for each twin (N = 130). One-way ANOVA indicated differential use of the 4 strategies (main effect: $P < 0.001$). The mean frequency of use was 2.5 ± 1.4, 4.9 ± 1.6, 3.1 ± 1.8, and 3.6 ± 2.1 for reward, verbal praise, easy access, and restricted access, respectively. There was a positive association between the use of each strategy and its perceived effectiveness (Spearman rho: 0.27 - 0.64; $P < 0.001$). These findings indicate that parents report using a variety of feeding strategies, with varying degrees of effectiveness, to promote intake of certain foods in their children. Identifying effective feeding strategies may foster the consumption of healthy foods and may aid in childhood obesity prevention.

Weight loss attenuates isoproterenol induced water intake of ovariectomized female rats.

E.G. KRAUSE, J.P. MARKLE, K.S. CURTIS, R.J. CONTRERAS.
Florida State University, Dept. of Psychology, Program in Neuroscience, Tallahassee FL 32306, USA.

Previous studies from our laboratory examining the effect of estrogen replacement on renin-angiotensin-system (RAS) induced water intake have shown that after injection of isoproterenol, a β-adrenergic agonist which activates the RAS, ovariectomized (OVX) rats treated with estrogen drank less water compared to oil-treated controls. This study provides evidence for estrogen modulation of RAS-elicited water intake; however, ovariectomy is associated with weight gain and subsequent estrogen replacement produces a modest decrease in body weight. Thus, it is possible that estrogen modulation of RAS-elicited drinking may be secondary to estrogen effects on body weight. We therefore examined the effect of weight loss on RAS-induced water intake. Ovariectomized rats were treated with oil (0.1 ml) for two consecutive days. On the third day, OVX rats were food restricted to produce weight loss comparable to that after estrogen treatment (~ 5%) or were given ad libitum access to chow. Twenty-four hours later, rats were injected with isoproterenol (ISOP; 30 µg/kg body weight) or the 0.15 M NaCl vehicle and then given water in graduated drinking tubes. Intakes were measured every 30 min for 2 h. Water intakes after injection of the 0.15 M NaCl vehicle were

not different between groups. In contrast, food restricted OVX rats drank significantly less water after ISOP (1.2 ± 0.4 ml/100 g body weight) than did ad libitum fed control (2.3 ± 0.3 ml/100 g body weight). These results suggest that estrogen attenuation of RAS-induced water intake may be due, in part, to the weight loss associated with estrogen replacement. Supported by NIH DC04785 and DK063754.

Analysis of AP-1 gene expression in the c-fos cells of c-fos-lacZ transgenic mice during conditioned taste aversion learning.

B.S. KWON, T.A. HOUPT.
Biological Sciences, Program in Neuroscience, Florida State University, Tallahassee, FL 32306, USA.

Conditioned taste aversion (CTA) occurs after pairing of a novel taste with a toxin (e.g. sucrose with LiCl). It has been demonstrated that c-fos is necessary for CTA acquisition, but because c-fos is induced by LiCl also in the absence of learning, c-fos alone is not sufficient: additional gene expression must be present in these cells during learning. We plan to target c-fos-positive cells for expression analysis using laser capture microdissection. To aid in the identification of c-fos-positive cells, we characterized β-galactosidase expression in transgenic mice carrying a c-fos-lacZ fusion gene (a gift from J. Morgan). Mice were injected with LiCl (40 ml/kg, 0.15 M, i.p.) or saline and perfused one hour later. Alternate 40-μm sections were processed for c-Fos immunohistochemistry and X-Gal staining to visualize b-galactosidase activity in the amygdala region. There was a close correlation of X-gal staining with c-Fos expression in the forebrain, e.g., high densities of both c-Fos- and X-gal-positive cells in cortex and hypothalamus. There was also increased c-Fos and X-gal staining in the central amygdala after LiCl injection; interestingly, c-Fos expression appeared more robust than X-gal staining specifically in the central amygdala. Nonetheless, c-fos-lacZ transgenic mice can be used to identify transcriptional activity of the c-fos gene in the amygdala after LiCl. Because X-gal staining requires less processing than immunohistochemistry, we anticipate greater preservation of other mRNA species for expression analysis after microdissection of X-gal-positive neurons. Supported by NIDCD 03198.

Feeding suppression by cholecystokinin is blocked by hindbrain administration of a selective gastrin-releasing peptide receptor antagonist.

E.E. LADENHEIM, R.R. BEHLES, T.H. MORAN.
Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.

The integration of long-term adiposity signals and short-term controls of food intake may depend on descending hypothalamic projections to caudal brainstem regions that are responsive to meal-related satiety signals. Although the chemical identity of the neurotransmitters comprising this pathway is currently unknown, one potential candidate is gastrin-releasing peptide (GRP). To determine whether hindbrain GRP signaling can modulate suppression of food intake by the meal-related satiety signal, cholecystokinin, (CCK), we evaluated the effects of fourth cerebral ventricular administration of the selective GRP receptor antagonist, [D-F5,Phe6,D-Ala11]bombesin-(6-13) methyl ester (BN-ME), on feeding suppression produced by i.p. CCK administration. Male Sprague-Dawley rats (n = 12) were injected into the fourth ventricle with either 0.9% saline or 1 nmol BN-ME five min prior to receiving an i.p. injection of 0.9% saline or 0.32 nmol/kg CCK-8. Five min later they were given access to Ensure liquid diet for 30 min. Our results indicate that Ensure intake

following fourth ventricular administration of BN-ME did not differ significantly from intake following saline injection ($P > 0.05$). Administration of CCK, in the absence of BN-ME, significantly suppressed 30 min Ensure intake by 28% compared to intake after saline injection ($P < 0.05$). By contrast, the satiety effect of i.p. CCK was completely blocked by prior injection of BN-ME into the fourth ventricle ($P > 0.05$). These results suggest that hindbrain GRP, possibly of hypothalamic origin, participates in feeding suppression by i.p. CCK. Supported by NIH grant DK46448.

A low-energy-dense diet is associated with the consumption of a greater weight of food and fewer calories in US adults.

J.H. LEDIKWE[a], H.M. BLANCK[b], L. KETTEL KHAN[b], M.K. SERDULA[b], J. SEYMOUR[b], B.C. TOHILL[b], B.J. ROLLS[a].

[a]Department of Nutritional Sciences, The Pennsylvania State University, 226 Henderson Building State College, PA 16802, USA; [b]Centers for Disease Control and Prevention, Division of Nutrition and Physical Activity, 4770 Buford Highway MS K-34, Atlanta, GA 30341, USA.

Dietary energy density (ED; kcal/g) has been shown to influence energy intake in laboratory studies. The present epidemiological study investigated the relationship of ED to energy and food intake in a representative sample (94-96 CSFII) of adults (= 20 y) not pregnant/lactating or on a special diet (final n = 7500). ED was calculated using two recalls, excluding beverages. Analyses compared persons with low, medium, and high ED diets, as defined by ED tertiles, to identify differences in energy intake and weight of food and beverages. Individuals with a diet having a low ED reported a lower intake of total energy, energy from food, and energy from beverages than those with a diet having a high ED ($P < 0.0001$). While the total weight of food and beverage intake did not differ by the ED of the diet, those with a diet having a low ED reported consuming more food and less beverages than those with a diet having a high ED ($P < 0.0001$). A low ED diet was associated with the consumption of a greater weight of food and fewer calories. This evidence suggests that a reduction in dietary ED as a weight loss strategy would allow individuals to consume fewer calories without reducing the weight of food consumed. Supported by CDC/ORISE, DK039177, DK059853.

Lithium increases hippocampal cholinergic neurostimulating peptide in PC12 cells and choline acetyltransferase in the rat septo-hippocampal cholinergic system.

J.Y. LEE, G.T. KIM, S.B. YOO, J.W. JAHNG.

Department of Pharmacology, BK21 Project for Medical Science, Yonsei University College of Medicine, Seoul, 120-752, Korea.

Lithium chloride, conventional US in conditioned taste aversion (CTA) learning, induces neuronal activation, referred by c-fos expression, in the brain regions. We examined the proteome pattern of PC12 cells after lithium treatment (5 mM LiCl for 24 h) using MALDI-TOF peptide analysis system, in order to determine which genes are expressed by lithium. Gene expression of hippocampal cholinergic neurostimulating peptide (HCNP) was found to be increased in PC12 cells by lithium. It has been reported that cholinergic signals initiated by novelty are crucial for taste memory formation, and that mice with hippocampal dysfunction showed impairments in CTA learning. We examined if lithium increases expression of choline acetyltransferase (ChAT), which is known to be increased by HCNP, in the rat septo-hippocampal cholinergic system. Male Sprague-Dawley rats (300 - 450 g) received intraperitoneal injection of LiCl (0.15 M, 12 ml/kg), and were decapitated 6 h later. The

hippocampus, the medial septum and the preoptic magnocellular nucleus were rapidly dissected on ice and processed for Western blot analysis with ChAT antibodies. ChAT expression was increased in all three brain regions of lithium injected rats, more obviously in the medial septum, compared to the saline injected controls. This result together with the proteome analysis of PC12 cells suggests that lithium may activate the septo-hippocampal cholinergic system, at least partly by increasing expression of ChAT, perhaps HCNP as well, and that the activation of the septo-hippocampal cholinergic system may contribute to the formation of lithium-induced CTA. Supported by a KISTEP Grant (JWJ).

Hypothalamic peptides and palatable foods.

S.F. LEIBOWITZ, O. KARATAYEV, G-Q. CHANG.
The Rockefeller University, New York, NY 10021, USA.

Hypothalamic peptides that stimulate feeding can be divided into two distinct classes: 1) one that is closely related to low energy, carbohydrate- or sugar-rich foods, including neuropeptide Y and agouti-related protein in the arcuate nucleus; and 2) one that is closely related to energy dense, fat-rich foods, including galanin in the paraventricular nucleus and orexins in the perifornical lateral hypothalamus. The former produce a stronger feeding response and are endogenously stimulated by a high-carbohydrate diet, food deprivation, glucoprivation, glucocorticosteroids and reduced adiposity. This contrasts with galanin and orexins, which have a stronger effect when stimulating intake of a fat-rich diet and are, in turn, increased by a high-fat diet along with a rise in adiposity. These carbohydrate- and fat-stimulated peptides are potentiated by short periods of diet consumption, perhaps less than an hour, in close relation to circulating levels of glucose and triglycerides, respectively. Also, administration of these metabolic fuels differentially modulates these hypothalamic peptides. Most intriguing are recent findings showing that the opioids, enkephalin and dynorphin, also fall in the class of fat-stimulated peptides. This evidence has led us to propose the existence of non-homeostatic, positive feedback loops involving dietary and circulating nutrients, as well as hypothalamic peptides related to glucose and lipids. These non-homeostatic systems may stimulate meal size and produce overeating when carbohydrate- and fat-rich diets are readily available.

24h satiety, GLP-1, ghrelin, energy- and substrate metabolism during a high protein diet measured in a respiration chamber.

M.P.G.M. LEJEUNE, K.R. WESTERTERP, T.C.M. ADAM, N.D. LUSCOMBE-MARSH, M.S. WESTERTERP-PLANTENGA.
Maastricht University, Department of Human Biology, P.O. Box 616, 6200 MD Maastricht, The Netherlands.

The mechanism of protein-induced satiety remains unclear. We investigated 24h satiety, related hormones and, energy- and substrate metabolism during a high-protein diet in a respiration chamber. Subjects were twelve healthy females (BMI: 20 - 25 kg/m2, age: 18 - 40 y). They were fed in energy balance (EB) a normal-protein (NP: 10/60/30 en% of protein/carbohydrate/fat) or a high-protein (HP: 30/40/30 en% of protein/carbohydrate/fat) diet in a randomized cross-over design. 24h energy expenditure (EE), substrate oxidation, appetite profile, and ghrelin and GLP-1 concentrations were measured. Sleeping metabolic rate (6.40 ± 0.47 versus 6.12 ± 0.40 MJ/d; $P < 0.05$), DIT (0.91 ± 0.25 versus 0.69 ± 0.24 MJ/d; $P < 0.05$) and satiety were higher during the HP diet, activity-induced EE (1.68 ± 0.32 versus 1.86 ± 0.41; $P < 0.05$), RQ (0.84 ± 0.02 versus 0.88 ± 0.03; $P < 0.0005$), and hunger

were lower. 24h EE during the HP diet tended to be higher (P = 0 .05). While energy intake was not different, subjects were in EB during the HP diet and in positive EB during the NP diet. Satiety was related to 24h EE ($P < 0.05$; $r^2 = 0.40$) and energy intake ($P < 0.01$; $r^2 = 0.53$) during the HP diet, while in EB. Ghrelin concentrations were not different between diets whereas GLP-1 concentrations after dinner were higher in the HP diet condition ($P < 0.05$). We conclude that a HP diet as compared to a NP diet when fed at EB during 4 days increased 24h satiety, related to energy-metabolism, and not to ghrelin or GLP-1 concentrations. Accordingly, protein-induced satiety seems to be rather thermogenic than hormonal.

Teaching portion size control can block the freshman weight gain.

D.A. LEVITSKY, J. GARAY.
Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853-6301, USA.

Our previous research indicated that freshman women at Cornell University gain approximately two kilograms over the course of their first 12 weeks at College. We observed that a large portion of the variance in weight gain could be accounted for by the number of times they ate in the "all-you-can-eat" dining halls where the cost of the eating is independent of the amount of food that students serve themselves. We, and others, have found that the amount of food on the plate is a significant determinant of the amount consumed. This study examined the effect of providing a group of freshman with two one hour "lessons" at the beginning of their first semester of how to estimate appropriate portion sizes. The result was that this group gained no weight while the untreated controls gained approximately 2 kg during the first 12 weeks of the semester.

Dose-related effects of the fatty acid, lauric acid, on antropyloroduodenal (APD) motility and energy intake in healthy men.

T.J. LITTLE[a], K.L. FELTRIN[a], M. HOROWITZ[a], A.J.P.M. SMOUT[b], A.N. PILICHIEWICZ[a], J.H. MEYER[a], T. RADES[a], C. FEINLE-BISSET[a].
[a]*Departments of Medicine, University of Adelaide, South Australia;* [b]*Gastroenterology, University Hospital Utrecht, The Netherlands.*

Free fatty acids mediate the slowing of gastric emptying and appetite suppression induced by fat. These effects are dependent on the chain length of fatty acids. We have recently reported that duodenal infusion of a low dose of lauric acid (C12) (0.375 kcal/min, 106 mM) stimulates isolated pyloric pressure waves (IPPWs), inhibits antral and duodenal pressure waves (PWs) and suppresses energy intake much more than an isocaloric decanoic acid (C10) infusion (*AJP* 2004;287:R524-R533). In this study, C12 infusion, at the concentration used, was associated with nausea, confounding interpretation of the results. We have now evaluated the effects of different intraduodenal doses of C12, at lower concentrations, on APD motility and energy intake. 13 healthy men were studied on four occasions. APD pressures were measured during 90 min intraduodenal infusions of C12 at (1) 0.1 (14 mM), (2) 0.2 (28 mM) or (3) 0.4 (56 mM) kcal/min and (4) saline (control), all at 4 ml/min. Energy intake at a buffet meal following the infusion was determined. The studies were well tolerated without nausea. C12(0.2) and C12(0.4) stimulated IPPWs and suppressed duodenal PWs ($P < 0.05$) compared with both control and C12(0.1); these effects were dose-related ($R > 0.29$, $P < 0.05$). Only the highest dose of C12(0.4) suppressed energy intake ($P < 0.05$). In conclusion, (1) the effects of C12 on APD motility are dose-related, (2) the threshold dose of C12 for changes in APD motility is lower than that required to suppress energy intake.

Effects of glucagon-like peptide-1 (GLP-1) on gastric emptying (GE) and intragastric distribution of a mixed solid/liquid meal in healthy men.

T.J. LITTLE[a], A.N. PILICHIEWICZ[a], A. RUSSO[a], K.L. JONES[a], M. NAUCK[b], M. HOROWITZ[a], C. FEINLE-BISSET[a].

[a]*Department of Medicine, University of Adelaide, South Australia;* [b]*Diabeteszentrum, Bad Lauterberg, Germany.*

GLP-1 has been reported to slow GE and inhibit energy intake. We have shown that energy intake after a meal is related to distal gastric content much more closely than to total or proximal gastric content (*AJCN* 2004;80:656-67). We have now evaluated the relationship between the slowing of GE by GLP-1 and intragastric distribution. 10 healthy men were studied on 3 separate days. Subjects received either i.v. (1) GLP-1, 0.3 pmol/kg/min [0.3], (2) GLP-1, 0.9 pmol/kg/min [0.9] or (3) saline [C], commencing 30 min before ingestion of a radiolabeled solid/liquid meal (270 kcal). GE was evaluated scintigraphically for 120 min. GLP-1 0.3 and 0.9 slowed GE of both solid (retention at 100 min: 28 ± 5, 53 ± 6, 58 ± 7%, for C, 0.3, 0.9) and liquid (T50%: 28 ± 2, 42 ± 7, 50 ± 9 min, for C, 0.3, 0.9) (0.3 and 0.9 versus C, $P < 0.05$ for both), with no difference between 0.3 and 0.9. GLP-1 increased the amount of both solid and liquid in the distal stomach compared with C ($P < 0.05$), and the amount of liquid ($P < 0.05$), but not solid, in the proximal stomach. In conclusion, the slowing of GE by GLP-1 is associated with increased retention of solid and liquid in the distal stomach, and increased retention of liquid in the proximal stomach. This may potentially account for the reported suppression of energy intake by GLP-1.

The effect of exchanging dietary fat for protein on ghrelin homeostasis and appetite before and after weight loss.

N.D.LUSCOMBE[a], L.J.MORAN[b], M.NOAKES[b], G.A.WITTERT[a], J.B.KEOGH[b], P.FOSTER[b], P.M.CLIFTON[ab].

[a]*Department of Medicine, University of Adelaide, Australia;* [b]*Health Science and Nutrition, CSIRO, Adelaide, Australia.*

The effect of two isocaloric equivalent carbohydrate diets on fasting and postprandial ghrelin concentrations were compared and the relationship between the changes in ghrelin with changes in body weight and appetite were examined. 25 men and 32 women (50 ± 10 yrs, BMI 33.8 ± 3.4 kg/m^2) followed either a high protein (HP) (34% protein) or a high fat (HF) (45% fat) diet for 16 weeks (12 at energy restriction [6 MJ/day] and 4 at energy balance [7.4 MJ/day]). Weight loss (9.2 ± 0.7 kg) and improvements in the glucose and insulin responses to test meals were similar in both diet groups. Following weight loss, fasting ghrelin increased (by 15.5 ± 3.4 pmol/l, $P < 0.001$) and post-prandial ghrelin decreased (by 81 ± 16 %, $P < 0.001$) independent of diet composition. The reduction in post-prandial hunger ($P = 0.018$) was associated with the reduction in post-prandial ghrelin ($r^2 = 0.11$, $P = 0.024$). At week 0 and week 16, subjects desired less to eat following the HP than the HF meal ($P = 0.02$); the reduction was not associated with the reduction in post-prandial ghrelin. We conclude that both diets produced similar weight loss and improvements in ghrelin homeostasis but ghrelin did not mediate the reduction in appetite observed with the HP diet.

Ghrelin Immunodrug(TM) reduces body weight gain in male mice.

T.A. LUTZ[a], B. CETTUZZI[a], N. WALSER[a], A. FULURIJA[b], K. SLADKO[b], P. SAUDAN[b], M. BACHMANN[b].

[a]*Institute of Veterinary Physiology, Vetsuisse Faculty, University of Zurich, 8057 Zurich, Switzerland;* [b]*Cytos Biotechnology AG, Zurich-Schlieren; Switzerland.*
Ghrelin is the only peripheral hormone known to increase food intake. Ghrelin is mainly secreted during fasting from endocrine cells in the gastric mucosa. Food intake reduces ghrelin levels, which seems to be mediated by glucose, insulin and amylin. Ghrelin may, therefore, be a signal to initiate meals and ghrelin increases feeding after peripheral or central administration. Due to its potent orexigenic effect, ghrelin has been considered a potential target for the treatment of obesity. Here, we aimed at neutralizing circulating ghrelin by inducing the production of ghrelin-specific antibodies. We hypothesized that this should lead to a decrease in body weight gain and/or food intake. Male mice fed a fat-enriched diet were vaccinated in two to four-week intervals with the Ghrelin Immunodrug(TM) (ghrelin peptides coupled to the virus-like particle, Qb). Animals vaccinated against Qb served as controls. The Ghrelin Immunodrug(TM) induced a robust ghrelin-specific immune response two to four weeks after the first vaccination. Mice vaccinated with the Ghrelin Immunodrug(TM) had a lower body weight gain than control animals. When the experiment was repeated with mice fed a pelleted low-fat food and which were housed in an automated feeding system, we also observed a decrease in body weight gain relative to the starting weight. However, in this experiment, we did not see a marked difference in food intake between vaccinated and control mice. We conclude that production of ghrelin antibodies, which presumably neutralize circulating ghrelin, leads to a decrease in body weight gain in mice. This may be an interesting strategy deserving further research for the prevention or treatment of obesity.

The (C)atkins diet helps to resolve diabetes mellitus in obese cats - preliminary results.

T.A. LUTZ[a], F. TSCHUOR[ab], D. FURRER[a], K. KAUFMANN[ab], C. REUSCH[b].
[a]*Institute of Veterinary Physiology,* [b]*Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zurich, 8057 Zurich, Switzerland.*
The pathophysiology of feline diabetes mellitus (DM; disturbed insulin secretion, peripheral insulin resistance and islet amyloid deposition) is similar to human type 2 diabetes. The prevalence of feline DM increases with age (often > 7 years). Male cats are affected more often than females, and more than 60% of diabetic cats are obese. It has been hypothesized that in cats as true carnivores, commercial diets high in carbohydrate may have detrimental metabolic effects. Here, we report on the outcome of treating diabetic cats with insulin plus a high-protein/high-fat diet ("diet"; 54% protein; 25% fat). So far, five client-owned cats with confirmed DM were included in the study. All cats were transferred to the diet and received insulin b.i.d. Three of five cats were obese (BW 6 - 10 kg). In these, blood glucose levels and serum fructosamine levels almost normalized over 4 - 6 weeks. Interestingly, the insulin dose could be markedly reduced during this period and DM seemed to resolve, i.e. DM was transient, despite stable BW. None of the cats with low to normal BW (approx. 4 kg) had a transient course of DM. Blood glucose profile also improved, but insulin treatment in these animals could not be discontinued up to the present time. We conclude that obese diabetic cats can be treated successfully with insulin plus a high-protein/high-fat diet. The transient course of DM in these cats is most likely due to the resolution of glucotoxicity. The exact mechanisms underlying the beneficial effect of this diet in obese cats need to be elucidated in future studies.

Water ingestion by desalivated rats eating high-salt diet: significant roles of gastric chyme and of visceral osmoreceptors.

R.E. MANESH, M.L. HOFFMANN, E.M. STRICKER.
Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA.
Last year we reported that after surgical removal of all salivary secretions, rats consumed more water when eating dry laboratory chow containing 8% NaCl instead of 1% NaCl. Measurement of the gastric fluid in these animals indicated that the amount of water consumed, when mixed with the NaCl content of the ingested high-salt food, produced an isotonic saline solution. Interestingly, unlike the dense gastric chyme formed in the stomachs of intact control rats, in the "desalivated" rats food particles were suspended in a large quantity of ingested liquid. Because those rats ate only 1 - 2 g during the feeding test (after overnight food deprivation), further experiments were done to determine the effects of greater food consumption. The results indicated that although desalivated rats drank more water when they ate 2 - 4 g than when they ate less food, they no longer drank enough to dilute all the ingested NaCl to isotonicity in the stomach. However, a relatively dense chyme was found in the stomachs of these animals. Thus, it seems likely that some of the ingested NaCl remained associated with food particles in the chyme and that the remainder was in the supernatant fluid, whose concentration approached isotonicity. Such findings would be consistent with previous hypotheses that the formation of a dense gastric chyme is adaptive in reducing the early osmotic consequences of eating high-salt diet, and that visceral osmoreceptors can detect the concentration of the fluid leaving the stomach and promptly stimulate thirst.

Obese OLETF rats show augmented ingestive and motor responses to dopamine D2 receptor stimulation.

W.M. MARGAS[a], N.K. ACHARYA[a], M. COVASA[b], A. HAJNAL[a].
[a]*Department of Neural and Behavioral Sciences, The Pennsylvania State University, Hershey, PA 17033, USA;* [b]*Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA 16803, USA.*
Dopamine D2 receptors (D2Rs) are involved in feeding regulation and have also been associated with obesity. To investigate this relationship, the D2R agonist quinpirole was injected (0.05, 0.5 mg/kg, s.c.) in OLETF male rats (n = 10, 24 wks) that lack CCK-1 receptors, are hyperphagic, develop obesity and type-2 diabetes. For controls, age-matched non-mutant lean LETO males were used (n = 10). Under baseline conditions, daily food and 30-min sucrose (0.3 M) intake were higher in OLETF than LETO (24-hr chow: +19.3 ± 5.6%, $P < 0.05$; sucrose: +99.0 ± 13.95%, $P < 0.01$). The high dose of quinpirole significantly reduced intake in OLETF but not LETO (chow: -44.1 ± 5.3%, $P < 0.01$ versus -3.4 ± 5.9%, ns; sucrose: -67.5 ± 6.2%; $P < 0.01$ versus -44.2 ± 16.6%, ns). The low dose of quinpirole also decreased intake more in OLETF (chow: -9.6 ± 5.9%, sucrose: -19.4 ± 8.8%) than LETO (chow: -2.6 ± 9.0%, sucrose: +1.3 ± 10.3%). Whereas the high dose of quinpirole increased motor activity in both strains equally (120 min ambulatory move time: OLETF: +88.4 ± 17.9%; LETO: +76.7 ± 17.9%; $P < 0.01$), the low dose attenuated ambulatory move time more in OLETF than LETO (-45.1 ± 5.1%; $P < 0.01$, versus -29.3 ± 2.1%; $P < 0.05$). These data indicate that D2Rs in obese OLETF rats are more sensitive than in lean controls with the dose-response effect pointing to the involvement of autoreceptors. Thus, a reduced basal dopamine in the OLETF, due to the lack of CCK-1 receptor stimulation, may contribute to the obese phenotype. Supported by NIH DK065709.

**Martinez no address, co-authors?

Temporal course of the effect of reserpine and adrenal medullectomy on the ingestive behavior, catecholamine content in different tissues, and other metabolic variables.
R. MARTÍNEZ-OLIVARES, M. PIÑON, R. RACOTTA.
Escuela Nacional de Ciencias Biológicas. I.P.N., Mexico D.F. 11340.
Intraperitoneal (ip) administration of adrenaline (ADR) produces hypophagia, which suggests the participation of endogenous catecholamines (CA) and the porto-hepatic region in preabsortive satiety (satiation). The CA sources for the tissues are the sympathetic endings and secretory non-neuronal cells. In the present work we used non-specific chemical sympathectomy induced by reserpine (R) to identify the role of the catecholaminergic activity in satiation. R effects on tissue CA concentrations, daily food intake, boby weight, and ingestive response to ADR i.p. in rats after excision of their adrenal-medulla (AMx) were determined. Additionally, the temporal evaluation of R and AMx effect on the oxygen consumption (VO_2) and respiratory quotient in response to cold temperature was made. R-treatment significantly depleted tissue CA concentrations but increased temporally the adrenal ADR synthesis. AMx did not modify the CA depleting effects of R. R-treatment decreased temporally the daily food intake and produced loss of body weight without participation of AMx. In R-treated rats, the ADR-induced hypophagia was increased with some participation of adrenal CA in the ingestive reflex. R-treatment increased the VO_2 in response to cold. The results indicate that the R-induced CA deficit increased temporally the sensibility or the number of beta-adrenoreceptors related with the increment of CA-induced hypophagia and facultative thermogenesis. This sympathetic activity could be important to the peripheral metabolic information that should be integrated to express feeding behavior. R. Martínez-Olivares is fellow of CONACYT and PIFI, IPN. R. Racotta is fellow of DEDICT-COFAA, IPN.

Energy density of a supplemental food affects caloric homeostasis in rats.
C.M. MATHES, N.E. ROWLAND.
Department of Psychology, University of Florida, Gainesville, FL 32611-2250, USA.
The purpose of these studies is to examine the role of energy density in a treat or snack on caloric regulation in rats. This model is analogous to snacking or binging in humans and so may be of relevance to human obesity. We used a 'dessert protocol' that enables us to assess the effect of freely available supplemental calorie sources in conjunction with standard maintenance diet on the distribution and overall caloric intake in rats. We presented adult female Sprague Dawley rats with uninterrupted 8 h nocturnal access to a dessert of either high or low caloric density. The rats were allowed to eat as much or as little dessert and chow as they chose in that period. When presented with a sugar gel of low caloric density (0.31 kcal/g), rats overcompensated for calories eaten from gel by reducing chow intake, subsequently consuming fewer calories than baseline and losing weight. However, when presented with a sugary fat whip of high caloric density (7.35 kcal/g), rats consumed a large proportion of calories from dessert and failed to adequately reduce chow intake, thus increasing overall intake and gaining weight. Our data show that the ability of female rats to appropriately balance dessert and chow intake is an effect of the caloric density of the dessert with which they are presented. The caloric density of snack foods may play a large role in meal size, caloric regulation, and weight change as demonstrated in human populations (e.g. de Castro JM, *J. Nutr.* 2004;134:335-341).

Comparison of binge-like behavior in rats with limited access to Crisco or nutritionally complete high fat.

S.J. MELHORN, J.U. HEIMAN, A.D. STRADER, D.J. CLEGG, S.C. BENOIT.
University of Cincinnati, Department of Psychiatry, Cincinnati, OH 45237, USA.

Previous research suggests that limited access (e.g., 2 hr access every 3 days) to a palatable diet can result in excessive intake or a 'binge' of that diet. Here, we examined consequences of 'binging' on two different palatable diets. Rats were maintained on ad-libitum chow and given limited access to either a nutritionally complete high fat diet (HF) or to Crisco. Forty-two male LE rats were divided into five groups: 1) Chow only (Con), 2) Crisco-everyday (CRE), 3) Crisco every 3 days (CR3), 4) High Fat everyday (HFE), and 5) High Fat every 3 days (HF3). Rats were housed in a 12 hr LD cycle and given access to HF or Crisco for 2 hr in the middle of the light. Total caloric intake over 24 hr revealed a binge/compensate pattern in groups CR3 and HF3. These groups had increased total intake on "binge" days followed by decreased total caloric intake on subsequent days. Unexpectedly, neither CR3 nor HF3 groups exhibited increased intake of the "binge" diet relative to groups CRE and HFE. Furthermore, neither cumulative food intake nor body weight was significantly different between rats consuming the HF or Crisco every day and rats with access every third day. Predictably, rats that consumed Crisco had significantly reduced post-prandial blood glucose, relative to rats consuming HF diet. These data suggest that Crisco and HF diet yield similar effects on "binge" behavior in rats, though an apparent "binge" may not be due to the expected increased intake of the palatable diet.

Estradiol modulates the orexigenic and dipsogenic effects of MCH in ovariectomized rats.

M.M. MESSINA[a,c], G. BOERSMA[a,c], J.M. OVERTON[b,c], L.A. ECKEL[a,c].
[a]Departments of Psychology, [b]Nutrition, Food and Exercise Sciences, [c]Program in Neuroscience, Florida State University, Tallahassee, FL 32306, USA.

Melanin-concentrating hormone (MCH) is an orexigenic, hypothalamic neuropeptide that is also implicated in the control of water intake (WI) in male rats. Here, we determined the orexigenic and/or dipsogenic effects of MCH in ovariectomized rats treated with estradiol benzoate (EB) or oil. First, we assessed dark-phase food intake (FI) and WI for 4 h after lateral ventricular infusion of 5 µg MCH or 2.5 µl saline, administered 30 min prior to dark onset. In oil-treated rats, MCH increased 2 h and 4 h FI. In EB-treated rats, MCH increased 4 h, but not 2 h, FI indicating that EB delays, but does not prevent, the orexigenic effect of MCH. EB also decreased the orexigenic strength of MCH; at 4 h, the increase in FI following MCH was greater in oil-treated rats, compared to EB-treated rats. In contrast, WI was not increased by MCH. In fact, at 2 h and 4 h following MCH infusion, the ratio of WI to FI was suppressed in both oil- and EB-treated rats. Next, we assessed light-phase WI, in the absence and then presence of food, for 4 h after 5 µg MCH or 2.5 µl saline infusion, administered 30 min prior to the drinking test. Immediately following infusions, food was removed and then returned 2 h later. In oil- and EB-treated rats, MCH failed to increase light-phase WI either in the absence or presence of food. We conclude that EB attenuates the orexigenic effect of MCH in ovariectomized rats and, unlike male rats, MCH fails to induce a dipsogenic effect in female rats. Supported by MH63932.

Effects of central and peripheral administration of apelin on food intake, water intake, and blood pressure.

A. MITRA, J. GROBE, M.J. KATOVICH, N.E. ROWLAND.
Departments of Psychology & Pharmacodynamics, University of Florida, Gainesville, FL 32611, USA.
Apelin is the endogenous ligand for the orphan APJ receptor. Cleavage of a precursor, preproapelin, produces four known active fragments, Apelin-12, 13, 17, and 36. Apelin and the APJR are found in forebrain regions implicated in body fluid regulation. ICV injection of Apelin-13 has been reported to produce a robust water intake in sated rats (Taheri et al., *Biochem. Biophys. Res. Comm.* 2002;291:1208-1212) and Apelin-12 decreased nocturnal food intake (O'Shea et al., *Nutr. Neurosci.* 2003;6:163-167). There have been mixed reports concerning blood pressure. The present studies were designed to confirm and extend some of these observations. In our first study, we found that lateral ICV injections of Apelin-13 did not stimulate water intake in male Sprague-Dawley rats at doses reported effective by Taheri et al. We found a similar result using third ventricular injections. We also showed that these injections produced only modest increase in Fos-ir in PVN and SON, and none in the circumventricular organs. We then investigated the effect of peripheral injection of Apelin-13 on 24-hr food and water intake in male and female rats. We found a small but consistent reduction in food intake in males, and a small increase in water intake in females. In rats equipped with carotid catheters for direct blood pressure recording, we found that peripheral administration of either Apelin-12 or 13 fragments caused a dose-related decrease in arterial pressure in anesthetized animals. In conscious rats, administration of Apelin-13 was also found to cause a decrease in pressure.

High fat diets and hepatic 11 ß hydroxysteroid dehydrogenase-1 in Long-Evans male rats.

J. MOORE[a], E.Z. PARSONS[a], M. HARDY[b], L.M. BROWN[c], D. CLEGG[c], T.W. CASTONGUAY[a].
[a]*Department of Nutrition and Food Science, University of Maryland, College Park, MD 20742, USA;* [b]*The Population Council, New York, NY, USA;* [c]*Obesity Research Center, Department of Psychiatry, University of Cincinnati School of Medicine, Cincinnati, OH 45237, USA.*
11ß hydroxysteroid dehydrogenase-1 (11ß HSD-1) plays an integral role in the control of intracellular glucocorticoids in both liver and adipose tissue. Adipose tissue 11ß HSD-1 message is elevated in obese humans and rats. Curiously, hepatic 11ß HSD-1 message is reportedly low in obese Zucker rats. The present study determined both message and protein of 11ß HSD-1 in the livers of 21 Long Evans rats fed one of seven diets: 3 high fat diets, 3 low fat diets, or standard chow. Either butter or corn oil or olive oil was used as the source of fat. Each rat was maintained on one of these diets for 10 weeks, after which it was sacrificed, exsaguinated, and their liver was dissected and frozen. Total RNA was extracted and used to make liver cDNA templates that were used to amplify message by PCR in duplicate. Photos were analyzed by densitometry. 11ß HSD-1 / ß Actin ratios were calculated, and differences between dietary groups were compared. 11ß HSD-1 message was lowest in the low fat Olive Oil group. It was highest in rats fed either chow or HF Olive Oil diets. Similarly, 11ß HSD-1 protein was lowest in the LF Olive Oil group. It was highest in rats fed either chow, HF Olive Oil or LF Corn Oil diets. The correlation between message and protein varied widely between dietary groups. The importance of measuring both message and protein in developing an understanding of the role of 11ß HSD-1 in obesity will be discussed.

Caffeine pre-exposure, food deprivation, and the aversive conditioning effects of caffeine in rats.

K.P. MYERS.
Department of Psychology, Bucknell University, Lewisburg, PA 17837, USA.

Some inconsistencies exist in the literature describing the aversive/reinforcing effects of caffeine in rats, measured by learned avoidance or preference for a caffeine-paired flavor cue. Rats typically avoid flavors that have been paired with caffeine, but there is some evidence that caffeine can condition flavor preference (Fedorchak, et al., *Behav. Neurosci*. 2002;116:334-346). It is also unclear how significantly rats' prior caffeine exposure mediates its aversive/reinforcing effects, despite clear evidence that caffeine consumption history mediates these effects in humans (Tinley, et al., *Psychopharm*. 2003;166:416-423, and *Physiol. Behav*. 2004;82:317-324). In the present research, food-restricted, caffeine-naive rats were trained on alternating days with two differently-flavored palatable solutions – one containing caffeine, the other without caffeine. Rats decreased intake of the caffeine-flavor solution over days, but not the no-caffeine-flavor solution. In a choice between the flavors (without caffeine) they avoided the flavor previously paired with caffeine. Following several days of consuming large amounts of caffeinated water, rats were re-trained with new caffeine-paired and non-paired flavors. Their avoidance of the caffeine-paired flavor was significantly weaker, indicating some effect of caffeine consumption history. In a third experiment, conditioning occurred daily following chow rations, rather than prior to rations. Rats now neither avoided nor preferred the caffeine-paired flavor, suggesting caffeine's effects may differ with food deprivation. The effects of food deprivation state on caffeine conditioning were replicated in an additional experiment using between-groups design (daily training before or after chow rations) in naive rats, indicating separate effects of food restriction and prior caffeine consumption history.

Amylin's inhibitory effect on food intake is not due to visceral malaise in rats.

S. NAEVE, D.G. PARKES, K.D. LAUGERO.
Amylin Pharmaceuticals, Inc., San Diego, CA 92121, USA.

The pancreatic β-cell peptide hormone, amylin, inhibits feeding in animals, and the human amylin analog, pramlintide, decreases food intake in humans. To determine if this action is due to malaise, we tested in male, Sprague-Dawley® rats for effects of amylin (1 – 300 μg/kg, i.p.) on kaolin ingestion, an index of visceral malaise in rodents. In parallel, we studied the effects of salmon calcitonin (sCT), a potent amylin agonist, on kaolin ingestion. The chemotherapeutic and emetic cisplatin was used as a positive control to induce malaise. Food intake was determined at 2 and 24 hours after injection, and kaolin intake was determined 24 hours after injection. Amylin (10 – 300 μg/kg) reduced chow intake below vehicle by 60 – 80% at 2 hours after injection ($P < 0.05$), but did not stimulate kaolin intake ($P > 0.05$). Of the amylin treatments, only the 300 μg/kg dose of the peptide suppressed food intake (16% below vehicle) at 24 hours after injection ($P < 0.05$). sCT (1 – 100 μg/kg) suppressed feeding at 2 hours post injection (43 – 83% below vehicle; $P < 0.05$), and 10 and 100 μg/kg doses of the peptide suppressed food intake at 24 hours after injection (57 – 76% below vehicle; $P < 0.01$). sCT did not stimulate kaolin ingestion ($P > 0.05$). Cisplatin (3 mg/kg) reduced chow intake below vehicle by 64% at 24 hours after injection ($P < 0.05$), and also increased kaolin ingestion up to 20 X that of vehicle ($P < 0.05$). While malaise might contribute to the anorexigenic actions of cisplatin, amylin's inhibitory effect on feeding may be specifically related to satiety, and not to malaise.

Persistence of food reinforcement after a caloric preload in women is correlated with binge eating score and hunger in the fasted state.

J.A. NASSER, A. GELIEBTER, F.X. PI-SUNYER.
New York Obesity Research Center, Department of Medicine, St. Luke's-Roosevelt Hospital Center, New York, NY 10025, USA.

Food reinforced operant task performance is reported to be dependent on food deprivation state. However, we have observed a relationship between binge eating tendency (BES) and operant task performance (FBP) that persists after caloric feeding. A non-clinical sample of 6 women with BES ranging from 0 - 21 consumed 600 ml of flavored water or 600 kcal of a liquid mix meal after 2 hours of food deprivation, and rated their hunger before and after each preload. The FBPs after the two preloads were significantly correlated with each other ($r = 0.92$, $P = 0.026$). In addition, FBPs (water and mixed meal respectively) correlated with BES scores ($r = 0.84$, $P = 0.034$; $r = 0.91$, $P = 0.012$), as well as with prefeeding hunger ratings ($r = 0.86$, $P = 0.07$; $r = 0.93$, $P < 0.001$). There was no correlation of FBPs with post feeding hunger score ($r = 0.65$, $P = 0.24$). Also of interest was the correlation of prefeeding hunger scores with BES ($r = 0.89$, $P = 0.018$; $r = 0.82$, $P = 0.047$; water and mixed meal respectively). In conclusion, food-reinforced operant task performance persists after caloric feeding in relation to BES, and prefeeding hunger ratings may represent a combination of physiological and psychological desires.

Stimulation of hindbrain and hypothalamic receptors with prostaglandin E_2 triggers thermal and feeding responses.

K.M. NAUTIYAL, J.M. KAPLAN, H.J. GRILL.
Psychology and Neuroscience, University of Pennsylvania, Philadelphia, PA 19104, USA.

The LPS treatment cascade results in production of PGE_2 which in turn acts on brain EP receptors to trigger effector circuits for feeding and thermal responses. Hypothalamic nuclei express EP-Rs that are hypothesized to mediate the observed febrile and anorexic responses. These receptors, however, are widely distributed including representation in dorsal medulla. We pursue the hypothesis that hypothalamic as well as hindbrain EP-Rs can trigger both responses through delivery of PGE_2 to the 4th v. and to the 3rd v. with and without aqueduct occlusion. 4th icv delivery in the light phase yields a robust, short-latency hyperthermia (BAT_T; $Core_T$) that peaks at 30 minutes with baseline temperatures restored by 2 h. The response is dose-related (0.01 to 2 μg) and, interestingly, stable with repeated dosing (no tolerance). 3rd icv delivery of 2 μg evokes a response of the same character as that observed for this dose in the 4th v. and thereby suggests that a comparable febrile response is driven by EP-Rs accessed by the two ventricles. (Dose-response and aqueduct occlusion experiments are in progress.) Markedly different anorexic responses to PGE_2 stimulation are observed from the two sites. 4th icv delivery (5 μg) triggers an anorexia first observed at 3 h. The latency of the anorexia is shorter (1 h) and the intake suppression greater (3 h) when the same dose is delivered to the 3rd ventricle. The data described are consistent with the hypothesis that the febrile and feeding responses to PGE_2 can be driven by stimulation of disparate receptor populations. Supported by DK-21397.

Energy label on preload does not affect subsequent test meal size.

L.J. NOLAN, J. FERRERI.
Department of Psychology, Wagner College, Staten Island, New York 10301, USA.

Several studies indicate that food label information about calories and macronutrient content affects food intake. For example, Caputo & Mattes (*Int. J. Obesity* 1993;17:237-240) found that participants consumed more when a food was labeled "low fat." Restrained eaters in particular have been shown to eat more snacks when told they are low fat (Miller et al., *Am. J. Clin. Nutr.* 1998;68(2):282-90). In the present study, we examined whether a label denoting the caloric content of a preload (42 g granola bar served in a clear plastic bag with a white printed label) would influence the amount of a test meal (500 g macaroni and cheese) consumed 20 minutes after consumption of the preload. 50 (mean age = 19.63 years; mean BMI 24.62) participants (restrained and unrestrained) were given the same foods to consume but were randomly assigned to receive one of two labels on the preload: one group (N = 24) was given a label that read "Fat Free, 90 Calories" and the other group's (N = 26) label read "6 grams of fat, 180 Calories." Participants' BMI, TFEQ score, hunger and fullness (and other) ratings were recorded. Participants were identified as restrained or nonrestrained and as normal weight, overweight or obese. A three-way ANOVA (label X restraint X BMI) revealed no main effects or interactions on test meal intake. Men ate significantly more (mean = 313.72 g, SEM = 33.75) than women (mean = 228.54 g, SEM = 17.80) but there was no sex X label interaction. It appears that preload caloric labels do not affect subsequent test meal intake.

The effect of relaxation on food consumption in stressed emotional eaters.

L.J. NOLAN, L.B. HALPERIN, M.J. BEACH, J. BUDDENSICK.
Department of Psychology, Wagner College, Staten Island, New York 10301, USA.

Emotional eaters increase food consumption when experiencing positive and negative emotions including stress (Lindeman & Stark, *Eating Disorders* 2001;9:251-259). Relaxation techniques such as listening to music have been shown to reduce stress (Scheufele, *J. Behav. Med.* 2000;23:207-28). In the present study, we stressed emotional eaters in the laboratory by asking them to prepare a speech on habits they did not like about themselves (a procedure that has been shown to be a significant short term stressor; Oliver et al., *Psychosom. Med.* 2000;62:853-65). After completing questionnaires (EMAQ, DEBQ) and preparing a speech, participants (men and women) were randomly assigned to one of three experimental groups (10 min of classical music, 10 min of silence, or neither) and the amount of snack foods (cookies, chocolate candies and pretzels) they consumed during an afternoon snack was measured. BMI, how long since the last meal also measured. Of 48 participants tested, 40 met the criterion for emotional eating. Preliminary results (one-way ANOVA) indicate that participants in the music condition ate less than those in the other conditions. Results suggest that use of relaxation technique may reduce intake in emotional eaters in stressful situations.

Influence of gender and corpulence on sodium depletion in Zucker rats.

S.T. OMOUESSI[a], M. LESHEM[b], S.N. THORNTON[a].
[a]EA 3453 SNCI, Université Henri Poincaré, Nancy, France. [b]Department of Psychology & Brain and Behavior Center, University of Haifa, Israel.

The Zucker obese rat is an important model for the metabolic syndrome, obesity-associated insulin resistance, vascular impairments, salt-sensitivity, and associated cardiovascular disease. Sodium restriction is one therapeutic approach, but animal research has shown that repeated restriction of sodium can actually enhance spontaneous sodium intake. Here we investigate sodium appetite and sodium depletion in a rat model of obesity, the Zucker rat. Despite their greater body weight, obese rats ingested less sodium than leans, and male rats

less than females. Relative to their increased body weight, obese Zuckers also drank less water, lost more dilute urine, and lost more sodium. These findings indicate that the obese are less able to regulate sodium and water in response to challenge. We also find that Zucker females have a greater predilection for sodium than their males, and are also better at conserving it. All these responses are enhanced when sodium depletion is repeated, suggesting that repeated sodium depletion sensitizes the rat's responses.

Bizarre food concocting as a feature in anorexia and bulimia nervosa but not binge-eating disorder: dieting versus stress as triggers.

K.D. OSWALD[a], E. SHUMAN[b], C.R. MALDONADO[c], A.I. ARTIGA[a], M.M. BOGGIANO[a].
[a]*Department of Psychology, University of Alabama at Birmingham, Birmingham, AL 35294-1170, USA;* [b]*WellCentered, Inc., Cincinnati, OH, USA;* [c]*Department of Psychology, University of Texas at El Paso, TX, USA.*

The semistarvation literature is rife with accounts of bizarre mixing of food ingredients but this behavior has not been examined closely in eating disorder populations. N = 307 adult men and women were classified as healthy controls, anorexic (AN), bulimic (BN), or binge-eating disorder (BED) on the basis of strict DSM-IV-R criteria and responded to a detailed questionnaire on strange food-mixing (concocting) behavior, a dietary restraint scale (DEBQ-R), and questions regarding affect surrounding their eating habits. As expected from semistarvation accounts, ANs and BNs, who scored higher on dietary restraint than BEDs and controls ($P < 0.001$), also concocted more frequently than these groups ($P < 0.001$). Dieting was associated with use of cereals, bread, and peanut butter in concoctions. Out of multiple emotions and reasons precipitating a binge, stress and shame accounted for the widest use of ingredients in concoctions, while loneliness and depression were associated only with the use of chocolate. Among ANs and BNs refined carbohydrates (e.g., cereal, bread) and chocolate, both quick sources of energy, were most often used to concoct. Controls reported using salty snacks most often, which may reflect normalcy even in subjective "strange" mixing because these foods are often used with other foods in social events. Concocting frequency was positively associated with increased engagement in other semistarvation-associated chaotic-eating behaviors, negative affect, increased attempts to restrain binge-eating, and more consequences as a result of binge-eating. Concocting in BN and AN may be a symptom of severe dietary restraint and may contribute to worsening psychopathology if not addressed openly.

Motivational trades-off in food and drug addiction.

M.L. PELCHAT[a], A.R. CHILDRESS[b], J. VALDEZ[b], C. BYKOWSKI[a], J.D. RAGLAND[b].
[a]*Monell Chemical Senses Center, Philadelphia, PA 19104, USA;* [b]*University of Pennsylvania, Philadelphia, PA 19104, USA.*

Although there is evidence for common brain mechanisms for all types of cravings, it is unclear how abstinence from cocaine affects responses to natural rewards such as food. We predicted that in abstinent cocaine abusers, food cravings would be stronger and more common than in controls. A food craving questionnaire was administered to 21 male abstinent cocaine addicts and 33 healthy males. Ninety-five per cent of addicts reported food cravings in the past year as compared with 67% of controls (Fisher's exact test, $P = 0.0175$). So, abstinent addicts were more likely to express food cravings. In an fMRI study of food cravings in abstinent cocaine addicts, the pattern of patient activation was similar to that in healthy subjects. As previously, activation accompanying food craving was seen unilaterally

in the fusiform gyrus, the amygdala and parahippocampal gyrus, thalamus, caudate nucleus, and middle frontal gyrus. In contrast, patients showed bilateral rather than left hemispheric activation in most regions. Patients also produced activation in several additional regions. Thus, there may be a greater spatial extent of craving-related fMRI activation in patients and this is also consistent with the notion of greater food craving in patients. These results bolster the argument that drug addiction may alter the response natural rewards. Although, alternatively, the increased frequency of food cravings in the addicted sample may be the result of pre-existing individual differences. Funded, in part, under a grant with the Pennsylvania Department of Health. The Department specifically disclaims responsibility for any analyses, interpretations or conclusions.

Amygdalar and prefrontal pathways to the lateral hypothalamus are activated by a learned cue that stimulates eating in sated rats.

G.D. PETROVICH, P.C. HOLLAND, M. GALLAGHER.
Department of Psychological and Brain Sciences, Johns Hopkins University, 3400 N. Charles St., Baltimore, MD 21218, USA.

Experimental animals that are trained to associate a cue with food consumption when hunger prevails will subsequently consume a greater amount of food when that cue is presented under conditions of satiety. This phenomenon of conditioned potentiation of feeding is abolished by neurotoxic lesions restricted to the basolateral region of the amygdala (BLA), and by disconnection of the BLA and lateral hypothalamus (LHA). Here we combined immediate early gene (IEG) and tract tracing methods to map functional BLA-LHA circuitry that is engaged when potentiated feeding is produced by Pavlovian conditioning. Sated rats were assessed for food consumption in the presence of a cue that was previously paired with food (CS+), or in the presence of another cue that was never paired with food (CS-), in two consecutive tests temporally arranged for activation of effector IEGs, Arc and Homer 1a. We examined the selective induction of the IEGs by tests with CS+ or CS- presentations in BLA neurons that project to LHA, as identified with a retrograde tracer. We also examined neurons in several other brain regions (the prefrontal cortex, central amygdalar nucleus and nucleus accumbens) that receive strong inputs from the BLA and, in turn, innervate the LHA. Our results indicate that a learned cue, which promotes eating in sated rats (CS+), activates a functional network formed by direct pathways from the BLA and orbitomedial prefrontal cortex to the LHA.

Twenty-four hour food intake is reduced following muscarinic receptor antagonism of the nucleus accumbens or anterior dorsal striatum.

W.E. PRATT, A.E. KELLEY.
Department of Psychiatry, University of Wisconsin, Madison, WI 53719, USA.

Recent electrophysiological, lesion, and behavioral pharmacology experiments have implicated the striatal acetylcholine interneuron as an important mediator of rewarding stimuli. We have previously demonstrated that nucleus accumbens muscarinic (but not nicotinic) receptor activation is required for the learning and performance of an instrumental response for food reward, and that this was the result of reduced motivation for the sucrose pellet. In order to examine whether muscarinic receptor blockade within the anterior striatum has long-term consequences on food intake, we injected rats with a single dose of 0, 5, or 10 micrograms (in 0.5 microliters saline) scopolamine bilaterally into the nucleus accumbens or anterior dorsal striatum. All drug treatment groups significantly and dramatically reduced

their subsequent 24-hour food intake compared to controls. The brains of the control and high dose drug group were then prepared for semi-quantitative in situ hybridization targeting preproenkephalin (PPE) and prodynorphin (PD). Twenty-four hours following treatment, drug treated animals showed significant trends for PPE downregulation across multiple striatal regions. The anterior dorsal group also showed PD upregulation in anterior dorsal striatal regions following muscarinic receptor blockade. As the activation of striatal mu-opioid receptors has been shown to increase food intake, it is possible that scopolamine-induced hypophagia is the result of its effects on opioid mRNA expression within medium spiny neurons. Supported by NIDA DA09311 & DA04788.

Mechanisms of oleoylethanolamide (OEA)-induced changes in feeding behavior and motor activity.

K. PROULX, D. COTA, T.R. CASTANEDA, M.H. TSCHOP, D.A. D'ALESSIO, P. TSO, S.C. WOODS, R.J. SEELEY.
Department of Neuroscience, University of Cincinnati, 2170 East Galbraith Road, Cincinnati, OH 45237, USA.

Oleoylethanolamide (OEA), a lipid synthesized in the intestine, reduces food intake and stimulates lipolysis through peroxisome proliferator-activated receptor-alpha (PPAR-α). OEA also activates transient receptor potential vanilloid type 1 (TRPV1) in vitro. Because the anorexigenic effect of OEA is associated with delayed feeding onset and reduced locomotion, we examined whether i.p. administration of OEA results in non-specific behavioral effects that contribute to the anorexia. Moreover, we determined whether circulating levels of other gut hormones are modulated by OEA, and whether cholecystokinin (CCK) is involved in OEA-induced anorexia. We found that OEA reduced food intake without causing a conditioned taste aversion or reducing sodium appetite. However, OEA induced changes in posture and reduced spontaneous activity in the open-field. This likely underlies the reduced heat expenditure and sodium consumption observed after OEA injection, which disappeared within 1 hour. The effects of OEA on motor activity were similar to those of the TRPV1 agonist capsaicin, and were also observed with the PPAR-α agonist Wy-14643. Plasma levels of ghrelin, peptide YY (PYY), glucagon-like peptide 1 (GLP-1) and apolipoprotein A-IV (apo A-IV) were not changed by OEA. Finally, antagonism of CCK-1 receptors did not affect OEA-induced anorexia. These results suggest that OEA suppresses feeding without causing visceral illness, and that neither ghrelin, PYY, GLP-1, apo A-IV nor CCK play a critical role in this effect. Despite that OEA-induced anorexia is unlikely to be a due to impaired motor activity, our data raise a cautionary note in how specific behavioral and metabolic effects of OEA should be interpreted.

Daily, intermittent intravenous infusions of peptide YY(3-36) decrease daily food intake and body weight gain in rats.

R.D. REIDELBERGER, A.C. HAVER, P.K. CHELIKANI.
VA-Nebraska Western Iowa Health Care Ssystem, Omaha, NE 68105, USA.

PYY(3-36) is postulated to act as a hormonal signal from intestine to brain to inhibit food intake. We determined the effects of daily, intermittent i.v. infusions of PYY(3-36) on food intake and body weight in rats tethered via infusion swivels to computer-controlled pumps. Study-1: Two groups of 15 rats received 2, 3-h infusions of vehicle during hours 1-3 and 7-9 of the dark period each day for 3 days, followed by vehicle or PYY(3-36) at 50 pmol/kg/min during the same periods for 7 days. Food intake was determined from continuous computer

recordings of changes in food bowl weight. PYY(3-36) significantly reduced 17-h food intake each day for the first 6 days by 14, 18, 17, 19, 13, and 13%, respectively, and reduced body weight gain across the 7-d period from 5.0 ± 2.0 to 0.2 ± 1.6 g. No desensitization occurred across PYY(3-36) infusion periods; however, rats became hyperphagic between PYY(3-36) infusions. Study-2: Two groups of 15 rats received 1-h vehicle infusions every other hour for 1-week, followed by 1-h infusions of vehicle or PYY(3-36) at 50 pmol/kg/min every other hour for 10 days. PYY(3-36) reduced food intake each day by 31, 20, 24, 21, 25, 17, 19, 16, 15 and 23%, respectively, and reduced body weight gain across the 7-d period from 12.9 ± 1.9 to -1.9 ± 3.1 g. Thus, daily, intermittent i.v. infusions of PYY(3-36) can reduce daily food intake and body weight gain without producing desensitization. Supported by Department of Veterans Affairs and NIH grant DK55830.

Ghrelin is an orexigenic signaling molecule with anxiogenic activity in discrete regions of the hypothalamus.

E.M. RIGSBEE, C.D. COIRO, T.P. SWANN-STERNBERG, E. FREEMAN-DANIELS, S. ANOLIK, K. HINCHCLIFF, A. PANDOLFI, P.J. CURRIE.
Department of Psychology, Barnard College, Columbia University, New York, NY 10027, USA.

Ghrelin, an endogenous ligand of the growth hormone secretagogue receptor (GHS-R), is a 28 amino acid acylated peptide recently identified in the rat stomach. Gene expression in the stomach is increased by tail pinch stress and by starvation. We have previously reported that injections of ghrelin into the arcuate and paraventricular nuclei stimulate eating and alter energy substrate utilization and energy expenditure. These effects are blocked by urocortin pretreatment. Recent evidence suggests that peripherally administered ghrelin significantly increases corticoptropin releasing hormone (CRH) mRNA and increases serum corticosterone, while ventricular treatment induces anxiety-like behaviors in the rat. In the present study we assessed the orexigenic and anxiogenic action of ghrelin following microinjection into the arcuate nucleus (Arc), paraventricular nucleus (PVN), perifornical hypothalamus (PFH) and the ventromedial nucleus (VMN). To assess ghrelin's role in anxiogenic behavior, separate groups of rats were injected with vehicle, 50 pmol or 200 pmol and then placed in an elevated plus maze for 10 min. Each test was performed as a single trial per animal. PVN and PFH ghrelin treatment significantly decreased the number of entries and time spent in the open arms of the maze. In separate testing, injection of the peptide into all hypothalamic areas significantly increased food intake over 2 h. These findings are consistent with the argument that ghrelin mediates neuroendocrine and behavioral responses to stress in addition to its role as a hypothalamic orexigenic peptide.

Dehydration anorexia is attenuated in oxytocin deficient mice.

L. RINAMAN, R.R. VOLLMER, J. KARAM, D. PHILLIPS, X. LI, J.A. AMICO.
Departments of Neuroscience, Pharmaceutical Sciences, and Medicine, University of Pittsburgh, Pittsburgh, PA 15260, USA.

Evidence in rats suggests that central oxytocin (OT) signaling pathways contribute to suppression of food intake during dehydration (i.e., dehydration anorexia). The present study examined water deprivation-induced dehydration anorexia in wild type and OT -/- mice. Mice were deprived of food alone (fasted, euhydrated) or were deprived of both food and water (fasted, dehydrated) for 18 hr overnight. Fasted wild type mice consumed significantly less chow during a 60 min refeeding period when dehydrated compared to their intake when

euhydrated. Conversely, fasting-induced food intake was slightly but not significantly suppressed by dehydration in OT -/- mice, evidence for attenuated dehydration anorexia. In a separate experiment, mice were deprived of water (but not food) overnight for 18 hr, then were anesthetized and perfused with fixative for immunocytochemical analysis of central Fos expression. Fos was elevated similarly in osmo- and volume-sensitive regions of the basal forebrain and hypothalamus in wild type and OT -/- mice after water deprivation. OT-positive neurons expressed Fos in dehydrated wild type mice, and vasopressin-positive neurons were activated to a similar extent in wild type and OT -/- mice. Conversely, significantly fewer neurons within the hindbrain dorsal vagal complex were activated in OT -/- mice after water deprivation compared to activation in wild type mice. These findings support the view that OT-containing projections from the hypothalamus to the hindbrain are necessary for the full expression of compensatory behavioral and physiological responses to dehydration.

Estradiol's inhibitory effect on food intake is attenuated by antagonism of central, but not peripheral, estrogen receptors.

H.M. RIVERA, G. BOERSMA, L.A. ECKEL.
Program in Neuroscience, Florida State University, Tallahassee, FL 32306, USA.

The relative contribution of peripheral versus central estrogen receptors (ERs) to estradiol's inhibitory effect on food intake is unclear. Here, we addressed this issue by examining food intake following treatment with ICI-182,780, a pure antiestrogen that does not cross the blood brain barrier. In Experiment 1, food intake was assessed following subcutaneous administration of 0.5 mg ICI-182,780 or vehicle in ovariectomized rats treated with 2 µg estradiol benzoate (EB) or oil. Peripheral administration of ICI-182,780 alone did not influence 24 h food intake in oil-treated rats (ICI/OIL: 26.1 ± 1.2 g versus VEH/OIL: 26.7 ± 1.3 g) and, when given in combination with EB, it failed to attenuate EB's inhibitory effect on 24 h food intake (e.g., ICI/EB: 22.9 ± 1.4 g versus VEH/EB: 23.2 ± 1.8 g). We are confident that adequate peripheral blockade of ERs was achieved as ICI-182,780 blocked EB's uterotrophic effect. Because peripheral blockade of ERs failed to attenuate EB's inhibitory effect on food intake, our data suggest that this action of EB is mediated centrally. Thus, in Experiment 2, 24 h food intake was assessed following lateral ventricular administration of 10 nM ICI-182,780 or vehicle in ovariectomized rats treated with 2 µg EB or oil. Preliminary data indicate that central administration of this dose of ICI-182,780 attenuates EB's inhibitory effect on food intake (ICI/EB: 26.5 ± 1.9 g versus VEH/EB: 19.5 ± 0.6 g). We conclude that estradiol inhibits food intake largely via a central, rather than peripheral, mechanism. Supported by MH63932 and DC000044.

Dissociation of acute food intake and locomotor activity effects in rats after peripheral treatment with rat amylin.

J. ROAN, J. WILSON, D. PARKES, C. MACK.
Amylin Pharmaceuticals, San Diego, CA 92121, USA.

Amylin is a ß-cell hormone that reduces food intake in rodents. To help dissociate mechanistic (effects of energy balance pathways) versus locomotor effects, which can produce reductions in food intake, the current experiments compared the effects of amylin on acute food intake and locomotor activity in rats (average weight = 400 - 500 g, n = 5 - 11/group). 30 min food intake was measured in overnight fasted rats following a single intraperitoneal (IP) injection of amylin (1, 10 or 100 µg/kg). A second group of rats was administered amylin i.p. at identical doses, and spontaneous locomotor activity monitored for

30 min. The effects of sibutramine and phentermine, as well as cisplatin (an emetic agent)and the benzodiazepine lorazepam, were also examined. Compared to controls, amylin reduced food intake ($P < 0.05$ at 10 and 100 μg/kg, maximal suppression = 47%) but had no effect on locomotor activity. Sibutramine reduced food intake ($P < 0.05$ at 1.5 and 3 mg/kg, maximal suppression = 96%); at 1.5 and 3 mg/kg, small but significant reductions in locomotor activity were observed (24% and 18% respectively, *P's* < 0.05). Phentermine, while decreasing food intake ($P < 0.05$ at 1, 2.5 and 5 mg/kg, maximal suppression = 99%), increased locomotor activity ($P < 0.05$ at 2.5 and 5 mg). Cisplatin reduced food intake ($P < 0.05$ at 1, 3, and 10 mg/kg, maximal suppression = 85%), while suppressing locomotor activity by 49% at 10 mg/kg ($P < 0.05$). Treatment with lorazepam decreased food intake ($P < 0.05$ at 0.25 and 0.5 mg/kg, maximal suppression = 95%) and locomotor activity ($P < 0.05$ at 0.1, 0.25 and 0.5 mg/kg, maximal suppression = 71%). In summary, amylin reduced food intake at doses that do not affect locomotor activity, further supporting a role of this peptide in energy-related appetite suppression.

Diminished food intake in rats during amphetamine-induced acute withdrawal appears to be due to changes in appetitive rather than consummatory processes.

S.L. ROY, W. WHITE.
Psychology Department, Morehead State University, Morehead, KY 40351, USA.

A rebound occurs in a variety of measures (activity, interoceptive cues, temperature, REM sleep) around hour 20 post-amphetamine administration, indicating the presence of an acute withdrawal state at this time. Food intake, however, is diminished both immediately after amphetamine administration and twenty hours later. The purpose of this research was to determine whether the reduction in food intake 20 hours after amphetamine administration was due to a change in appetitive or consummatory processes. Groups of rats were administered different doses of amphetamine at lights on, and at different times subsequent to administration, appetitive and consummatory behavior were assessed. Appetitive behavior was assessed using the progressive ratio procedure. On this procedure, the number of lever presses required to produce access to 0.5 ml of sucrose solution was progressively increased. Breakpoint was assessed 20 hours post-amphetamine treatment (during the rebound) and 25 hours post-treatment (during a putative recovery phase). Consummatory behavior was assessed using a free intake test. Sucrose solution was available for a one hour period during the rebound or during the putative recovery phase. Appetitive behavior was decreased, as indicated by a lowered breakpoint, 20 hours after amphetamine treatment relative to saline treatment. However, consummatory behavior was not decreased at this time, as indicated by the amount of sucrose solution consumed. The diminished food intake during amphetamine-induced acute withdrawal reflects unwillingness to work for reward, but not unwillingness to consume it. The acute withdrawal state appears to modify processes or mechanisms that modulate appetitive rather than consummatory behavior.

DMV and gastric motility effects produced by activation of melanocortin 4 receptor in the rat.

N. SAHIBZADA, M. CRUZ, A. JONES, J. VERBALIS, S. VICINI, R.A. GILLIS.
Departments of Pharmacology, Medicine (Endocrinology) and Physiology, Georgetown University Medical Center, Washington, DC 20057, USA.

Melanocortin 4 receptor (MC4R) activation in the CNS exerts an anorectic action. This receptor is highly expressed in the dorsal motor nucleus of the vagus (DMV) (Kishi et al., *J.*

Comp. Neurol. 2003;457:213-235) and this nucleus is known to influence gastric function. The purpose of our study was to assess what effect activation of MC4R would have on DMV neurons and gastric motility. *In vitro* cell-attached or whole-cell recordings were made from DiI labeled antrum projecting DMV neurons. Bath application of the MC3/4R agonist, MT-II (100 nM) reduced the frequency of action potentials (n = 24; $P < 0.01$) and EPSCs (n = 18, $P < 0.01$). In contrast, exposure to MT-II enhanced the frequency of IPSCs (n = 35, $P < 0.01$). These effects were blocked by the MC4R antagonist SHU9119 (100 nM) (n = 5) and TTX (1 μM). *In vivo* microinjection of MT-II (20 and 50 pmol/30 nl) into the DMV of anesthetized rats while monitoring gastric activity produced an initial, transient increase in intragastric pressure followed by a more prolonged inhibition of gastric motility (n = 10; $P < 0.05$). These effects of MT-II were abolished by ipsilateral vagotomy or administration of atropine methylbromide (0.1 mg/kg, i.v.). Our data indicate that MC4-R stimulation in the DMV reduces spontaneous discharge due to an increase in GABA and a decrease in glutamate release. We suggest that these effects may be responsible for the prolonged decrease in gastric motility observed after microinjection of MT-II into the DMV. We speculate that this decrease in gastric motility could contribute to the anorexic effect of MC4R stimulation.

Cues associated with food deprivation increase subsequent feeding responses in sated rats.

N.M. SANDERS, W. DAUMEN, D.P. FIGLEWICZ LATTEMANN.
VA Puget Sound Health Care System, Seattle, WA 98108, USA.

Many factors contribute to the initiation of food intake. For example, a conditioned cue associated with food will elicit feeding in sated rats. In the present experiment, we tested whether rats exposed to a prior metabolic "experience" of hunger and increased food intake would demonstrate a conditioned feeding response to cues associated with the metabolic experience. Rats (n = 30) were subjected to 3 episodes of 24hr food deprivation followed by re-feeding over 12d; control rats (n = 10) were handled. Prior to re-feeding, rats were injected with saline (conditioned cue; 1 ml/kg, s.c.). One, three or fifteen days after the last food deprivation/re-feeding episode, 3hr food intake in response to a saline injection was assessed. At 1d, rats exhibited a significant increase in food intake relative to controls (6 ± 0.3 versus 1.3 ± 0.20 g, respectively, $P < 0.05$). This elevated feeding response to a saline injection was still present at 3d (5 ± 0.40 g) and 15d (4.5 ± 0.5 g) and was not secondary to an overall energy deficit, since body weight was not different from controls at the time of the feeding tests. Rats did not compensate for the elevated feeding response as 24hr food intake 1d, 3d and 15d after the last food deprivation/re-feeding episode was significantly increased above that in controls (30 ± 1 versus 25 ± 0.73 g (1d), respectively). These findings demonstrate that prior metabolic experience can induce persistent conditioned and uncompensated feeding responses in sated rats.

Development and extinction of reduced sensitivity to CCK in high-fat maintained rats.

D.M. SAVASTANO, M. COVASA.
Department of Nutritional Sciences, College of Health and Human Development, The Pennsylvania State University, University Park, PA 16802, USA.

Adult rats maintained on high-fat (HF) diets exhibit diminished cholecystokinin (CCK)-induced satiation. Here we examined changes in feeding responses to CCK in pups maintained on HF diet. Pups fed isocaloric (3.9 kcal/g) HF or low fat (LF) diets from

postnatal day 25 received i.p. CCK injections beginning on day 7 of diet adaptation. Unlike adult rats, pups were resistant to 0.125 and 0.250 μg/kg CCK by week 2. Compared to LF, HF adapted pups exhibited reduced sensitivity to1.0 μg/kg by week 4 and to 0.5 μg/kg CCK by week 5. We also examined the time course of development and extinction of reduced sensitivity to CCK in adult rats. HF maintained rats displaying diminished response to CCK (0.25 μg/kg) were switched to LF diet while LF maintained rats were switched to HF diet. Sensitivity to CCK (0.25 μg/kg) was tested. Rats previously fed HF diet regained sensitivity to CCK by the end of week 2 on the LF diet while HF rats previously fed LF diet developed reduced sensitivity to CCK by the end of week 1 from diet switch. Similar findings were observed when rats were switched back to their original diets following an 8-week diet maintenance period. These results demonstrate that 1) regardless of diet, pups are less sensitive to doses of CCK known to elicit satiation in adults, 2) diminished sensitivity to CCK in HF fed pups occurs in response to higher doses of CCK compared to adults, and 3) diminished CCK sensitivity in adult rats seems to develop within one week of HF feeding whereas restoration of CCK sensitivity requires a minimum of 2 weeks.

Effects of pinealectomy on food-hoarding behavior in rats.

G. SCALERA.
Dipartimento Scienze Biomediche, Sezione Fisiologia, Universita' di Modena & Reggio Emilia, Via Campi 287, 41100 Modena, Italy.

Four experiments were performed to ascertain whether the pineal gland influences food-hoarding behavior. Twenty-four Sprague-Dawley rats housed individually and maintained under controlled conditions were kept on a 12h:12 h light/dark cycle. During baseline food-hoarding period, rats that hoarded more than 2/3 of available pellets were designed as high hoarding (HH; n = 12); rats hoarding less than 1/3 of pellets were designed as low hoarding (LH; n = 12). In the 1st experiment, all rats were subjected to 24 h continuous light. After 3 weeks, food-hoarding was significantly lower than that of the baseline period, in all rats. In 2nd experiment, 6 HH and 6 LH rats received pinealectomy (HH-Px; LH-Px); 3 HH and 3 LH were sham-operated (HH-S; LH-S); 3 HH and 3 LH were left intact (HH-NS; LH-NS). After 3 weeks, the HH-Px and LH-Px rats decreased significantly the number of pellets hoarded. In the 3rd experiment, rats were implanted subcutaneously with Melatonin-implants (2.7 mg Melatonin/ implant; Melatonin daily release rate: 10 μg/day). After 3 weeks, the food-oarding behavior decreased significantly in HH-Px, HH-S, HH-NS rats, but was almost unchanged in LH-Px, LH-S, LH-NS rats. In the 4th experiment, Melatonin-implants were removed from all rats and after 2 and 3 weeks, food-hoarding increased significantly in HH-S and HH-NS rats, but decreased in HH-Px rats and LH-Px, and it was almost unchanged in LH-S and LH-NS rats. In conclusion, the data here reported confirm the involvement of pineal gland and its hormone (Melatonin) in food-hoarding behavior, in rats.

Age-related obesity: Interventions with gene therapy.

P.J. SCARPACE, N. TUMER.
Department of Pharmacology, University of Florida, GRECC, VA Medical Center, Gainesville, FL 32611, USA.

Obese rats and humans, whether from diet-induced or age-related obesity have elevated leptin and impaired responses to exogenously administered leptin, and are hence considered leptin resistant. To investigate if elevated leptin contributes to leptin resistance or is simply secondary to the consequence of obesity, we chronically elevated central leptin by

recombinant adeno-associated viral mediated leptin (rAAV-leptin) gene delivery in young lean and aged-obese rats. Although there was an initial robust response to leptin gene delivery, lean rats became completely refractory to leptin (gene delivery or endogenous pharmacological administration) independent of obesity. Aged rats demonstrated a more rapid onset of this leptin resistance following leptin gene therapy, and rats of both ages were fully responsive to downstream activation by alpha-melanocyte stimulating hormone (alpha-MSH) agonist, suggesting the leptin resistance lies within the first order hypothalamic neurons expressing leptin receptors. Gene therapy with proopiomelanocortin (POMC), the precursor to alpha-MSH was effective in both young and aged rats, improving both obesity and insulin sensitivity. Moreover this rAAV-leptin induced leptin resistance exacerbates diet-induced obesity. On a high fat diet, the leptin resistant rats consumed more calories, gained more weight and accumulated greater visceral fat mass than controls. These data suggest that leptin resistance is both a consequence and cause of obesity.

Maternal and genotype effects on weight gain in nursing rat pups lacking CCK-A: "competition" and cross-fostering studies.

M. SCHROEDER, O. ZAGOORY-SHARON, Y. AVNON, A. WELLER.
Department of Psychology and Gonda Brain Research Center, Bar-Ilan University, Israel.

OLETF rats lacking expression of functional CCK-A receptors are used to study the early origins and neurobiology of obesity. We followed-up the patterns of body-weight gain and fat-pad distribution of OLETF and LETO (control) male and female rats, from postnatal day 1 to 65. OLEFT pups were significantly heavier since birth and gained weight more dramatically from the third postnatal week. OLETF tended to significantly accumulate white fat from the post weaning period and on compared to controls. Next, we compared the ability of pups' to gain weight from the same nursing episode. In a "competition" experiment, OLETF and LETO pups were fed together by a dam (OLETF or LETO). OLETF pups gained weight significantly more than LETO. In order to assess how the maternal environment affects the developmental trajectory of OLETF pups towards obesity, similar-sized litters were cross-fostered and diurnal nursing behavior was examined. Preliminary results showed more nursing in OLETF litters in the third, but not in the first and second postpartum weeks. OLETF pups raised by LETO dams remained obese. LETO pups raised by OLETF dams were overweight until weaning, and (in females) returned to normal average weight afterwards. The results suggest a maternal influence on weight gain during lactation, and a strong obesity-prone phenotype in OLETF pups.

"Bitter" taste in the gut? Flavor avoidance conditioned by intragastric denatonium in rats.

A. SCLAFANI[a], K. ACKROFF[a], J.I. GLENDINNING[b].
[a]Brooklyn College of CUNY, Brooklyn, NY 11210, USA; [b]Barnard College, New York, NY 10027, USA.

Recent studies demonstrate the expression of bitter taster receptors (T2Rs) and other taste signaling proteins (T1Rs, gustducin) in the rodent gastrointestinal tract. These findings suggest that bitter tastants may act in the gut as well as in the mouth to promote avoidance of potential toxins. This issue was investigated by training rats to associate a novel flavor with intragastric infusions of denatonium benzoate, a bitter, but relatively harmless compound. Male rats were trained 30 min/day with one novel solution (e.g., grape saccharin, CS+) paired with a matched IG infusion of 2.5 mM denatonium benzoate and a different solution (e.g.,

cherry saccharin, CS-) paired with IG water infusion. In a CS+ versus CS- choice test with no infusions, the rats were indifferent to the CS+ (46% preference). They were next trained with a new CS+ (e.g., orange-saccharin) paired with IG infusion of 10 mM denatonium, and new CS- (e.g., lemon-lime saccharin) paired with IG water. The rats consumed less CS+ than CS- during training and avoided the CS+ (22%) in the two-bottle test. Oral CS+ intakes during training diluted the denatonium concentration in the gut to 1.25 mM and 5 mM, which are within the concentration range that rats avoid in oral taste tests. The physiological process responsible for the denatonium-conditioned flavor aversion remains to be established, but the data are consistent with a role of gut taste receptors in the avoidance of bitter tastants. Supported by NIH DK31135.

Flavor preferences conditioned by intragastric sucrose infusions in C57BL/6J and 129 mice.

A. SCLAFANI[a], J.I. GLENDINNING[b].
[a]*Brooklyn College of CUNY, Brooklyn, NY 11210, USA;* [b]*Barnard College, New York, NY 10027, USA.*

C57BL/6J (B6) mice consume more of various sweeteners than do 129 mice. Strain differences are most profound with caloric sweeteners, perhaps due to differential responsiveness to postoral actions of sugars. This was investigated by training B6 and 129 mice with a novel flavor (CS+) paired with intragastric (IG) infusions of 16% sucrose and a different flavor (CS-) with IG water infusions (22 hr/day). In choice tests, the B6 mice displayed stronger CS+ preferences than 129 mice when the CS flavors were unsweetened (83% versus 62%) or sweetened with 0.2% saccharin (98% versus 88%). The 129 mice also consumed less CS during training, which may have contributed to their reduced preference. To equate training intakes, new 129 and B6 mice were trained with flavors made "isosweet" by adding different amounts of sucrose (2% or 0.4%) and saccharin (0.2% or 0.04%) to the CS solutions. IG infusates were adjusted to equate total sugar intakes (oral+IG). In training, the 129 and B6 mice consumed similar amounts, and CS+ intakes were twice that of CS- intakes demonstrating a sucrose-conditioned flavor acceptance. In the two-bottle test, 129 and B6 mice displayed equally strong CS+ preferences (98% versus 96%). The results suggest that 129 and B6 mice are equally responsive to the postoral stimulating action of sucrose. We propose that B6 mice typically consume more sucrose than 129 mice because their stronger taste response stimulates greater intake, leading to greater stimulation of postoral nutrient detectors which promote ingestion. Supported by: NIH DK31135, DK59630 and DC007475.

PYY(3-36) fails to increase CCK induced suppression of food intake in Rhesus monkeys.

K.A. SCOTT, T.H. MORAN.
Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD 21205, USA.

CCK and PYY(3-36) are gastrointestinal peptides that have been shown to reduce food intake and suppress gastric emptying in non-human primates. We investigated whether these compounds would have an additive effect on suppression of food intake when administered peripherally. The dose of 1.0 nmol/kg PYY(3-36) was chosen as it has previously been shown to reduce gastric emptying and food intake in non-human primates. CCK was given at doses of 1.0 nmol/kg and 3.0 nmol/kg, with or without PYY(3-36). Rhesus monkeys (n = 3) that had been trained to lever-press for food pellets were injected intramuscularly (IM), 15 minutes prior to the start of a 6 hour feeding period. The latency to first pellet taken was increased

with 3.0 nmol/kg CCK with or without PYY(3-36) and by 1.0 nmol/kg CCK with PYY(3-36). Cumulative intake was calculated on an hourly basis. CCK suppressed food intake in a dose-dependent manner, with the 3.0 nmol/kg dose exerting the greater effect. Suppression was greatest during the first 2 hours of feeding. The dose of 1.0 nmol/kg PYY(3-36) inhibited food intake during the first 3 hours of feeding in comparison to the saline treatment. However, combining 1.0 nmol/kg PYY(3-36) with either dose of CCK did not increase the degree of feeding inhibition, indicating that there is not an additive suppressive effect when PYY(3-36) is administered in combination with CCK. Supported by DK19302.

Compensation after visceral and subcutaneous fat removal is sexually dimorphic.

H. SHI, A.D. STRADER, S.C. WOODS, R.J. SEELEY.
University of Cincinnati, Cincinnati, OH 45237, USA.

Surgical removal of selective fat pads leads to enlargement of nonexcised pads in many species, suggesting that total body fat is regulated. Leptin and insulin levels are correlated with subcutaneous and visceral fat. Females have more subcutaneous fat and female brains are more sensitive to leptin than occurs in males. Males have a larger percentage of visceral fat and male brains are relatively more sensitive to insulin. We therefore tested the hypothesis that males and females respond differently to removal of subcutaneous or visceral fat. FVBN mice had either the internally-located retroperitoneal or the subcutaneous inguinal pad removed (RWATx and IWATx, respectively) or were sham-operated. Food intake was measured weekly, energy expenditure was assessed every 3 weeks, and fat distribution was assessed 12 weeks after surgery. Body fat decreased in IWATx males but had recovered by 2 weeks after surgery due to increased food intake with no change of energy expenditure. In contrast, RWATx females decreased energy expenditure without changing intake. IWATx and RWATx males had comparable carcass fat distribution. In contrast, RWATx females had significantly less subcutaneous fat whereas IWATx females had the same distribution as shams. In conclusion, male and female mice compensated after selective fat removal by increasing body fat overtime, but they used different strategies. Interestingly, IWATx females returned to a typical 'female' fat distribution whereas RWATx females did not. Both male groups resumed normal 'male' distribution. These data point to fundamental differences in the regulation of body fat in male as compared to female mouse.

Role of mu-opioid receptor antagonist CTAP on Agrp-induced feeding in the rat brain.

Y. SHRESTHA, I.M. VENTURA, K. WICKWIRE, S.Q. GIRAUDO.
Department of Foods and Nutrition, University of Georgia, Athens, GA 30602, USA.

This study focuses on understanding the interaction of two hypothalamic systems, the melanocortins and opioid peptides involved in feeding behavior. They are often colocalized and share a common precursor. Agouti-related protein (Agrp), which antagonizes melanocortin receptors, has a long-lasting but delayed effect on feeding suggesting an involvement in the maintenance rather than the initiation of feeding. Agrp prolonged stimulation of feeding can be blocked by the nonspecific opioid antagonist, naltrexone 24 h after initial Agrp administration. Thus the question arises whether Agrp is recruiting the opioid system to maintain the prolong effect on feeding behavior. To investigate the interaction between these two systems, we assessed the role of the mu-opioid receptor (implicated in control of food intake) in mediating the orexigenic effects of Agrp. Rats were fitted with a lateral ventricle (ICV) cannula. After recovery, animals received via cannula, 0.9% saline or 1 nmol of Agrp. Twenty-four hours later a second 3 µl volume injection of

either saline or 2 nmol of CTAP (mu-specific opioid receptor antagonist) was administered through the cannula. As a positive control an injection of naltrexone (1 mg/kg body weight) was given subcutaneously to the rats that did not receive CTAP. Food intake was measured utilizing the Automated Feeding System BioDAQ. CTAP effectively and significantly suppressed Agrp-induced feeding up to 24 h after CTAP administration whereas naltrexone suppressed Agrp-induced feeding up to 12 h after administration. These results together with prior research suggest that mu-opioid receptors could mediate the orexigenic effect of Agrp.

Hedonic enhancement of jaw movements in rabbits in a pavlovian model of external stimulus control of learned ingestive responses.

K.J. SIMANSKY, J. QUINN, A. SPOR, D.M. NICKLOUS, A.G. ROMANO.
Department of Pharmacology & Physiology, Drexel University College of Medicine, Philadelphia, PA 19102, USA.

Pavlovian conditioning of jaw movement responses (JMR) offers a robust model for analyzing forebrain circuits, sensory pathways and effector systems mediating external stimulus control of ingestion. Male Dutch-belted rabbits were restricted to their normal daily chow intake. They were conditioned daily (30 trials/30 min) for 4 days, using a 5-sec, 1 KHz tone as the conditioned stimulus (CS), an unconditioned stimulus (US) of 20 or 40% sucrose (1 ml/1 sec) and a CS-US interval of 4 sec. A JMR amplitude exceeding mean pretrial baseline + 10 SD was the response criterion on each trial. A conditioned response (CR) was a JMR that began before US onset. Rabbits (8/group) satisfied the stringent criterion on 26 ± 2 trials (20% sucrose US) and 28 ± 1 trials (40% sucrose) on day 1 and for each of the 4 days of conditioning. CR's increased from 8 ± 2 (for each US) on day 1 to plateaus of 15 ± 2 (20%) and 18 ± 2 (40%) on day 4 ($P < 0.01$ for days; ns for sucrose concentration). Next, we compared 40% sucrose and water as the US's. With sucrose, rabbits made 27 ± 2 responses on day 1 and throughout training. In contrast, water elicited half as many JMR's ($P < 0.01$ versus sucrose). Furthermore, rabbits made 14 ± 3 CR's by Day 4 with sucrose reward but only 7 ± 2 CR's with water as US. These data implicate hedonic enhancement of the probability of responding and level of acquisition of learned ingestive responses under external stimulus control. Supported by DK58669 to KJS.

Metabolic effects of oral fat perception.

A.J.P.G. SMEETS[a,b], M.S. WESTERTERP-PLANTENGA[a].
[a]*Maastricht University, Department of Human Biology, Maastricht, The Netherlands;* [b]*Wageningen Centre for Food Sciences (WCFS), Wageningen, The Netherlands.*

The aim of the study was to provoke cephalic and metabolic responses due to vagal stimulation with different high-fat meals in the postprandial state. A randomized parallel design with 3 groups (26 females and 10 males, 12 subjects in each group). Vagal stimulation was achieved by the modified sham feeding (MSF) technique. Five hours after a high-fat breakfast, the subjects were given 1 of 3 test meals in random order: a high-fat lunch, water or the same lunch as MSF. The main fat sources in the high-fat lunch and MSF were olive oil, an oil rich in linoleic acid and an oil rich in oleic acid. During 3 h after the test meal blood samples were taken for metabolite analysis, and Visual Analog Scales on the appetite profile were completed. The cephalic response and vagal stimulation appeared to be achieved by MSF in that we observed a relative increase in insulin and glucose during 15 - 90 minutes. Non-esterified fatty acids increased significantly compared to water ingestion, in the case of olive oil ($P < 0.0001$) and linoleic acid ($P < 0.05$). MSF provoked a significantly higher

increase in triacylglycerol and glycerol compared to water ingestion in the case of linoleic acid ($P < 0.05$). Satiety/fullness was significantly increased in the eating condition and in the sham feeding condition ($P < 0.0002$, for all oils) compared to water ingestion. We conclude that vagal stimulation by different fats increases concentrations of metabolites and stimulates satiety or fullness, with linoleic acid showing the strongest response.

Gastric emptying of ingested fluid when hypovolemic rats drink water or isotonic saline.

C.A. SMITH, E.M. STRICKER.
Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA.

The present experiments sought to determine the basis of the early inhibition of fluid consumption by hypovolemic rats. Rats were injected with 30% PEG (5 ml, s.c.) and deprived of food and water overnight. They were then given access to either water or 0.15 M NaCl solution and allowed to drink until they stopped, at which time they were killed by decapitation and their stomachs, small intestines, and blood were collected for analysis. The PEG treatment produced 30-40% plasma volume deficits. The rats drank comparable amounts of water and saline (~ 1 ml/min for 5 - 9 min), with drinking rates diminishing in proportion to plasma volume deficit. Gastric emptying of ingested water by PEG-treated rats while they were drinking (49%) was smaller than gastric emptying of saline (61%). Thus, less fluid remained in the stomach when rats drank saline than when they drank water. However, the total volume of ingested fluid in the stomach and small intestine was similar regardless of which fluid the rats drank; indeed, the relation between fluid intake and gastrointestinal fill resembled that seen when rats drank water or saline after water deprivation or other treatments that elicit thirst or salt appetite. These results are consistent with the hypothesis that the ingestion of water or saline solution by rats is constrained by a rapid inhibitory feedback signal associated with distention of the stomach and small intestine. Ongoing studies are investigating whether water ingestion by hypovolemic rats has an early inhibitory effect on vasopressin secretion.

Genetic and psychophysical measures reveal associations between oral sensation and tobacco use.

D.J. SNYDER, V.B. DUFFY, A.C. DAVIDSON, J.R. KIDD, K.K. KIDD, W.C. SPEED, A.J. PAKSTIS, J.F. CUBELLS, S.S. O'MALLEY, L.M. BARTOSHUK.
Yale University, New Haven, CT 06520-8041, USA.

Multiple reports indicate that nontasters of certain bitters (e.g., quinine, PTC, PROP) are more likely than tasters to use tobacco. However, most of these studies use methods that fail to capture the full range of oral sensory variation; they also fail to account for pathologic sensory change. Recent advances in genetic analysis allow identification of polymorphisms underlying threshold differences between PTC/PROP nontasters and tasters; modern psychophysical scaling allows suprathreshold classification of tasters into medium tasters and supertasters. Using these techniques, we compared distributions of PTC/PROP status between smokers (N = 149) and nonsmokers (N = 91). By itself, genetic classification (which identifies nontasters and tasters only) produced no difference between smokers and nonsmokers. When genetic analysis was combined with suprathreshold PROP taste intensity (which identifies supertasters and controls for oral sensory pathology), significant differences emerged: Consistent with earlier reports, both male and female smokers are less likely to perceive PROP bitterness. Pairwise comparisons show that this effect is largely due to an absence of supertasters among smokers. Overall, these data confirm reports that link smoking

with nontaster status; more importantly, they indicate that supertasters avoid tobacco use. We believe that multifactorial testing enhances the accuracy and predictive power of sensory assessments. Supported by NIDCD (LMB), NRICGP/USDA (VBD), NIGMS (KKK), NIDA/NCI (SSO), NSF/Pangborn Sensory Science Fund (DJS).

Social defeat and footshock increases body and lipid mass in male Syrian hamsters.

M.B. SOLOMON[a], M.T. FOSTER[b], T.J. BARTNESS[a, b], K.L. HUHMAN[a].
[a]*Department of Psychology,* [b]*Department of Biology, Center for Behavioral Neuroscience, Georgia State University, Atlanta, GA 30303, USA.*

Defeated rodents and non-human primates are known to exhibit behavioral and physiological changes including increases in stress hormone secretion, suppression of immune function, and changes in food intake and body mass. Following defeat, rats and most mice become hypophagic and subsequently lose body mass, but the opposite is true of Syrian hamsters which become hyperphagic and subsequently gain body mass. We did not know whether the stress-induced increases in body mass and food intake was limited to a social stressor. Therefore, the purpose of this study was to determine if a nonsocial stressor, footshock, was capable of producing similar increases in body mass and food intake in Syrian hamsters. Animals were randomly assigned to non-stressed control, footshock, or defeat groups. Consistent with previous findings, defeated animals gained significantly more body mass in comparison to non-stressed controls. Similarly, animals that were exposed to a brief footshock stressor gained significantly more body mass in comparison to non-stressed controls. There were no significant differences in body mass between footshock and defeated animals. In addition, the footshock and defeated groups had significantly increased white adipose tissue (WAT) pad masses (i.e. mesenteric and epididymal WAT) in comparison to non-stressed controls. Contrary to our previous findings, there were no significant differences in food intake among any of the groups. Taken together these data demonstrate that both social and nonsocial stressors are capable of producing increases in body and lipid mass in male Syrian hamsters. Supported by NIH RO1 MH 62044 to KLH, NIH RO1 DK35254 to TJB and supported in part by NSF under agreement #IBN-9876754.

Satiation of need-related sodium appetite in rats.

L.J. STARR, N.E. ROWLAND.
Department of Psychology, University of Florida, Gainesville, FL 32611-2250, USA.

Jalowiec (*Behav. Biol.* 1974;10:313-327) who pioneered the acute diuretic protocol using furosemide, found that sodium depleted rats often consumed more NaCl than their physiological loss. He thus hypothesized that there appeared to be no satiation mechanism for sodium appetite. Additionally, while some studies have showed that gastric preloads of NaCl can reduce subsequent intake of a NaCl solution, none have challenged the notion that, unlike food or water intakes, that of salt may not have a natural inhibitory mechanism. Previously, we reported that in contrast to the typical results in free consumption tests, rats depleted chronically of sodium and made to work for NaCl on a progressive ratio (PR) schedule showed a reasonably need-related satiation or break point. Behavioral satiation was also correlated in time with reductions in plasma aldosterone and renin activity. The studies to be reported further investigate this satiation mechanism. In particular, we will present the results of studies in which consumption of NaCl is spread out in time and also studies on preloads in this protocol. We hypothesize that if indeed work (as an example of an environmental adversity) acts to cause the rats to cease consuming the NaCl solution once they have repleted

their deficit, then a simply longer interval of time allowed to access the NaCl solution should not stop the rats from overconsuming. Additionally, we hypothesize that a NaCl preload should perhaps cause the rats to stop bar-pressing earlier in a PR protocol than was previously shown in our earlier work.

Incentive value of food images is modulated by hunger.

L.E. STOECKEL, M. GIDDINGS, E.W. COOK III, J.E. COX, R.E. WELLER.
Department of Psychology, University of Alabama at Birmingham, Birmingham, AL 35294-1170, USA.

The incentive value of foods varies as a function of degree of hunger. We plan to study the mediation of this effect using functional brain imaging (fMRI). As a preliminary study, we sought to demonstrate visual alliesthesia in subjects viewing pictures of food. Two groups of subjects were studied, fasted and non-fasted. Subjects were two groups of college students, non-fasted (N = 369) and fasted (N = 257). The latter subjects were asked not to eat for 12 hours before the session. We hypothesized (1) that ratings of food images, but not non-food images, would be higher in fasted compared to non-fasted subjects and (2) that ratings of food images in non-fasted subjects would be positively correlated with subjective hunger ratings. Each subject viewed one of six 100-item lists containing pictures of foods and non-foods. Subjects rated each image on valence (pleasantness) using a 9-point scale (1-low; 9-high) and also rated their degree of hunger. Our results supported our hypotheses. Fasted subjects rated food images higher on valence (6.07 ± 0.09) than did non-fasted subjects (5.53 ± 0.07) ($P <$ 0.001). In contrast, fasted subjects rated non-food images lower on valence (5.03 ± 0.06) than did non-fasted subjects (5.26 ± 0.05) ($P = 0.005$). In non-fasted subjects, there was a positive correlation between hunger rating and mean valence rating for food images ($r = 0.34$, $P <$ 0.001). These results suggest that we have successfully demonstrated alliesthesia in a paradigm we can transfer to our fMRI studies.

Healthy food choices during school lunches and their effect on palatability.

N. STROEBELE[a], R. BARZ[b], J. O. HILL[a].
[a]*Center for Human Nutrition, University of Colorado Health Sciences Center, Denver, CO 80262, USA;* [b]*Leprino Foods, Denver, CO, USA.*

About 15% of children are overweight and the percentage is increasing. To address obesity, interventions could target individual behavior change, the eating and physical activity environment or both. One way to improve diet is to help children substitute healthier foods for those less healthy. This is difficult since foods that might contribute to excessive energy intake, such as pizza and other high-fat foods, are favored by children. An alternative strategy is to modify foods to improve their nutritional value without reducing the acceptability of the foods. The aims of this study were to determine whether small changes to favorite school foods could be made to make them healthier and palatable to the children during lunch. We hypothesized that changes to the foods would not alter meal participation, palatability or appearance ratings. With help from food manufacturers and the Denver Public School's food service staff, we made small changes to three popular foods. Food manufacturers provided the schools with lower fat and lower calorie French fries, chicken fingers, and pizza. Information about meal participation and palatability was obtained from the original and modified versions of each food. Meal participation and palatability did not change when children were given the altered versions, suggesting that children did not detect the small nutritional

changes. Thus, small environmental changes might be an effective tool in implementing healthier foods in children's lives.

Effects of consistent and inconsistent snack food-calorie relationships on regulation of food intake in rats.

S.E. SWITHERS, A. DOERFLINGER, C. STUDEBAKER, T.L. DAVIDSON.
Department of Psychological Sciences and Ingestive Behavior Research Center, Purdue University, West Lafayette, IN 47907, USA.

Associations between the taste of a food and the consequences of consuming that food may provide one mechanism for regulation of energy balance. Consequently, disrupting the ability of the sensory properties of food to predict the caloric consequences of consuming that food may impair regulation of food intake and body weight. For example, previous work from our lab has demonstrated that rats provided with a sweet-tasting, liquid diet that sometimes predicts the delivery of calories and sometimes predicts the delivery of no calories show differential regulation of food intake and body weight compared to rats for which sweet-tasting liquid diets always predict calories. In the present experiments, we examined whether a similar effect would be observed using a different diet. Young male rats were given a daily dietary supplement of 10 g potato chips. For the first group of animals, these potato chips were always high fat and high calorie (5.6 kcal/g; group Consistent). For the second group, the potato chips were sometimes high fat and high calorie, and sometimes were manufactured with a non-caloric fat substitute (2.8 kcal/g; group Inconsistent). Thus, for group Inconsistent, the taste of potato chips was sometimes associated with high calories, and sometimes provided low calories. Results of this experiment indicated that food intake over 24 hours was significantly higher in the Inconsistent group compared to the Consistent group. Thus, impairing the ability of the sensory properties of a food to predict the caloric consequences may affect an animal's ability to regulate food intake.

High cholesterol levels in neuronal cells impair the insulin signaling pathway and interfere with insulin's neuromodulatory action.

C. TAGHIBIGLOU, C. BRADLEY, Y. WANG.
Brain Research Centre, Department of Medicine, University of British Columbia, Vancouver, V6T 2B5 Canada.

Insulin plays important roles in CNS physiology including memory and normal cognition, neuronal cell survival and neuromodulatory actions. Using cultured neurons, we investigated plasma membrane distribution of insulin receptors and their functionality in the different compartments. Furthermore, we studied effect of high cholesterol on the insulin signaling cascade and its neuromodulatory consequences. PM flotation studies revealed that the majority of IRs are localized in the non-raft compartment with only a small portion recovered from lipid rafts. Insulin stimulation resulted in tyrosine-phosphorylation of non-lipid raft IRs with no effect on receptors localized in lipid rafts. We hypothesize that incubation of neuronal cells in high cholesterol, by expanding the raft component of the plasma membrane, impairs the insulin signaling pathway and interferes with the neuromodulatory action of the hormone. Filipin and Cholera toxin-B subunit recovery assays showed a significant increase of lipid raft-like structures in the PM of cholesterol-treated neurons. Cholesterol incubation significantly reduced insulin-induced tyrosine-phosphorylation of IR, IRS-1 and IRS-2, suggesting induction of insulin resistance in cholesterol treated cells. In biotin-labelled cultured neurons, insulin reduced AMPA receptor PM expression to 60.32 ± 6.06% of the

basal level (to 61.49 ± 3.8% in brain slices) whereas it failed to induce any additional reduction in the cholesterol-treated cultured neurons. Under the same conditions, insulin increased PM localized GABAA receptor to 177.52 ± 11.2% of the basal level, while failed to show similar effects on cholesterol treated cells. Based on our data, high cholesterol treatment of neurons induces insulin resistance leading to impairment of the neuromodulatory action of insulin.

Chronic social stress effects on food intake and energy expenditure.

K.L.K. TAMASHIRO[a,b], M.M.N. NGUYEN[a,b], L.Y. MA[b], D.A. D'ALESSIO[c], S.C. WOODS[b], R.R. SAKAI[b].

[a]Neuroscience Program, [b]Department of Psychiatry, [c]Division of Endocrinology, University of Cincinnati Medical Center, Cincinnati, OH 45237, USA.

Male rats in mixed-gender rat colonies form dominance hierarchies when housed in a visible burrow system (VBS), a laboratory model of chronic social stress. Subordinate (SUB) males consistently lose a significant amount of body weight over 14 days in the VBS, while dominant (DOM) males maintain or lose very little weight. Food intake was measured while the animals were in the VBS by the AccuDiet ID system. SUB were hypophagic during social stress in the VBS. Body composition analysis showed that both DOM and SUB lost adipose tissue, but SUB lost lean tissue as well. When allowed to recover in individual cages, SUB re-gained weight primarily as fat and this is exacerbated by repeated exposures to social stress. In addition, SUB preferentially deposited fat in visceral rather than subcutaneous depots. SUB were also hyperinsulinemic and hyperleptinemic compared to DOM and CON after VBS stress and recovery. While there were no differences among the groups in an oral glucose tolerance test prior to stress, SUB cleared the glucose load faster with lower insulin secretion than DOM and CON after 14 days of social stress and thus had more efficient glucose tolerance. After 2 cycles of stress and recovery both DOM and SUB groups had become more efficient at clearing the glucose load compared to CON. The data suggest that neurochemical and peripheral endocrine changes associated with chronic social stress influence systems involved in food intake and body weight regulation and may result in metabolic disorders over long-term, repeated exposures.

Enhancement of satiety by an environmental signal of nutrient influx in rat.

N.L. TARNER, Z.S. WARWICK.

Department of Psychology, University of Maryland Baltimore County, Baltimore, MD 21250, USA.

The magnitude of postprandial satiety (herein defined as the reduced willingness to ingest additional food following a meal) is influenced by a multiplicity of factors including the macronutrient profile of the meal, flavor-cued expectancies of the meal's satiating potency, etc. The present study investigated the impact of an environmental cue on the magnitude of satiety produced by a nutritive load. All rats received four daily intragastric infusions (17 kcal each) of an evaporated milk/sucrose mixture, given at 3 hr intervals from 6 pm - 3 am. A 4-minute buzzer-light conditioned stimulus (CS) preceded each infusion for some animals (SIGNALLED), while for other animals, this stimulus was not temporally associated with the infusion (NOT SIGNALLED). Chow was available ad lib. Preliminary results (n = 6/group) indicate lower chow intake (mean 25.4, s.e. 4.8 kcal), and thus lower total daily kcals, in SIGNALLED animals relative to the NOT SIGNALLED group (mean 32.4 s.e. 4.9 kcal).

This suggests that the CS enhanced the satiating (intake-suppressing) effect of the nutritive infusion. Supported by NIDDK 55367.

Reductions in dietary fat produce symptoms of drug withdrawal.

S.L. TEEGARDEN, T.L. BALE.
Department of Animal Biology, Neuroscience Graduate Group, and Institute of Neurological Sciences, University of Pennsylvania, PA 19104, USA.

Levels of obesity in America are currently reaching epidemic proportions, with nearly 65% of the adult population classified as overweight or obese. Obesity is associated with a number of serious health complications including hypertension and type II diabetes. One likely factor in the growing prevalence of obesity is the increasing availability of highly palatable and energy-dense foods, especially those high in fat. Recent studies in both humans and animals have shown that palatable foods high in dietary fat activate many of the same brain reward areas as drugs of abuse such as cocaine and nicotine. Therefore, we propose that obesity may be viewed as a disease with addiction-like characteristics. We investigated whether reductions in dietary fat following acute exposure would produce symptoms of withdrawal in mice. As a model of withdrawal, mice were fed either high or low fat diets for four weeks and then returned to regular house chow. Following withdrawal, mice were assessed for behavioral and physiological signs of withdrawal at multiple time points. Mice were sacrificed either 24 hours or 1 week post-withdrawal and their brains examined for biochemical and molecular changes associated with withdrawal. Our results show that reductions in dietary fat produce physiological, behavioral, molecular, and biochemical alterations that mimic those found during drug withdrawal. These findings support an addictive capacity of foods high in dietary fat as a possible contributor to obesity development and increased risk for dietary relapse.

Genetic taste influences on dietary behavior and body weight.

B. TEPPER.
Department of Food Science, Rutgers University, 65 Dudley Road, New Brunswick, NJ 08901, USA.

Genetic variation in sensitivity to the bitter taste of 6-n-propylthiouracil (PROP) is a marker for individual differences in taste perception and food preferences. Those who are taste blind to this substance (i.e. non-tasters) are shown to have lower taste perceptions for a variety of oral sensations including bitterness, spiciness and fattiness, and paradoxically they show higher preferences for foods with these sensory qualities. In contrast, those who are sensitive to PROP (including tasters and super-tasters) show the opposite sensory and hedonic responses to these foods. These data suggest that the PROP polymorphism could have far reaching implications for guiding food selection and dietary intake, ultimately influencing body weight. Thus, we have hypothesized that the non-taster phenotype is associated with higher fat and energy intakes and greater adiposity than taster phenotypes. This talk will examine current evidence supporting this hypothesis. New data will be presented linking PROP status with body weight variation in different study populations.

***NO PUBLICATION in APPETITE.

Evidence that glucocorticoids increase salt appetite by increasing urinary excretion.

R.L. THUNHORST, T.G. BELTZ, A.K. JOHNSON.

Departments of Psychology, Pharmacology, Exercise Science, and the Cardiovascular Center, University of Iowa, Iowa City, IA 52242-1407, USA.
Mineralocorticoids, such as aldosterone (Aldo) and deoxycorticosterone acetate (Doca), stimulate salt appetite through central mechanisms. Glucocorticoids, (e.g., corticosterone, dexamethasone) greatly potentiate salt appetite during mineralocortioid treatment. It is postulated that glucocorticoids enhance salt appetite by acting at sites in the brain to facilitate mineralocorticoid effects. However, glucocorticoids have major effects on water and sodium homeostasis through actions on the kidney to increase excretion of water and sodium. Wolf suggested 40 years ago that glucocorticoids might increase salt appetite by promoting excretion of the ingested sodium load. We gathered evidence for this possibility by determining water and sodium intakes, excretions and balances during daily injections of Doca, the glucocorticoid agonist dexamethasone (Dex) and their co-administration (Doca + Dex). Doca progressively increased sodium ingestion. Water and sodium intakes were greater than their urinary excretion, resulting in positive water and sodium balances. During Dex treatment, water and sodium intakes did not change, and excretion outpaced ingestion resulting in negative water and sodium balances. Doca + Dex treatment stimulated rapid, large increases in sodium ingestion while maintaining positive sodium balances. However, water excretion outpaced water ingestion (including water from saline, i.e., total fluid intake) resulting in negative water balances. The negative water balances during Dex and Doca + Dex were paralleled by diminishing body weights indicating likely volume contraction. We conclude that glucocorticoid effects on urinary excretion provide additional, or alternative, mechanisms to postulated central effects that may explain their potentiation of salt appetite.

Does restrained eating reflect actual or perceived deprivation?
J. TUTTMAN MARKOWITZ, M.R. LOWE.
Drexel University, Department of Psychology, Philadelphia, PA 19102, USA.
Restrained eating refers to an effort to restrict energy intake for the purposes of weight loss or maintenance. Restrained eaters are not in negative energy balance; indeed, restraint measures predict future weight gain. Therefore, measures of restrained eating may reflect eating less than one wants, not less than one needs, a phenomenon labeled Perceived Deprivation (PD) by Timmerman and Gregg (*WJNR* 2003;25:405-418). Using a 5-point Likert scale, we measured PD in 53 college females by asking two questions each day for one week that were summed and averaged to produce a single PD score: 1) Do you feel like you ate enough food today? and 2) Do you feel like you ate what you wanted today? The correlation between the two items was substantial ($r = 0.71$, $P < 0.01$). Timmerman and Greg found in obese adult women that a similar measure of PD was not correlated with daily caloric intake, but was correlated with the Restraint Scale (RS). The current study was aimed at replicating and extending this finding. PD correlated with the RS ($r = 0.27$, $P = 0.06$), a trend that was due to PD's correlation with the RS' dietary concern factor ($r = 0.35$, $P = 0.01$) rather than its weight fluctuation factor ($r = 0.07$, ns). Results were unchanged when BMI was used as covariate. These results support a new view of restrained eating as reflecting the effort to eat less than wanted, rather than less than needed.

Effects of central and peripheral ghrelin on feeding in dietary obese leptin-resistant rats.
J.R. VASSELLI, J. MORENO, J. JOHNSON, V. GAREL, P. CURRIE.
St. Luke's-Roosevelt Hospital and Barnard College, Columbia University, New York, NY 10027, USA.

Ghrelin increases feeding by stimulating NPY/AGRP neurons in the arcuate nucleus, while leptin reduces feeding by inhibiting these neurons. Also, ghrelin levels decrease with increasing body fat, while leptin levels increase. These alterations suggest that the feeding-stimulatory effects of ghrelin may be reduced in obesity. However, obesity can be accompanied by leptin resistance, which diminishes leptin-induced inhibition of the NPY feeding pathway. We therefore tested whether ghrelin retains its feeding-stimulatory ability in obesity. Groups of 12 wk old male Sprague-Dawley rats (n = 6 - 8) were fed either chow (CH) or 45% high fat diet (HF) for 6 months. Following habituation to respective saline injection test procedures, groups were administered rat ghrelin (Biopeptide Co.) either icv or i.p., and feeding was measured hourly for 4 hr. Mean BW at time of testing was CH 578.3 ± 57.3 versus HF 751.9 ± 80.6 g ($P < 0.001$), and HF rats were leptin resistant in response to 1.0 mg/kg leptin i.p. Significant increases in feeding in response to icv ghrelin were observed between hrs 0 - 2 in both CH (50 pmol, + 208%; 200 pmol, + 643%, *P's* < 0.01) and HF groups (50 pmol, + 61%; 200 pmol, + 309%, *P's* < 0.01). Likewise, significant increases in feeding to i.p. ghrelin were observed between hrs 0-2 in CH (30 ug/kg, + 227%; 100 ug/kg, + 137%, *P's* < 0.05) and HF groups (30 ug/kg, +157%; 100 ug/kg, + 52%, *P's* < 0.02). We conclude that both central and peripheral ghrelin retain significant feeding-stimulatory ability in dietary obese leptin-resistant rats.

Conditioned flavor avoidance in melanocortin receptor 4 knockout mice.

C.H. VAUGHAN[a], M.C. MOORE[b], C. HASKELL-LUEVANO[b], N.E. ROWLAND[a].
[a]*Departments of Psychology,* [b]*Medicinal Chemistry, University of Florida, Gainesville FL 32611-2250, USA.*

Overeating in melanocortin receptor knockout (MC4RKO) mice is linked to their housing environment. MC4RKO mice show a long latency to acquire an operant task, in comparison to wild type mice. The objective of this study was to assess neophobia and associative learning in MC4RKO mice using a conditioned flavor aversion test. To avoid possible genotype differences in effects of deprivation, this test used a flavored gelatin "dessert". Ad libitum fed wild type, heterozygous and MC4RKO mice first received a daily 30 min presentation of a flavored gelatin containing 10% Polycose to determine baseline intake. Mice were then given a 30 min exposure to a novel flavor of the gelatin dessert (CS) on four occasions followed immediately by intraperitoneal injection of either 0.15 M LiCl (6 meq/kg) or 0.15 M saline (40 ml/kg). The pairing sessions were separated by two day intervals. To test extinction of the avoidance, all mice received the CS again on five more occasions, again at two day intervals, but no subsequent injections. All three genotypes rapidly acquired comparable intakes of the dessert and of the novel CS on the first day. Mice that received LiCl injections developed a conditioned avoidance of the CS that was almost complete after 3 pairings. There were no differences between genotypes. Intake of mice that received saline injections was unaffected. The three genotypes also showed only slight extinction of the avoidance in extinction, with females tending to reverse faster than males. Thus, MC4RKO mice are capable of learning a conditioned flavor avoidance and show no differences from wild type controls in this regard.

The inhibition of intake when thirsty rats drink water.

J.E. VAUGHAN, M.L. HOFFMANN, E.M. STRICKER.
Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA.

Previous experiments indicated that rats deprived of drinking water (but not food) overnight, when given water again, drink almost continuously for 4 - 5 min. Although ingested water emptied rapidly from the stomach and traveled far into the small intestine, the cessation of water ingestion was not related to systemic rehydration. Instead, this early inhibition of thirst appeared to result from a distension signal associated with the volume of ingested fluid in the stomach and small intestine. It seemed noteworthy, however, that the amount of solids in their stomachs were quite low (< 0.4 g), presumably because the rats ate little while water-deprived (dehydration anorexia). Thus, it seemed possible that the rapid emptying of ingested water resulted from the relatively empty stomachs that rats had while they drank. To test this hypothesis, rats were made thirsty acutely by intraperitoneal injection of hypertonic saline (2 M NaCl, 2 ml). These animals had substantial amounts of stomach solids (0.8 - 3.0 g) when they began drinking. Nonetheless, gastric emptying of ingested water was comparably rapid as when dehydrated rats drank water; furthermore, the distance traveled by water in the small intestine was comparably far, and systemic hypernatremia persisted when rats stopped drinking. On the other hand, the relation between water intake and gastrointestinal fill resembled that seen when rats drank water after water deprivation. These results are consistent with the hypothesis that the ingestion of water by thirsty rats is constrained by a rapid inhibitory feedback signal associated with distention of the stomach and small intestine.

A mathematical model for switching between ingestion and rejection based on disinhibition.

S. VENUGOPAL, J.B. TRAVERS, D. TERMAN.
The Ohio State University, Columbus, OH 43210, USA.

Numerous studies provide evidence for a multifunctional network in the lower brainstem capable of generating ingestion (licks) and rejection (gapes), oromotor behaviors distinguished by the phase, amplitude and rate of lingual and masticatory muscle contractions (Travers & Norgren, *Behav. Neurosci.* 1986;100:544-555). To generate these behaviors, pre-oromotor neurons in the brainstem reticular formation (RF) are hypothesized to change their firing patterns based on gustatory input relayed through the solitary nucleus (NST) and parabrachial nuclei. Further, based on the distribution of QHCl-elicited Fos-like immunoreactivity (Harrer & Travers, *Brain Res.* 1996;711:125-37.) and medullary infusions of the GABA antagonist bicuculline, we have posited that QHCl causes disinhibition within the RF to effect the transition from licks to gapes (Chen & Travers, *AJP* 2003;285:R68-83.). Here we have tested the adequacy of the disinhibition hypothesis using a computer-based mathematical model (XPP: Rinzel & Ermentrout, 1998, In: *Methods in Neuronal Modeling: From Ions to Networks*, pp.251-291. MIT Press, Cambridge, MA, 2nd.ed.). A hypothetical network consisting of 3 conductance-based bursting neurons corresponded to 3 classes of interneurons: (1) pre-lingual protrudor; (2) pre-lingual retractor and (3) pre-jaw-opener. NST input to the network consisted of an excitatory current to all 3 interneurons and a tonic inhibitory input to the jaw-opener interneuron. In response to excitatory input and tonic inhibition, a lick pattern ensued in which lingual protrudor activity coincident with jaw-opener was followed by lingual retraction. Removal of tonic inhibition produced a gaping pattern in which jaw-opener activity coincident with lingual protrusion activity was both preceded and followed by lingual retractor activity. This model suggests a differential distribution of GABA receptors on specific classes of pre-oromotor interneurons. Supported by DC00417.

Childhood obesity: BMI tracking and parental influences.

N. VOGELS, M.S. WESTERTERP-PLANTENGA.
Maastricht University, PO Box 616, 6200 MD Maastricht, the Netherlands.

The problem of childhood obesity is accelerating throughout the world. To get more insight in the development of childhood obesity 105 children have been followed from birth till 12y. Anthropometrical measurements were made at birth, 1y, 2y, 3y, 4y, 7y and 12y. At 12y body weight and BMI (of children and parents), waist circumference, body composition, attitude towards eating (of children and parents), and physical activity (Baecke questionnaire) were determined. Children's mean BMI at 12y was 19.0±2.6 kg/m2, 15.2% was classified as overweight. BMI-1y was significantly associated with BMI-7y ($r = 0.44$, $P < 0.001$) and with BMI-12y ($r = 0.24$, $P = 0.02$). BMI-7y was strongly associated with BMI-12y ($r = 0.73$, $P < 0.001$). Overweight children showed significantly higher growth during their first year (6.9 ± 0.8 versus 6.4 ± 0.9, $P = 0.05$). Fathers of overweight children had a significantly higher BMI (27.9 ± 7.0 versus 25.7 ± 3.4, $P = 0.05$) and mothers were more disinhibited/emotional eaters (4.7 ± 2.2 versus 3.2 ± 2.1, $P = 0.01$) as compared to fathers/mothers of normal-weight children. Overweight children showed higher dietary restraint scores (7.1 ± 3.8 versus 4.8 ± 3.2, $P = 0.01$) and disinhibition/emotional eating scores (3.6 ± 1.3 versus 2.6 ± 1.3, $P < 0.01$), and tended to be less active (7.9 ± 1.4 versus 8.3 ± 0.9, $P = 0.08$). We confirmed the tracking of BMI during childhood, which may be due to early rapid growth and parental influences, i.e. BMI as well as attitude towards eating. Dietary restraint, disinhibition/emotional eating and low physical activity were considered as effects of childhood obesity.

Relationship of weight maintenance and dietary restraint with PPARg2, GRL and CNTF polymorphisms.

N. VOGELS, E.C.M. MARIMAN, F.G. BOUWMAN, M.S. WESTERTERP-PLANTENGA.
Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands.

Genetic variation in the PPARγ2, GRL and CNTF genes may play an important role in the etiology of obesity. We examined different determinants associated with weight maintenance (WM) after weight loss. 120 subjects followed a 6wk VLCD, followed by a period of 1y WM. Body weight (BW), body composition, leptin concentration, dietary restraint, physical activity and the polymorphisms of the PPARγ2, GRL and CNTF genes were measured. BW loss during VLCD was 7.0 ± 3.1 kg. After 1y, 21 subjects were successful (<10% regain) and 99 unsuccessful (>10% regain). Comparing these, successful subjects increased their dietary restraint significantly more (ΔF1: 4.8 ± 5.0 versus 1.8 ± 3.9, $P < 0.01$), whereas their general hunger feelings were significantly reduced (ΔF3: -4.0 ± 4.9 versus -1.2 ± 2.7, $P < 0.05$). Successful subjects showed a significantly different frequency distribution for all three genes (PPARγ2: $\chi^2 = 27.02$, GRL: $\chi^2 = 28.13$, CNTF: $\chi^2 = 6.12$, $P < 0.01$) as compared to the whole group. In addition, these relatively more successful genotypes showed significantly different characteristics as compared to the other genotypes, such as a higher baseline BMI (PPARγ2: 31.3 ± 3.9 versus 29.7 ± 3.0, $P = 0.05$), a decrease in disinhibition (GRL: -1.9 ± 1.9 versus –0.4 ± 1.8, $P < 0.05$) and hunger feelings (GRL: -2.6 ± 5.8 versus C/C –0.5 ± 2.6, $P < 0.05$), and a smaller decrease in leptin concentrations (CNTF: -13.4 ± 9.6 versus -19.3 ± 14.5, $P < 0.05$). In relation to particular genotypes of the PPARγ2, GRL and CNTF genes, successful WM was favored by a higher baseline BMI and waist circumference, an increased dietary restraint score and decreased hunger feelings.

Chronic prevention of mu-opioid receptor G-protein coupling in the external nucleus of the lateral parabrachial nucleus of the rat does not alter food intake.

H.G. WARD, V.J. ALOYO, K.J. SIMANSKY.
Drexel University College of Medicine, Philadelphia, PA 19102, USA.

Unilateral infusion of the mu-opioid receptor (MOR) agonist, DAMGO ([D-Ala2, N-Me-Phe4, glycinol5] enkephalin) into the lateral parabrachial nucleus (LPBN) increases consumption of standard laboratory chow. Conversely, infusion of the competitive MOR antagonist, CTAP (D-Phe-Cys-Trp-Arg-Thr-Pen-Thr-NH2), decreased consumption. In vitro [^{35}S] GTP-?-S autoradiography shows that infusion of the irreversible MOR antagonist, β-funaltrexamine (β-FNA), into the external nucleus of the LPBN decreased DAMGO-stimulated G-protein coupling for at least 5 days, predicting that bilateral infusion of β-FNA into the LPBN of rats should persistently decrease food intake. Surprisingly, infusion of β-FNA (4.0 nmol/0.5 μl) into the LPBNe did not alter consumption of either palatable ENSURE® (β-FNA: 24.2 ± 1.3ml, saline: 26.2 ± 1.1 ml; 4 h) or chow (β-FNA: 30.5 ± 1.3g, saline: 33.3 ± 1.4; 20 h) for 5 days. We infused CTAP (10 nmol/0.5 μl) bilaterally into the LPBNe of the same rats on day 6. CTAP decreased chow intake in rats that received saline (saline: 32.0 ± 1.2 g, CTAP: 23.7 ± 1.8 g, $P < 0.001$) or β-FNA (saline: 37.6 ± 2.9 g, CTAP: 20.5 ± 1.2 g, $P < 0.001$) on day 0, but not ENSURE consumption (saline/saline: 30.7 ± 1.1 ml, saline/CTAP: 34.8 ± 2.3 ml; β-FNA/saline: 26.4 ± 2.3 ml, β-FNA/CTAP: 28.1 ± 3.2 ml). Presumably, the larger dose of CTAP than β-FNA inhibited a larger field of MORs in the LPBN. Thus, either a minimum area or locus of receptor inhibition within the LPBN is critical for MOR-modulation of feeding. Therefore, MORs within the LPBNe may modulate an aspect of feeding not involving palatability. Supported by DK067648 to KJS.

Changes in rat leptin and ghrelin 24 h after traumatic brain injury or club drug use.

M. WARREN, F. KOBEISSY, J. JEUNG, M. GOLD.
University of Florida, College of Medicine, Gainesville, FL 32610, USA.

Traumatic brain injury (TBI) and club drug use such as Ecstasy and Speed are known to be anorexia-inducing phenomena. Club drugs are also known to produce hyperthermia and increased energy expenditure. However, little is known about the mechanism of these effects. Leptin is a protein hormone which regulates body weight and metabolism by affecting the hypothalamic centers on feeding behavior, hunger, body temperature and energy expenditure. Increases in leptin decrease hunger and food consumption, mediated by inhibition of neuropeptide Y, and also increase body temperature. Ghrelin increases hunger through its actions on the hypothalamic feeding center and upregulation of growth hormone. We conducted a pilot study using radioimmunoassays to measure the levels of leptin and ghrelin in rat serum 24 h after the experience of TBI or injection of Ecstasy or Speed. A controlled cortical impact device was used to model TBI at a level of 1.6 mm. These rats were compared to naïve animals receiving no injury. For club drug use, groups of rats receiving levels of MDMA (10 mg/kg, 20 mg/kg, or 40 mg/kg) were used as well as 40 mg/kg of Meth and compared to rats receiving only saline. The hormone levels changed significantly and in opposite directions, but to our surprise the leptin levels were decreased while the ghrelin levels were increased. There may be a complex feedback system in play with the leptin and ghrelin hormones unsuccessfully trying to combat the anorexia. In the future we wish to repeat this study using multiple time points as well as concurrent measurements of body mass and food consumption over time.

The absence of caloric density-associated flavor cues enhances intake in rats.

Z.S. WARWICK, K.R. BELL-WARREN, N.L. TARNER.
Department of Psychology, University of Maryland Baltimore County, Baltimore, MD 21250, USA.

Flavor-calorie associations are known to influence short-term (meal) intake in rats, but less is known of their potential impact on longer-term energy intake. To address this question, varying amounts of water were added to semi-solid (gelled) chow to produce high-density (1.2 kcal/g), mid-density (0.8 kcal/g), and low-density (0.4 kcal/g) diets. Flavored powder (grape; cherry; orange Koolaid) was added at 1% wt/wt. All rats received the high-, mid-, and low-density diet on consecutive days; the 3-day cycle was repeated 6 times. For Group CONSISTENT, each diet density had a consistent, unique flavor. Group INCONSISTENT received random flavor-density pairings. Group ONEFLAVOR had a monotonous flavor added to all densities. Between-group comparison of intakes during the final 3 cycles revealed the effect of density-predictive flavor cues: average energy intake by INCONSISTENT (mean 98.2, s.e. 3.0 kcal) and ONEFLAVOR (mean 104.2, s.e. 3.4 kcal) exceeded CONSISTENT (mean 85.6, s.e. 3.0 kcal). Since all animals had received identical exposure to the high-, medium- and low-density diets, the higher intake by INCONSISTENT and ONEFLAVOR indicates that the absence of density-predictive flavor cues increases energy intake. Supported by NIDDK 55367.

Influence of fluid deprivation on alcohol intake of fawn hooded rats.

R.S. WEISINGER[a], A.J. LAWRENCE[b].
[a]*School of Psychological Science, La Trobe University, Victoria 3086, Australia;* [b]*Howard Florey Institute of Experimental Physiology and Medicine,Victoria 3010, Australia.*

Angiotensin II infused into the brain can stimulate ethanol intake in some animals (e.g., C57BL mice, Sprague Dawley rats and sheep). We have recently investigated the influence of fluid deprivation, a potent stimulator of angiotensin release in the brain, on ethanol consumption and preference in the Fawn-Hooded (FH) rat, a rat that manifests both an excessive water and alcohol intake. Under basal conditions, animals had ad lib access to food, water and 7.5% ethanol solution. Under experimental conditions, the animals were deprived for 24 h of either ethanol solution or ethanol solution and water. After the deprivation period, either water alone or water and ethanol solution were returned. The results indicated that under basal conditions, the FH rat manifested a large preference for ethanol solution. Following deprivation, ethanol preference did not change, but the consumption of ethanol solution almost doubled, such that total fluid intake over 24 hours was greater in rats given a choice between ethanol and water than in rats given water only after deprivation. In contrast, rats given water only, drink 12 ml in the first 2 hours after deprivation whereas rats given a choice of ethanol and water consume ~ 25% less fluid over this time frame but maintain their elevated preference for ethanol. Thus, following fluid deprivation preference for ethanol is unaltered, although consumptive behaviour is increased. The role of brain mechanisms underlying this behaviour are currently being explored.

Involvement of meal-related signals and vagal afferents in hydroxycitric acid induced satiety.

P.Y. WIELINGA, E.H.E.M. VAN DER WALL, G. VAN DIJK, A.J.W. SCHEURINK.
Department of Neuroendocrinology, University of Groningen, PO Box 14, 9750 AA Haren, The Netherlands.

Hydroxycitric acid (HCA) is known to inhibit food intake, although the mechanism remains unknown. We hypothesized that food intake inhibiting effect of HCA is mediated by peripheral meal-related signals. The aim of the present study was to examine the effect of HCA on baseline levels and stimulated response to glucose of a selection of meal-related signals (GLP-1, PYY and ghrelin). Furthermore, the involvement of vagal afferents in the anorectic effect of HCA is investigated, since most of the meal-related signals inform the CNS through vagal afferents. Blood samples for GLP-1, PYY and ghrelin were collected from rats pre-treated with Regulator HCA (310 mg/kg, 2 hours prior to glucose) or vehicle before and after an intragastric glucose infusion (9 ml in 5 min, 123 mg/ml). No effect of HCA on baseline levels was observed. After glucose infusion, no significant differences in the responses of GLP-1, PYY and ghrelin between HCA and vehicle group were observed. Another group of rats, neonatally injected with capsaicin, which destroys primary sensory vagal afferents, was used to investigate the role of vagal afferents. Food intake was significantly reduced in both capsaicin ($P < 0.001$) and vehicle treated rats ($P < 0.01$) after one single oral injection of Regulator HCA. These results show that vagal afferents and the meal-related signals GLP-1, PYY and ghrelin are probably not involved in the food intake inhibiting effect of HCA.

Leptin enhances the hindbrain catecholamine neuronal response to cholecystokinin.

D.L. WILLIAMS[a], M.W. SCHWARTZ[a], J.E. BLEVINS[a], D.G. BASKIN[b].
[a]*Department of Medicine,* [b]*VA Medical Center, University of Washington, Seattle, WA 98104, USA.*

Available data provides compelling support for the hypothesis that leptin reduces food intake in part by enhancing satiety and hindbrain responses to gastrointestinal signals, including cholecystokinin (CCK). In rats, CCK-induced c-fos expression in the nucleus of the solitary tract (NTS) is augmented by pre-treatment with leptin. We hypothesized that this synergistic interaction between leptin and CCK is mediated in part by NTS catecholamine neurons, which are known to play a critical role in the feeding response to CCK. In the present study, rats were given 3rd-ventricular injections of leptin (3.5 μg/2.5 μl) or vehicle 60 min prior to CCK treatment (1.4 μg, i.p.), and were euthanized 90 min later. Using immunohistochemical techniques, hindbrain sections were stained for c-fos and tyrosine hydroxylase (TH, the rate-limiting enzyme for catecholamine synthesis). With vehicle pre-treatment, this low dose of CCK induced a small but significant amount of c-fos-like immunoreactivity (cFLI) in the NTS, but few TH-positive cells were stained for cFLI. After leptin pre-treatment, however, NTS cFLI was increased 3-fold ($P < 0.01$), and the number of TH cells expressing c-fos was increased 6-fold ($P < 0.001$). The disproportionately large increase in NTS TH cell responsiveness to CCK identifies hindbrain catecholamine cells as potential mediators of the synergistic interaction between leptin and CCK. Ongoing studies have successfully employed laser capture microdissection and real time PCR to identify the chemical phenotypes of NTS neurons that integrate input from leptin and CCK. Supported by Department of Veterans Affairs.

Increased blood glucose levels associated with food variety.

J.F. WILSON, Y. OGAWA, K. ENGLE.
Wittenberg University, Springfield, OH 45501, USA.

To test the hypothesis that food variety increases food intake, energy intake was measured in 32 undergraduates who came to the lab twice to eat dinner and were served water and cheese

pizza in one condition and mixed pizza (consisting of cheese pizza, sausage pizza, pepperoni pizza, and veggie pizza) in the other condition. The order of pizza conditions was counterbalanced. For each meal, blood glucose was measured before the meal and 15 and 30 minutes after the start of the meal. No differences were detected between the amount eaten in the cheese pizza condition (M = 370.8 kcal) and the mixed pizza condition (M = 388.1 kcal), t(31) = - 0.53, ns. Blood glucose before the meal did not differ between the cheese pizza (M = 84.1 mg/dl) and the mixed pizza (M = 83.3 mg/dl) conditions, t(31) = 0.33, ns. A significant difference was detected between blood glucose measured 15 minutes after the start of the meal in the cheese pizza (M = 88.6 mg/dl) and the mixed pizza conditions (M = 94.8 mg/dl), t(31) = -2.78, P = 0.016, although no difference was detected between blood glucose measured 30 minutes after the start of the meal in the cheese pizza (M = 104.6 mg/dl) and the mixed pizza conditions (M = 109.6 mg/dl), t(31) = - 1.68, ns. No increased eating was observed when a variety of pizzas was served. The increased blood glucose associated with the mixed pizza condition may have contributed to this finding.

Meal pattern analysis and body weight changes following peripheral administration of rat amylin and salmon calcitonin.

J. WILSON, J. ROAN, D. PARKES, C. MACK.
Amylin Pharmaceuticals, Inc., San Diego, CA 92121, USA.

Amylin and salmon calcitonin (sCT) reduce food intake in rodents through interaction with amylin binding sites. The current set of experiments examined dark-cycle feeding patterns to further explore the anorectic actions of these peptides. Amylin (100 µg/kg, n = 6 - 7) or vehicle (n = 6 - 8) was administered intraperitoneally (IP) to male rats (body weight = 500 g) at the onset of the dark cycle; food intake (45% kcal from fat) was measured for the following 20 hrs. Latency, meal size, meal duration, inter-meal interval, and satiety ratio were analyzed for the first meal. Under identical conditions, a second group of rats (body weight = 430 g) received sCT (5 µg/kg, n = 6) or vehicle (n = 6) once daily (IP) for 9 consecutive nights; food intake and body weight were monitored throughout the study. Amylin decreased cumulative food intake compared to controls for the first 3 hours post injection ($P < 0.05$). Analysis of the first meal showed amylin to reduce meal size (0.79 ± 0.2 g versus 1.5 ± 0.1 g, $P < 0.01$) and increase the satiety ratio ($P < 0.05$) compared to controls. Once daily injections of sCT suppressed food intake on each of the 9 nights, with a reduction in cumulative food intake at 23 hrs in sCT versus control-treated rats in 6 of the 9 nights (P's < 0.05). Body weight gain at the end of the study was reduced in sCT versus control treated rats (-14.9 ± 5.1 g versus 20.6 ± 2.9 g, $P < 0.01$, vehicle-corrected body weight loss = 8%). These data further support a role of amylin in energy balance through regulating satiety, and show the longer acting peptide, sCT, to reduce body weight when administered once daily.

No effect of exercise intensity on psychophysical ratings of hunger in postmenopausal women.

E.C. WUORINEN[a], K.T. BORER[a], C. BURANT[b].
[a]*Division of Kinesiology,* [b]*Department of Internal Medicine, The University of Michigan, Ann Arbor, MI 48109-2214, USA.*

Our understanding of how exercise affects perception of hunger or caloric intake is still incomplete. Dose-dependent suppression of hunger ratings and food intake in lean young men and women has been previously demonstrated. Purpose: To investigate the effects of moderate and high-intensity exercise in postmenopausal women on psychophysical ratings of

appetite, as assessed by a visual analog scale, and on end-of day compensatory caloric consumption. Methods: Six lean (BMI 20 - 25 kg/m^2) postmenopausal women were subjected to three treatments: a sedentary day, and a moderate and a high intensity (40% and 80% of maximal effort) exercise day where energy expenditure consisted of 800 kcal above their resting metabolic rate. They were provided calorically balanced intake in the form of three equal size meals at 07, 13, and 19 h. An ad libitum snack was offered at 21 h for a possible end-of day compensatory make-up the energy deficit generated by exercise. Energy expenditure was measured by indirect calorimetry. Results: In lean postmenopausal women, there was no significant effect of exercise at either intensity as compared to the sedentary condition on psychophysical ratings of appetite or the caloric intake during the ad libitum snack at 21 h. Conclusions: In contrast to our hypothesis, the moderate- and high-intensity walking exercise utilized in this study did not have an effect on psychophysical ratings of appetite or compensatory evening consumption of a snack in lean postmenopausal women. The subjects remained in negative energy balance during the exercise days. Supported by NIH grant M01-RR00042 to the General Clinical Research Center and a Blue Cross and Blue Shield of Michigan Student Award Grant to Elizabeth Wuorinen.

Effects of palatability on digestion, stress and immunity in rats.

C. YAMAMOTO, T. YAMAMOTO.
Department of Behavioral Physiology, Graduate School of Human Sciences, Osaka University, Osaka, Japan.

It is known that taste and smell play roles in appetite, food choices and nutrient intake. To further examine the role of taste in this respect, the following 3 experiments were performed in rats. First, we examined the effect of taste of food on its digestion in the stomach. Rats were randomly divided into 4 groups: each group was trained to eat a mash made up with powdered food and a liquid. The liquid was either distilled water, 0.05 M saccharin, 0.1 M sucrose or 0.01 M quinine. On the test day, the content of the stomach of each rat was measured 150 min after the start of eating the mash. It was shown that the food output from the stomach was increased by the palatable food, whereas it was decreased by the aversive food. In the second experiment, we measured the level of serum corticosterone (CORT) which is known as a stress hormone. The level of CORT was increased by ingestion of a bitter mash. In the third experiment, we measured the level of serum interleukin-1β (IL-1β) to examine the possible effect of taste on the immunity. The level of IL-1β was decreased by a bitter mash. This result shows that palatable taste increases the digestive function and immunity, whereas aversive taste decreases the digestive function and induces stress. The conclusion is that palatable foods are good for health if not overeaten.

Expression of acquired hedonic but not sensory properties of odours depends on current appetitive state.

M.R. YEOMANS, S. MOBINI.
Department of Psychology, University of Sussex, Brighton, BN1 9QH, UK.

For people who like sweet tastes, repeated retronasal experience of novel odours with 10% sucrose results in significant increases in both liking for and sweetness of the sweet-paired odour when assessed orthonasally. It is also known that expression of liking for a sweet taste itself can vary depending on the immediate nutritional needs of the consumer: sweet tastes are rated significantly more pleasant when hungry than when sated. What remains less clear is whether the same sensitivity to motivational state is seen for acquired liking, and indeed

whether this extends to acquired sensory as well as hedonic components of a sweet-paired odour. To test this, three groups of participants pre-selected as sweet-likers all evaluated the sweetness, bitterness and pleasantness of three novel odours before these odours were experienced retronasally, paired either with 10% sucrose, 0.2% quinine or water during 4 disguised training trials. Prior to re-evaluation of the odours, group sated [sated group] consumed 200 ml of a high energy soup [hungry group] the same volume of a sensory-matched low-energy soup [sated group] and 200 ml water [control group]. Odours were re-evaluated orthonasally 30 minutes after preload consumption. All three groups showed similar increases in the rated sweetness of the sucrose-paired odour, but liking for this odour had increased significantly only in the hungry and control groups. In contrast all groups rated the quinine-paired odour as more bitter and significantly less liked. These data provide the first clear evidence of acute sensitivity of acquired odour liking for sweetness to current motivational state, and further confirm the independence of acquired sensory and acquired hedonic properties of food-related odours.

Conditioning and extinction of flavor-flavor and flavor-nutrient preferences in rats.

Y.-M. YIIN[a], D. DWYER[b], A. SCLAFANI[a].
[a]*Brooklyn College of CUNY, Brooklyn, NY 11210, USA;* [b]*Cardiff University, Cardiff, Wales, UK.*

This study developed procedures to produce comparable flavor-flavor (FF) and flavor-nutrient (FN) preferences in rats. Two groups of food-restricted male rats (N = 10 or 11) were trained with grape or cherry-flavored saccharin solutions. The FN group had the CS+ solution paired with intragastric infusions of 8% glucose (US), and the CS- solution paired with water infusions. The FF group was not infused but had 8% fructose added to the CS+ solution. The US was presumed to be the sweet taste of fructose because fructose infusions do not condition preferences. During one-bottle training (8 x 30 min/day sessions), CS solutions were limited (10 g). Two-bottle extinction tests (12 sessions) were then conducted with the CS+ versus CS-. Both groups initially displayed similar CS+ preferences (78-79%) but with repeated trials, the preference extinguished in the FF group (50%) but not in the FN group (74%). Both groups were retrained as above but with unlimited CS access. In subsequent tests, the FF group recovered its CS+ preference (79%) which then declined to 69% with repeated extinction trials. The FN group displayed an enhanced preference (93%) which persisted throughout the 12 extinction trials (92%). These findings demonstrate that oral fructose and IG glucose condition flavor preferences of similar initial magnitude, but that the fructose, flavor-based preference extinguishes more rapidly than does the glucose, nutrient-based preference. This may occur, in part, because the oral fructose US (and lack thereof) is more salient to the animal than is the post-oral glucose US. Supported by NIH Grant DK31135.

The postprandial neuronal activation in the rat PVN and NTS did not occur by ingestion of a non-caloric palatable food mash.

S.B. YOO, V. RYU, J.W. JAHNG.
Department of Pharmacology, BK 21 Project for Medical Science, Yonsei University College of Medicine, Seoul, 120-752, Korea.

Oropharyngeal-esophageal and gastric cues contribute to meal-induced neuronal activation, referred by c-fos expression, in the paraventricular nucleus (PVN) and the nucleus tractus of solitarius (NTS). This study was conducted to determine if ingestion of tasty but non-caloric meal induces c-fos expression in brain regions. Male Sprague-Dawley rats (300 - 350 g)

underwent 48 h food deprivation, and received ad libitum access to standard rodent chow or non-caloric palatable food mash (2.5 parts by weight alpha-cellulose, 1.0 part mineral oil, and 10.0 parts of a deionized water solution containing 0.1 % sodium-saccharin and 0.2 % artificial vanilla extract) for 1 h. Rats were overdosed with pentobarbital, and transcardially perfused with 4 % paraformaldehyde. Free fed and 48 h deprived rats were included as control groups. Forty micron brain sections from the rostrocaudal extent of PVN and NTS were processed for c-fos immunohistochemistry. Food deprivation significantly decreased c-fos expression in the intermediate NTS, but not in the caudal NTS and the PVN. One hour of chow, but not the non-caloric, refeeding markedly increased c-fos-ir nuclei in all three brain regions, compared to the fed or the deprived controls. Although 1 h food intake by weight did not differ between the chow and the non-caloric groups, the stomach contents were markedly increased only in the chow group, compared to the fed or the deprived controls. These results suggest that ingestion of non-caloric meal may not produce effective oropharyngeal or gastric cues to induce neuronal activation in the PVN and NTS. Supported by a KISTEP grant (JWJ).

The correlation between fat pads, plasma oxytocin and leptin is dependent on reproductive status in female rats lacking CCK-A receptors.

O. ZAGOORY-SHARON, M. SCHROEDER, A. WELLER.
Department of Psychology & Gonda Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel.

OLETF rats lacking expression of functional CCK-A receptors have been used to study physiological and behavioral effects of the gut hormone cholecystokinin. We investigated the accumulation of fat pads (brown, retroperitoneal and inguinal) and plasma levels of glucose, leptin and oxytocin in OLETF and control (LETO) females. Virgin animals were tested as well as dams at the 7th and 15th lactation day, at weaning, and 8 weeks post-weaning. Inguinal WAT of LETO females was largest (when normalized to body weight) during lactation compared to the levels found in post-weaning and virgin females. LETO females accumulated fat during pregnancy and lactation, returning to their normal fat levels post-weaning. While the WAT depots of OLETF females were similarly heavier in the 7th postpartum day, they decreased dramatically during lactation; and accumulated fat after weaning, reaching the same levels as observed in virgins. Plasma leptin levels were positively correlated with the amount of white fat pad, in OLETF but not in LETO. Surprisingly we found a very high positive correlation between plasma oxytocin and leptin in OLETF but only a moderate correlation in LETO. We are currently analyzing fat cell size and density, in order to understand the hyperplasic and the hypertrophic processes of those fat pads. The results will be discussed. Supported by the US-Israel Binational Science Foundation.

Involvement of hypothalamic orexin-signaling in accumbens-induced high-fat feeding.

H. ZHENG, L.M. PATTERSON, H.-R. BERTHOUD.
Neurobiology of Nutrition Laboratory, Pennington Biomedical Research Center, LSU System, Baton Rouge, LA 70808, USA.

Activation of mu-opioid receptors with the selective agonist DAMGO injected into the nucleus accumbens elicits voracious eating of high-fat diet even in rats fully satiated on this highly palatable diet. Because (1) the nucleus accumbens has significant efferent projections to the hypothalamus, (2) accumbens DAMGO induces c-Fos in hypothalamic orexin neurons, and (3) orexin induces specific appetite for high-fat foods, we hypothesized that orexin-signaling might play a role in accumbens-induced high-fat intake. Here we show that

pretreatment with the selective orexin-1-receptor antagonist SB334867 (100 nmol/3 µl) injected into the lateral ventricle significantly attenuated (50 ± 10 %, $P < 0.01$) 2-h high-fat intake induced by DAMGO (250 ng/0.3 µl) injected 20 min later into the nucleus accumbens, without significantly reducing baseline food intake. Furthermore, while in WT mice, accumbens DAMGO in the dose range of 20 – 35 ng/mouse dose-dependently increased intake of 20% corn oil emulsion as measured by the number of licks 1-2h following the injection ($P < 0.01$), orexin null mice did not show this and ingested significantly less corn oil following the 35 ng dose as compared to the WT mice ($P < 0.01$). These results suggest an important role of orexin signaling in DAMGO-induced high-fat intake in both rats and mice. Because orexin projections to arcuate nucleus NPY neurons have been demonstrated both anatomically and functionally, the arcuate nucleus represents a likely candidate for critical orexin signaling. Overall, the findings provide further support for an important role of accumbens-hypothalamus projections in the overriding of metabolic satiety as represented by hypothalamic sensor systems by reward-driven signals from cortico-limbic systems. Supported by DK47348 and DK 071082.

Tracing nucleus accumbens-hypothalamic projections in rats tested for muscimol-induced food intake.

H. ZHENG, L.M. PATTERSON, H.-R. BERTHOUD.
Neurobiology of Nutrition Laboratory, Pennington Biomedical Research Center, LSU System, Baton Rouge, LA 70808, USA.

Robust food intake can be induced by injection of the GABAA-agonist muscimol into the medial shell of the nucleus accumbens. In an effort to identify the neural pathways responsible for this effect, we focused on efferent projections to the lateral hypothalamus, thought to be a unique feature of the shell as compared to the core of the nucleus accumbens. Sprague Dawley rats with chronic guide cannulas aimed at the shell were first characterized for their ingestive response to muscimol (100 ng/0.5 µl) or saline as a control. Rats eating > 4 g/hr more chow following muscimol as compared to saline were injected with biotinylated dextran-amine (BDA, 10% in 0.5 µl saline) through the same cannula. After 10 days survival, relevant brain sections were processed for BDA immunohistochemistry and in double-labeling experiments additionally for peptide-immunohistochemistry. Strongly labeled varicose axon profiles were not just confined to the lateral hypothalamus as reported earlier, but were distributed widely throughout most of the hypothalamus, including the perifornical, dorsomedial, arcuate, retrochiasmatic, paraventricular, periventricular, and medial tuberal, but not the ventromedial nuclei. Close anatomical appositions with orexin, MCH, POMC, CART, and oxytocin-ir neurons were numerous. These results are consistent with a role for accumbens-hypothalamus projections and targeted hypothalamic peptide systems in the robust feeding responses induced by the GABAA-agonist muscimol and the mu-opioid agonist DAMGO. This pathway might constitute a link by which reward-based non-homeostatic factors are integrated with the homeostatic control circuits in the hypothalamus, and may be responsible for externally driven hyperphagia and the development of dietary-induced obesity. Supported by DK47348 and DK 071082.